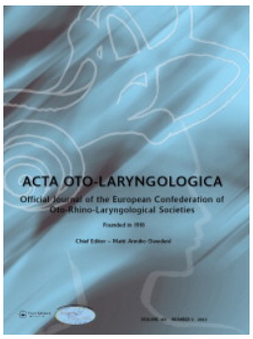

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RESEARCH ARTICLE

Self-reported symptoms of laryngopharyngeal reflux using the reflux symptom score in patients with obstructive sleep apnea syndrome

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ABSTRACT

Background: Obstructive sleep apnea (OSA) is associated with many chronic diseases among which is laryngopharyngeal reflux disease (LPRD).

Objective: To investigate the prevalence of laryngopharyngeal reflux (LPR)-related symptoms in patients with OSA using the Reflux Symptoms Score (RSS) and Reflux Symptom Index (RSI).

Methods: The medical records and video-recordings of patients with OSA who presented to a tertiary referral center were reviewed. The diagnosis of OSA was made using the STOP-BANG questionnaire and/or polysomnography. The prevalence of LPR-related symptoms was assessed using both the RSS and RSI questionnaires.

Results: Thirty-nine patients were included in this study. Twenty-seven patients (69.2%) had a positive RSS in comparison to only 7 (17.9%) using the RSI ($p=.052$). Subgroup analysis of those who had polysomnography ($n=24$) showed that 18 patients (75%) had a positive RSS in comparison to only 5 patients (20.8%) using the RSI. Patients in the high-risk category for OSA were also found to have a higher prevalence of LPR-related symptoms using both the RSS and RSI questionnaires in comparison to those in the lower risk categories.

Conclusion: The results of this investigation indicate that the prevalence of LPR-related symptoms is higher using the RSS in comparison to the RSI.

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Laryngopharyngeal reflux; obstructive sleep apnea; laryngology

Introduction

Obstructive sleep apnea (OSA) is a common morbid disease in the adult population [1]. It is characterized by intermittent decrease or cessation of airflow secondary to collapse of one or multiple sites of the upper airway. Anatomical areas of obstruction during awake and/or sleep endoscopy include the nasopharynx, oropharynx, hypopharynx, and larynx [2]. Patients with OSA suffer from an array of symptoms stratified as nocturnal vs diurnal [3]. Nocturnal symptoms include snoring, gasping, diaphoresis, and nocturia, whereas diurnal symptoms include sleepiness, morning headaches, apathy, a decrease in cognitive ability, and memory loss. Age, gender, obesity, and craniofacial anomalies are considered risk factors that prompt the need for early screening using validated questionnaires [4].

Obstructive sleep apnea is associated with many chronic diseases among which is laryngopharyngeal reflux disease (LPRD). LPRD is characterized by the retrograde movement of gastro-duodenal contents into the laryngeal and pharyngeal inlets resulting in atypical symptoms of reflux such as hoarseness, throat irritation, cough, and globus sensation. These symptoms are attributed to structural changes in the laryngeal and pharyngeal mucosa such as edema and granuloma formation, and to non-structural changes such as impaired laryngeal sensation and altered upper airway reflexes. The current literature suggests the occurrence of LPRD in almost one out of two patients with OSA [5–10]. In a meta-analysis review that included 870 patients with OSA, Magliulo et al. reported an overall incidence of LPRD in 45.2% of the cases [11]. The review included 10 studies, in 7 of which the diagnosis of LPRD was based primarily on the Reflux Symptom Index (RSI) and the Reflux Finding Score (RFS) developed and validated by Belafsky et al. [12,13].

The purpose of this investigation is to shed more information on the prevalence of laryngopharyngeal reflux (LPR)-related symptoms in patients with OSA using the Reflux Symptom Score (RSS) and to compare its prevalence with that using the RSI. The authors of this manuscript hypothesize that the prevalence of LPR-related symptoms in patients with OSA is higher using the RSS questionnaire in comparison to the RSI. Increasing the physician's awareness of the high prevalence of LPR-related symptoms using the RSS in patients with OSA can help improve patient care.

