ORIGINAL RESEARCH

Somatic anxiety in patients with laryngopharyngeal reflux

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Abstract

Objective: This study aimed to evaluate the relationship between larryngopharyngeal reflux (LPR) and anxiety in patients with LPR.

Design: Prospective, case-control study.

Setting: This study was conducted at a tertiary care center.

Participants: Sixty-four patients with LPR and 60 healthy controls.

Methods: Patients with LPR and healthy individuals (N = 64 and N = 60) were enrolled in this study. The Beck Anxiety Inventory (BAI) and reflux symptom index (RSI) were used to evaluate anxiety and reflux-related symptoms, respectively. The BAI can be classified into somatic and subjective symptom scales. The prevalence of anxiety was compared between patients with LPR and healthy individuals. This study evaluated the relationship between BAI and RSI scores.

Results: No statistical difference was found in the prevalence of anxiety between patients with LPR and healthy individuals (42.2% vs. 33.3%). However, the somatic anxiety symptom score was statistically higher in patients with LPR than in healthy individuals (p = .047). We observed a correlation between RSI and somatic anxiety scores of BAI in patients with LPR (rho = 0.286, p = .021).

Conclusion: Patients with LPR had more severe somatic anxiety symptoms, and somatic anxiety was associated with their LPR-related symptoms.

KEYWORDS

anxiety, laryngopharyngeal reflux, somatic anxiety

1 | INTRODUCTION

Laryngopharyngeal reflux (LPR) is defined as laryngopharyngeal conditions with mucosal inflammation that is caused by the retrograde reflux of gastric contents. Although the definition of LPR is clear, its symptoms and laryngeal findings are not specific to LPR. The nonspecific symptoms of LPR include changes in voice, chronic throat clearing, chronic cough, globus pharyngeus, and dysphagia. The laryngopharyngeal findings of LPR, such as pseudosulcus,

ventricular obliteration, laryngeal erythema, laryngeal edema, and posterior commissure hypertrophy, have been observed in the normal population.^{1,3} Previous studies have found no association between symptoms and laryngopharyngeal findings in patients with LPR.^{3,4} The mismatch between symptoms and laryngopharyngeal findings suggests that cofactors are required to explain the discrepancy. A previous study reported that patients with LPR had higher psychological distress than normal individuals, which could decrease their quality of life.^{5,6} Thus, psychological distress, such as anxiety,

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might be a candidate cofactor that influences symptom severity in patients with LPR.

Several studies have analyzed the relationship between LPR and psychological symptoms, such as anxiety and depression^{1,2,6–8}; however, the association between LPR and psychological symptoms remains controversial. Patients with globus are commonly related to various psychopathologic statuses.^{9,10} Among the psychopathologic statuses, we decided to focus on anxiety in this study. Therefore, this study aimed to discover the relationship between LPR and anxiety by analyzing the prevalence of anxiety and its correlation with LPR symptom severity.

2 | MATERIALS AND METHODS

2.1 | Study design and subjects

This prospective case-control study was designed to compare anxiety symptoms between patients with LPR and healthy subjects. To recruit patients with LPR, all patients who visited our clinic with common LPR-related symptoms were assessed using the reflux symptom index (RSI) and 24-h hypopharyngeal-esophageal multichannel intraluminal impedance pH monitoring (HEMII-pH). The inclusion criteria for patients with LPR were as follows: (1) age ≥ 18 years; (2) at least one of the common LPR-related symptoms, such as hoarseness, throat clearing, dysphagia, increased phlegm, and globus sensation; and (3) at least one pharyngeal reflux episode for 24 h via HEMII-pH monitoring. 11,12 To recruit healthy subjects, we assessed clinical study volunteers. The inclusion criteria for healthy subjects were as follows: (1) age ≥ 18 years. (2) not over 7 in RSI score, and (3) no previous medical history of reflux or laryngeal complaints. 13 The study population was recruited in a hospital between 2018 and 2020. We have received informed consent from all subjects for this study. This study was approved by the ethics committee of Kyung-Hee University Hospital at Gang-dong (approval number: 2018-05-021).

2.2 | Symptom Scale

We administered two questionnaires, the RSI and Beck Anxiety Inventory (BAI), to patients with LPR and healthy subjects. RSI is a self-administered instrument that consists of nine questions¹⁴ and is widely used by otolaryngologists to assess reflux-related symptoms. Each question has six grades of selectable answers, from zero (no symptoms) to five (severe symptoms), with a maximum total score of 45. The nine questions were as follows: (1) hoarseness or a problem with your voice, (2) clearing your throat, (3) excess throat mucus or postnasal drip, (4) difficulty swallowing food, liquids, or pills, (5) coughing after you ate or after lying down, (6) breathing difficulties or choking episodes, (7) troublesome or annoying cough, (8) sensations of something sticking in your throat or a lump in your throat, and (9) heartburn, chest pain, indigestion, or stomach acid coming up.

The BAI questionnaire consists of 21 items to assess anxiety symptoms, 15 with each item having four answers that range from one (not at all) to three (severe bother). The maximum total score was 63 points. The classification ranges of BAI are 0-7 (minimal anxiety), 8-15 (mild anxiety), 16-25 (moderate anxiety), and 26-63 (severe anxiety). The 21 items were as follows: (1) numbness or tingling, (2) feeling hot, (3) wobbliness in legs, (4) unable to relax, (5) fear of worst happening, (6) dizzy or lightheaded, (7) heart pounding/racing, (8) unsteady, (9) terrified or afraid, (10) nervous, (11) feeling of choking, (12) hands trembling, (13) shaking/unsteady, (14) fear of losing control, (15) difficulty in breathing, (16) fear of dying, (17) scared, (18) indigestion, (19) faint/lightheaded, (20) face flushed, and (21) hot/cold sweats. For further investigation, we classified the BAI questions into somatic or subjective subscales. 16 The somatic subscale included 14 BAI items (1-3, 6-8, 11-13, 15, 18-21), and the subjective subscale included seven BAI items (4, 5, 9, 10, 14, 16, 17).

2.3 | 24-hour hypopharyngeal-esophageal multichannel intraluminal impedance pH monitoring

HEMII-pH is an important tool for the diagnosis and management of LPR. HEMII-pH can detect and quantify pharyngeal reflux and temporally correlate symptoms with reflux. A multi-channel probe catheter (Sandhill Scientific, Inc., Highlands Ranch, CO, ZAI-BL-54, 55, 56, ComforTEC Z/PH single-use 2.3-mm-diameter probe) for HEMII-pH was used. The catheter has multiple impedance and pH electrodes that were placed in the pharynx and esophagus. The most proximal electrodes were placed 2–3 cm above the upper esophageal sphincter. The subjects were recommended to maintain a routine daily lifestyle and a common diet during HEMII-pH. After completion of HEMII-pH, the recorded monitoring data were analyzed by an otolaryngology specialist.

2.4 | Statistical analyses

Mann-Whitney test was used to compare parameters between patients with LPR and healthy individuals. The chi-squared test was used to compare the categorical variables. Multivariable logistic regression and backward elimination methods were used to identify important anxiety symptoms related to LPR. The Spearman's correlation was used to evaluate the relationship between the RSI and BAI. All statistical analyses were conducted using the R software (https://www.R-project.org, ver. 4.1.0).

3 | RESULTS

After screening 100 patients with LPR-related symptoms, 31 patients were excluded due to no pharyngeal reflux in HEMII-pH test, and 5 patients were excluded due to insufficient questionnaire data.

TABLE 1 Baseline characteristics of patients with laryngopharyngeal reflux and healthy individuals.

| Variable | LPR patients (N = 64) | Healthy individuals (N = 60) |
|-----------------------------------|-----------------------|------------------------------|
| Sex, n | | |
| Female | 43 (67.19%) | 46 (76.67%) |
| Male | 21 (32.28%) | 14 (23.33%) |
| Age, year | 52.98 ± 13.14 | 49.60 ± 9.20 |
| Pharyngeal reflux, n | 4.28 ± 3.98 | - |
| RSI, median [interquartile range] | 11.50 [8.00;14.00] | 2.00 [0.00;4.00] |
| Anxiety (≥ mild), n | | |
| Yes | 27 (42.19%) | 20 (33.33%) |
| No | 37 (57.81%) | 40 (66.67%) |

Abbreviation: RSI, reflux symptom index.

Among 82 volunteers of healthy controls, 22 individuals were excluded due to high RSI score (RSI > 7), and 60 individuals met inclusion criteria. Finally, total of 124 participants were enrolled in this study. The number of patients with LPR and healthy individuals were 64 and 60, respectively (Table 1). The mean age of patients with LPR was 52.98 ± 13.14 years, and the mean age of the healthy individuals was 49.60 ± 9.20 years (p = .096). The female-to-male ratio was 67.19% in patients with LPR and 76.67% in healthy individuals (p = .319). The average number of pharyngeal reflux episodes in patients with LPR was 4.28 ± 3.98 times for 24 h. The RSI scores were 11.50 [8.00;14.00] in the patients with LPR and 2.00 [0.00;4.00] in the healthy individuals (p < .001). No statistical difference was observed in the more than mild anxiety rate between patients with LPR and healthy individuals (27/64, 42.2% vs. 20/60, 33.3%; p = .406).