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Materials and methods

After having obtained the approval of the institutional review board (IRB ID: BIO-2022-0220), the medical records and video-recordings of all patients with a history of obstructive sleep apnea who presented to a tertiary referral center between January 1, 2020, and June 30, 2022, and who had filled the RSS and RSI were reviewed. The diagnosis of OSA was made using the STOP-BANG questionnaire and/or polysomnography. The STOP-BANG questionnaire is a validated questionnaire that consists of eight dichotomous questions related to the clinical features of sleep apnea and classifies patients into three categories; low risk of developing OSA if the score is between 0 and 2, intermediate risk of developing OSA if the score is 3–4, and high risk of developing OSA if the score is 5–8 [14]. Concerning the Apnea Hypopnea Index (AHI), patients were categorized as having 'mild OSA (AHI ≥ 5 to < 15/h), moderate (AHI≥ 15 to < 30/h), and severe (AHI ≥ 30/h)' [15].

The prevalence of LPR-related symptoms was assessed using the RSS [16] and the RSI questionnaires. The RSS is a self-reported questionnaire composed of 22 items that cover symptoms of the laryngeal, gastrointestinal, and respiratory systems. Each item is scored separately from 0 to 5 for its severity and frequency. The two scores are multiplied to obtain a total that ranges from 0 to 25 for each symptom. The sum of these 22 symptom scores is calculated to provide the final RSS score. According to ROC curve analysis, an RSS >13 was considered suggestive of LPR [16]. The RSI score was also computed and analyzed for comparison. A RSI > 13 was also suggestive of LPR [12]. Demographic data included age, gender, smoking, and body mass index (BMI).

A secondary outcome measure used in this study was the RFS described by Belafsky [13]. The RFS is an 8-item severity scale based on endoscopic findings suggestive of reflux with a score ranging from 0 to 26. A score of 7 or more is suggestive of LPRD. The video-recordings of the laryngeal endoscopic examination were blindly reviewed by two otolaryngologists and signs of LPR such as mucosal, edema, erythema, pseudosulcus vocalis, and ventricular obliteration were noted.

Statistical methods

Analyses were performed using Statistical Analysis Package for Social Sciences (SPSS, version 25.0 Chicago, IL, USA). Descriptive statistics were applied for different variable types. The Chi-Square test was used to determine the association between categorical variables. A one-way ANOVA test was used to compare means of three or more groups. For a two-group comparison of means, the independent sample *t*-test was used. Data were represented as means ± SD (standard deviation) and a *p*-value <.05 was considered significant.

Results

Demographic data

A total of 39 patients were included in this study. Of these, 33 were males (84.6%) and 6 were females (15.4%). The study population was mostly middle-aged ranging from 20 to 76 years, with a mean of 43.8 ± 13.7 years. The mean BMI was 29.03 ± 4.17 kg/m^2. The smoking status of the patients was divided into three categories: 17 patients were active smokers (43.59%), 7 were former smokers (17.95%), and 15 were never smokers (38.46%). See Table 1.

STOP-BANG score and AHI

All patients included in this study had filled the STOP-BANG questionnaire and were assigned accordingly to one of three categories: low, intermediate, or high risk for OSA. Most patients fell in the high-risk category (61.54% of the cases) while the rest belonged to the intermediate-risk category (38.46%). The mean STOP-BANG score of the total group was 4.84 ± 1.22. Of the 39 patients included in this study, 24 had polysomnography. The mean AHI score of those who had polysomnography was 27.75 ± 15.81. Based on the AHI score, patients were classified as having severe risk of OSA ($n = 9$), moderate risk of OSA ($n = 11$), and mild risk of OSA ($n = 4$).