The median total BAI score in patients with LPR was 6.00 [2.00;11.00], and the median total BAI score in healthy individuals was 3.50 [1.00;8.00] (p=.071) (Table 2). Although the total BAI score did not show a statistically significant difference, the somatic BAI score was significantly higher in patients with LPR than in healthy

| Questionnaires | LPR patients (N = 64) | Healthy individuals (N $=$ 60) | p-value |
|--|-----------------------|--------------------------------|---------|
| BAI items | | | |
| 1. Numbness or tingling ^a | 0.00 [0.00;1.00] | 0.00 [0.00;0.00] | .524 |
| 2. Feeling hot ^a | 0.00 [0.00;0.00] | 0.00 [0.00;0.00] | .658 |
| 3. Wobbliness in legs ^a | 0.00 [0.00;0.00] | 0.00 [0.00;0.00] | .448 |
| 4. Unable to relax ^b | 0.00 [0.00;1.00] | 0.00 [0.00;1.00] | .213 |
| 5. Fear of worst happening ^b | 0.00 [0.00;1.00] | 0.00 [0.00;1.00] | .321 |
| 6. Dizzy or lightheaded ^a | 1.00 [0.00;1.00] | 0.00 [0.00;1.00] | .011* |
| 7. Heart pounding/racing ^a | 1.00 [0.00;1.00] | 0.00 [0.00;1.00] | .065 |
| 8. Unsteady ^a | 0.00 [0.00;1.00] | 0.00 [0.00;1.00] | .891 |
| 9. Terrified or afraid ^b | 0.00 [0.00;1.00] | 0.00 [0.00;0.50] | .679 |
| 10. Nervous ^b | 0.00 [0.00;1.00] | 0.00 [0.00;1.00] | .482 |
| 11. Feeling of choking ^a | 0.00 [0.00;1.00] | 0.00 [0.00;0.00] | .007* |
| 12. Hands trembling ^a | 0.00 [0.00;0.00] | 0.00 [0.00;0.00] | .467 |
| 13. Shaky/unsteady ^a | 0.00 [0.00;0.00] | 0.00 [0.00;0.00] | .978 |
| 14. Fear of losing control ^b | 0.00 [0.00;0.00] | 0.00 [0.00;0.00] | .321 |
| 15. Difficulty in breathing ^a | 0.00 [0.00;1.00] | 0.00 [0.00;0.00] | <.001* |
| 16. Fear of dying ^b | 0.00 [0.00;0.00] | 0.00 [0.00;0.00] | .083 |
| 17. Scared ^b | 0.00 [0.00;1.00] | 0.00 [0.00;1.00] | .148 |
| 18. Indigestion ^a | 0.00 [0.00;1.00] | 0.00 [0.00;1.00] | .270 |
| 19. Faint/lightheaded ^a | 0.00 [0.00;0.00] | 0.00 [0.00;0.00] | .020* |
| 20. Face flushed ^a | 0.00 [0.00;1.00] | 0.00 [0.00;0.00] | .020* |
| 21. Hot/cold sweats ^a | 0.00 [0.00;0.50] | 0.00 [0.00;0.00] | .019* |
| Somatic BAI score | 3.50 [1.00;7.50] | 2.00 [1.00;5.00] | .047* |
| Subjective BAI score | 2.00 [0.00;5.00] | 1.00 [0.00;3.00] | .260 |
| Total BAI score | 6.00 [2.00;11.00] | 3.50 [1.00;8.00] | .071 |

TABLE 2 Comparison of anxiety symptoms between patients with laryngopharyngeal reflux and healthy individuals.

Note: All scores are presented as median [interquartile range].

Abbreviations: BAI, Beck Anxiety Inventory; LPR, laryngopharyngeal reflux.

^aSomatic BAI items.

^bSubjective BAI items.

TABLE 3 Odds ratio of the 'Beck Anxiety Inventory' related to patients with laryngopharyngeal reflux.

| Step | Variable | Odds ratio | Lower | Upper | p-value |
|-------|--|------------|-------|-------|---------|
| First | 1. Numbness or tingling ^a | 0.88 | 0.71 | 1.10 | .267 |
| | 2. Feeling hot ^a | 1.09 | 0.88 | 1.35 | .438 |
| | 3. Wobbliness in legs ^a | 1.03 | 0.83 | 1.29 | .777 |
| | 4. Unable to relax ^b | 0.96 | 0.79 | 1.16 | .667 |
| | 5. Fear of worst happening ^b | 1.02 | 0.84 | 1.25 | .819 |
| | 6. Dizzy or lightheaded ^a | 1.09 | 0.92 | 1.29 | .345 |
| | 7. Heart pounding/racing ^a | 0.99 | 0.83 | 1.20 | .957 |
| | 8. Unsteady ^a | 0.96 | 0.77 | 1.20 | .748 |
| | 9. Terrified or afraid ^b | 1.00 | 0.83 | 1.21 | .998 |
| | 10. Nervous ^b | 1.03 | 0.86 | 1.23 | .759 |
| | 11. Feeling of choking ^a | 0.95 | 0.73 | 1.23 | .684 |
| | 12. Hands trembling ^a | 0.81 | 0.60 | 1.08 | .157 |
| | 13. Shaky/unsteady ^a | 0.73 | 0.53 | 1.02 | .065 |
| | 14. Fear of losing control ^b | 1.03 | 0.74 | 1.44 | .863 |
| | 15. Difficulty in breathing ^a | 1.45 | 1.09 | 1.91 | .011* |
| | 16. Fear of dying ^b | 1.01 | 0.66 | 1.53 | .971 |
| | 17. Scared ^b | 1.06 | 0.86 | 1.30 | .606 |
| | 18. Indigestion ^a | 1.03 | 0.88 | 1.21 | .692 |
| | 19. Faint/lightheaded ^a | 1.35 | 0.90 | 2.04 | .153 |
| | 20. Face flushed ^a | 0.99 | 0.80 | 1.22 | .908 |
| | 21. Hot/cold sweats ^a | 1.08 | 0.84 | 1.39 | .560 |
| Final | 12. Hands trembling ^a | 0.79 | 0.62 | 1.01 | .058 |
| | 13. Shaky/unsteady ^a | 0.84 | 0.68 | 1.04 | .118 |
| | 15. Difficulty in breathing ^a | 1.44 | 1.22 | 1.71 | <.001* |
| | 19. Faint/lightheaded ^a | 1.40 | 1.07 | 1.82 | .015* |

Abbreviations: BAI, Beck Anxiety Inventory; LPR, laryngopharyngeal reflux.

^bSubjective BAI items.

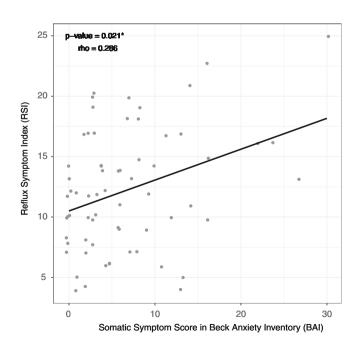


FIGURE 1 Correlation between reflux symptom index and Beck Anxiety Inventory somatic symptom score in patients with LPR.

subjects. The median somatic BAI scores in patients with LPR and healthy individuals were 3.50 [1.00;7.50] and 2.00 [1.00;5.00], respectively (p=.047). It was interesting to note that all items that showed statistical significance in patients with LPR, such as dizziness, feeling of choking, difficulty in breathing, faint, face flushing, and sweats, were included in the somatic subscale. A multivariate logistic regression analysis confirmed an association between the presence of LPR and the BAI items (Table 3). After the backward elimination process, four anxiety symptoms related to LPR were statistically selected. These items were trembling hands, shaky, difficulty in breathing, and faint symptoms. We evaluated the correlation between reflux symptoms and somatic anxiety symptoms in patients with LPR. A significant correlation was detected between the RSI and the somatic BAI scores in patients with LPR (Figure 1, rho = 0.286, p=.021).

4 | DISCUSSION

This study aimed to determine the relationship between LPR and anxiety and had two major findings. First, we discovered that patients

^aSomatic BAI items.

with LPR had more severe somatic BAI scores than healthy individuals. Second, the severity of RSI correlated with the severity of somatic BAI scores in patients with LPR.