The prevalence of LPR-related symptoms using the RSS and RSI questionnaires

Twenty-seven patients of the study group (69.2%) had a positive RSS (>13) suggestive of LPR disease, in comparison to only 7 (17.9%) using the RSI (p-value = .052). The mean RSS score of the total study group was 30.05 ± 23.21 compared to a mean RSI score of 7.1 ± 5.5.

When looking at the prevalence of reflux-related symptoms among the STOP-BANG risk categories, 70.8% of patients at a high risk of having OSA had LPR-related symptoms when using RSS compared to 20.8% when using RSI. See Table 2. Patients in the high-risk category of OSA had a higher risk for reflux compared to those in the intermediate-risk category of OSA using the RSS (70.8% vs 66.7%, respectively) (p-value = .784) and RSI (20.8% vs 13.3%, respectively) (p-value = .553).

Of the 24 patients with an AHI index, 18 patients (75%) were found to have LPR-related symptoms using the RSS, in comparison to only 5 patients (20.8%) using the RSI. When stratifying patients by AHI categories, patients with severe

Table 1. Demographic characteristics of the study population.

	Value
Demographic data ($N = 39$)	*n* (%)
Gender	
Male	33 (84.6)
Female	6 (15.4)
Smoking	
Active	17 (43.6)
Former	7 (17.9)
Never	15 (38.5)
	mean ± SD
Age (years)	43.8 ± 13.7
BMI (kg/m^2)	29.03 ± 4.17
STOP-BANG	4.84 ± 1.22
AHI	27.75 ± 15.81

BMI: Body Mass Index; AHI: Apnea/Hypopnea Index; SD: Standard Deviation.

and/or moderate OSA were considered to be at a higher risk for reflux compared to those with mild disease using the RSS (66.7% and 90.9% vs 50% respectively). A similar pattern was observed using the RSI (33.3% and 18.2% in patients with severe and moderate OSA, respectively, vs 0% in patients with mild OSA). See Table 3. When comparing the prevalence of LPR-related symptoms using the RSS and RSI in relation to the severity of OSA, notably there was a trend for a higher prevalence using the RSS.

Laryngeal findings in patients with OSA

The mean RFS of the total study group was 9.31 ± 2.09. Twenty-eight patients (71.8%) were found to have LPRD according to the RFS, which is commensurate with the percentage of patients with reflux according to the RSS (69.2%).

The most common endoscopic laryngeal findings were moderate vocal fold edema (36.1%), posterior commissure hypertrophy (33.3%), and diffuse erythema/hyperemia (19.4%). Inter-rater reliability analysis revealed an intraclass correlation coefficient (ICC) of 0.942, indicating excellent reliability between the two otolaryngologists who evaluated the endoscopic laryngeal findings ($p < .0001$).

Discussion

The results of this investigation indicate that the high prevalence of LPR-related symptoms using the RSI. Almost one out of five patients with OSA had a positive RSI score and the mean RSI of the study group was 7.1 ± 5.5. Moreover, the RSI increased with the increase in the risk of OSA and the severity of the disease as evidenced by the AHI. The findings of this investigation are in alignment with many studies indicating the high prevalence of extra-esophageal reflux disease in patients with OSA using the RSI and/or subjective laryngeal findings. In 2013, Xavier et al. examined the prevalence of LPR in 74 patients diagnosed with OSA and reported a prevalence of 89%. The authors used the RSI and RFS and noted a higher prevalence of symptoms and signs in obese patients vs. non-obese [5]. In 2016, Elhennawi et al. reported a mean RSI score of 9 in a cohort of 62 patients diagnosed with OSA by polysomnography. The authors also noted a correlation between the frequency and duration of reflux events and the severity of OSA [6]. In 2017, Caparroz et al. investigated LPR using the RSI and RFS in a cohort of 56 patients diagnosed with moderate to severe OSA and reported a prevalence of LPR symptoms and/or signs in 64.3% of the cases. The authors also noted worse AHI in those with positive RSI and RFS, alluding to a positive correlation between these two disease entities [7]. The same year, Kim et al. examined the prevalence of LPR using the RSI in 73 patients with OSA before and after upper airway surgery. The investigation showed a post-operative decrease in the prevalence of LPR (33% before vs. 9% after) and the mean RSI score (11.48 before vs. 4.95 after). The authors stressed the positive effect of multilevel airway surgery on LPR in patients with OSA [8]. In 2018, Lee et al. studied 88 patients with OSA who had completed polysomnography with drug-induced sleep endoscopy and reported no significant correlation between the severity of sleep apnea and laryngopharyngeal-related parameters. Laryngopharyngeal symptoms and signs were retrieved using the RSI and RFS questionnaires [9]. See Table 4.

The results of this investigation also indicate that the prevalence of LPR-related symptoms is higher using the RSS questionnaire in comparison to the RSI questionnaire. The higher prevalence can be ascribed to the broader query aspect of the RSS. Moreover, the prevalence of LPR-related symptoms increased with an increase in the AHI, although the increase was not significant. This is in alignment with a previous study by Bobin et al. [10]. The authors investigated the numbers of upright and daytime hypopharyngeal reflux events in patients with OSA and LPR and reported a significant positive association between a validated screening tool for OSA and the RSS quality of life score [10].

The pathophysiology of LPR in patients with OSA is multifaceted. To many authors, LPR is based primarily on the pressure gradient between the decreased esophageal pressure at end-inspiration and the positive gastric pressure [17]. It is postulated that OSA leads to an increase in trans-diaphragmatic pressure with a subsequent lower esophageal sphincter insufficiency, which in turn leads to reflux disease, although not all reflux events occur during OSA events. Kuribayashi et al. investigated the mechanism of gastro-esophageal reflux in 17 patients with OSA using pH recording and esophageal manometry and noted a significantly higher transient lower esophageal sphincter relaxation in comparison to healthy controls, which argues against the

Table 2. Prevalence and mean RSS and RSI in STOP-BANG categories.

		STOP-BANG categories		
		Intermediate ($n = 15$)	High ($n = 24$)	p-value
RSS	n (%)	10 (66.7)	17 (70.8)	.784
	mean ± SD	28.67 ± 23.9	30.92 ± 23.24	.773
RSI	n (%)	2 (13.3)	5 (20.8)	.553
	mean ± SD	5.33 ± 5.74	8.21 ± 5.14	.113

RSS: Reflux symptom score; RSI: Reflux symptom index; SD: standard deviation.

Table 3. Prevalence and mean RSS and RSI in AHI categories.

		AHI categories			
		Mild ($n = 4$)	Moderate ($n = 11$)	Severe ($n = 9$)	p-value
RSS	n (%)	2 (50)	10 (90.9)	6 (66.7)	.252
	mean ± SD	19.75 ± 17.2	38.36 ± 21.75	36.56 ± 32.43	.461
RSI	n (%)	0 (0)	2 (18.2)	3 (33.3)	.447
	mean ± SD	4 ± 3.9	8.82 ± 5.58	9.22 ± 5.54	.254

RSS: Reflux symptom score; RSI: Reflux symptom index; AHI: apnea/hypopnea index; SD: standard deviation.

Table 4. Summary of notable publications on the prevalence of reflux in OSA.