This study used the BAI to evaluate anxiety symptoms in patients with LPR. The BAI is one of the most widely used questionnaires for evaluating anxiety and was developed by Beck et al. (1990). The advantages of BAI are that its validity and reliability have been thoroughly verified. 17,18 Although BAI may not be specific for various types of anxiety, the simplicity of BAI makes it convenient to use in primary care. 18 Beck et al. introduced a two-factor model that consists of subjective and somatic symptoms, using exploratory factor analysis. 15 The investigators broadly defined subjective anxiety as "negative expectations, worries, and concerns about oneself, the situation at hand, and potential consequences" and somatic anxiety as "the perception of one's physiological arousal." This study used a two-factor model for the subscale analysis of BAI in patients with LPR. Several studies supported this two-factor model. 16-19

In this study, the mild-to-severe BAI-anxiety rate was not significantly higher in patients with LPR than in normal controls. Specifically, the total BAI score was 9.11 ± 10.27 in patients with LPR. This value is similar to those found in previous studies carried out in other countries, both with adults from the general population and with university students.²⁰ A few studies have been conducted to evaluate psychological distress in patients with LPR. Shin et al. failed to demonstrate any significant correlation between psychological distress and reflux-related symptom severity in patients with LPR.¹⁶ Mesallam et al. reported that there was no association between psychological disorders and LPR.¹⁹ The results of these studies are consistent with our results. In short, our results indicate that the prevalence of anxiety does not appear to be particularly high in patients with LPR.

We found that patients with LPR complained of more somatic anxiety than healthy individuals. Somatic anxiety, also known as somatization, is the physical manifestation of anxiety.²¹ Somatization refers to the phenomenon in which patients experience and express their feelings or emotions through physical complaints and distress.²² Although the term somatization is generally used, it needs to be differentiated from somatization disorder, 23 which is recognized as a distinct clinical psychiatric disorder.²³ Vázquez Morejón et al. observed that BAI-somatic scores were highly correlated with somatization dimension scores of Symptom Checklist-90-Revision.²⁴ A study using Symptom Checklist-90-Revision reported that the severity of irritable bowel syndrome significantly correlated with somatization subscale without gastrointestinal complaints.²⁵ Symptoms typically associated with somatization of anxiety include abdominal pain, dyspepsia, chest pain, fatigue, dizziness, insomnia, and headache.²¹ In this study, BAI-somatic symptoms, such as dizziness, feeling of choking, difficulty in breathing, fainting, and face flushing, were more frequently observed in patients with LPR than in healthy individuals. Although the frequent symptoms did not involve any gastrointestinal symptoms, patients with LPR showed a higher severity of BAI-somatic symptoms than healthy individuals.

Anxiety may present with somatic symptoms,²⁶ and the BAI-somatic symptom scale can be used to evaluate somatic anxiety.¹⁵ Psychologic distress itself may be a factor in provoking or

maintaining medical conditions or diseases.²¹ Katon found that those who experienced panic attacks had a significantly higher rate of hypertension than those who did not.²⁷ If psychologic distress is left and untreated, it may prolong or worsen a medical illness.²⁸ This study demonstrated a positive correlation between BAI-somatic symptom severity and RSI-symptom severity in patients with LPR.

A study reported the relationship between throat discomfort and psychological distress in the general population.²⁹ Another randomized controlled trial suggested that voice symptoms were also related to neuroticism, alexithymia, psychological distress, poor quality of life, and past medically unexplained symptoms.³⁰ The onset of throat symptoms could be related to significant life events and minor psychological hassles.³¹ There is long history of psychometric evidence on throat symptoms. On the other hand, the evidence for reflux therapy responsiveness is weak.³² Therefore, we need to evaluate psychological distress in patients with LPR. Although this study used BAI, other questionnaires such as the General Health Questionnaire also could be convenient screening tools to psychological problems.^{33,34}

Belafsky et al. analyzed 25 healthy controls and reported an RSI > 13 is abnormal. Since then, many studies have used 13 as a cut-off value of abnormal RSI. However, a recent study analyzing 91 asymptomatic subjects revealed that the 5%-95% range of RSI score in asymptomatic volunteers was 0-7 which amounts to be much lower than the previous criteria. Since we considered the latter criteria to be more suitable, we used RSI ≤ 7 as the inclusion criteria for the control group.

This study has some limitations. First, the size of the sample was relatively small. Second, The HEMII-pH was not performed on every control. No pharyngeal reflux event was observed in the controls who underwent HEMII-pH.

5 | CONCLUSION

Patients with LPR had more severe somatic anxiety symptoms, which were associated with LPR-related symptoms. Clinicians need to consider somatic anxiety symptoms during the treatment of patients with LPR.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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