Author's names	Number of subjects	Diagnostic tests used for LPR	Outcome of the study
Xavier et al. [5]	74	Reflux Symptom Index (RSI) Reflux Finding Score (RFS)	The prevalence of signs and symptoms suggestive of LPR (RSI and RFS-positive) in the studied population was 89%, with significantly higher rates seen in obese patients
Elhennawi et al. [6]	62	Reflux Symptom Index (RSI) pH probe studies (all patients)	Signs of LPR reflux were present in 34 (55%) patients. Mean RSI in the study group 9 and >13 in patients with severe OSA. Patients with severe OSA have significantly higher nocturnal LPR.
Caparroz et al. [7]	70	Reflux Symptom Index (RSI) Reflux Finding Score (RFS)	The prevalence of LPR in patients with OSA was 59.7% (defined as RSI and/or RFS positivity). The RSI was positive in 32.9% of the sample, while the RFS was positive in 38.8%. No statistically significant association between LPR and dysphagia.
Kim et al. [8]	73	Reflux Symptom Index (RSI)	24 (33%) reported an RSI score >13 and were thus classified as having reflux. The mean RSI score before surgery was 11.48. This number decreased to 4.95 after surgery and RSI positivity rate decreased from 33% to 9%
Lee et al. [9]	88	Reflux Symptom Index (RSI) Reflux Finding Score (RFS) LPR–health-related quality of life (LPR–HRQOL)	The mean RFS, RSI, and LPR–HRQOL were 6.4, 6.4, and 16.0, respectively. There was no significant correlation between OSAS severity and RFS, RSI, and scores of LPR–HRQOL.
Bobin et al. [10]	89	Reflux Symptom Score (RSS) Multichannel intraluminal impedance-pH monitoring (HEMII-pH)	Significant positive association between the Epworth Sleepiness Scale and the RSS quality of life score

trans-diaphragmatic pressure gradient hypothesis. The high number of transient lower esophageal sphincter relaxation events was attributed to shallow sleep and frequent arousals, which preceded the events [18]. Another possible cause for the co-occurrence of LPR and OSA is impaired laryngeal sensation. Patients with LPR are known to have decreased laryngeal sensation, which is also a common finding in patients with OSA. Aviv et al. investigated the presence of laryngeal sensory deficits in patients with LPR and showed that 78% of those with dysphagia and laryngeal edema of the posterior larynx had laryngopharyngeal sensory deficits [19]. Similarly, Payne et al. reported laryngeal inflammation suggestive of LPR in 90% of patients with OSA and the presence of a significant correlation between laryngeal inflammation, sensory deficits, and OSA severity using the apnea/hypopnea index [20]. Finally, it is worth noting that the laryngeal inflammation seen in patients with OSA suggestive of LPR may be the result of the repetitive collapse and re-opening of laryngeal tissues secondary to recurrent negative pressure swings. Almendros et al. investigated the effect of recurrent negative pressure swings on upper airway tissue in a rat model. The authors showed a significant increase in pro-inflammatory biomarkers, such as macrophage inflammatory protein (MIP)-2, interleukin (IL)-1b, and tumor necrosis factor (TNF)-alpha. The authors concluded that opening and closing of the upper airway in patients with OSA could lead to local inflammatory changes [21]. Laryngeal inflammatory changes may in turn contribute to the narrowing of the upper airway and increase in airway resistance.

The primary limitation of the present study is the small number of patients. Another limitation is the lack of objective diagnostic tests for LPR such as the hypopharyngeal-esophageal multichannel intraluminal impedance-pH monitoring. A larger prospective study using objective testing for LPR in OSA and its impact is in progress. Potential improvement in the severity of OSA because of a decrease in mucosal edema of the upper airway post-treatment of LPR warrants future investigation.

Conclusion

The results of our investigation indicate that LPR-related symptoms are very common in patients with OSA and that their prevalence increases with the severity of the disease. Our results also indicate that the prevalence of LPR-related symptoms is higher using the RSS in comparison to the RSI. This underscores the presence of non-laryngeal symptoms of LPR in patients with OSA that are often underdiagnosed. Our findings also highlight the need for a more comprehensive approach to the treatment of OSA-associated co-morbidities.

Ethical approval

This study was approved by the Institutional Review Board of the American University of Beirut Medical Center, Lebanon. IRB ID: BIO-2022-0220

Consent form

Verbal informed consent was obtained from the patients for their anonymized information to be published in this article.

Disclosure statement

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