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## Anxiety and its relationship to quality of life independent of depression in patients with obstructive sleep apnea

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### ABSTRACT

**Objectives:** The relationship between anxiety and obstructive sleep apnea (OSA) has not been well studied. We evaluated the factors associated with anxiety and whether anxiety is related to quality of life (QoL) independently of depression in OSA patients.

**Methods:** Data were collected from adults with newly diagnosed, untreated OSA. The State-Trait Anxiety Inventory-State Scale (STAI-S), the Beck Depression Inventory (BDI), the Epworth Sleepiness Scale (ESS), and the Short Form 36 Health survey (SF-36) were used. Anxiety and depression were defined as high levels of anxiety symptoms (STAI-S score  $\geq 40$ ) and depressive symptoms (BDI  $\geq 10$ ), respectively. Associations between anxiety and OSA were analyzed using multiple linear regression analysis.

**Results:** Of 655 OSA subjects included, the prevalence of anxiety and depression was 48.4% and 46.4%, respectively. The scores of STAI-S had strong correlations with BDI ( $r = 0.676, p < 0.001$ ). Female sex ( $p < 0.05$ ), excessive daytime sleepiness (ESS  $\geq 10$ ) ( $p < 0.05$ ), and a lower educational level ( $p < 0.05$ ) were identified as independent factors for predicting the presence of anxiety in OSA patients. The severity of OSA measured by the apnea-hypopnea index or respiratory distress index was not related to comorbid anxiety. In linear regression analysis, both anxiety ( $\beta = -10.196, p < 0.001$ ) and depression ( $\beta = -16.317, p < 0.001$ ) were independently associated with lower SF-36 scores in OSA patients.

**Conclusions:** The presence of anxiety can be predicted by female sex, daytime sleepiness, and a lower educational level. Both anxiety and depression were independently associated with a lower QoL in OSA patients.

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### Introduction

Obstructive sleep apnea (OSA) is the most common type of sleep apnea [1]. The characteristic feature of OSA is a transient and repetitive obstruction of the upper airway during sleep. These episodes of airway obstruction cause intermittent periods of oxygen desaturation and arousal from sleep, resulting in fragmented sleep. The prevalence of OSA was estimated from large population studies, such as the Sleep Heart Health study, to be up to 18% [2]. Untreated OSA is often associated with cardiovascular disease [3,4]. Symptoms reported by OSA patients include fatigue, daytime sleepiness, poor sleep quality, impaired concentration, memory loss, headache, and mood and affect disturbance [5]. OSA has a significant impact on individuals' daytime functioning, increasing traffic accidents and decreasing work productivity [6].

The physical effects of OSA and its treatment have been extensively investigated, but the psychological aspects of OSA, especially anxiety, have not drawn as much attention [7]. In fact, the relationship between

anxiety and OSA is not addressed in the clinical guidelines for the management of OSA [8]. The prevalence of anxiety ranges from 11% to 70% [7] in OSA patients and individuals with a diagnosis of sleep apnea have increased odds of receiving anxiety disorder diagnosis [9], whereas the relationship between anxiety and OSA is unclear [7]. For example, the severity of OSA was not found in previous investigations to be related to accompanying anxiety [5,7,10]. In addition, the effectiveness of continuous positive airway pressure (CPAP) treatment on anxiety is not consistent in the literature [7]. For example, Kingshott et al. [11] reported that anxiety significantly declined after 6 months of CPAP treatment. In contrast, Munoz et al. [12] failed to find a significant decline in anxiety after 3 and 12 months of CPAP treatment.

Although the role of OSA as a cause of anxiety is still unknown, it is clear that the presence of comorbid anxiety significantly impacts the health-related quality of life (QoL) of OSA patients [13]. In other diseases, depression is considered to be an extremely important determinant of QoL. For example, depression has a greater negative impact on QoL in patients with epilepsy than other clinical indicators such as seizure frequency [14]. In light of the strong association of depression and anxiety with OSA [10,13], it is possible that they strongly affect the QoL of OSA patients. However, the relationship between these mood disturbances and QoL in patients with OSA has not been well

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studied [13]. Therefore, in our current study, we investigated the relationship between OSA and comorbid anxiety in newly diagnosed, untreated OSA patients. The aims of our present analyses were three-fold: (1) to determine the prevalence of anxiety in OSA patients; (2) to identify the factors associated with anxiety in OSA patients; and (3) to determine whether anxiety is related to QoL independently of the status of depression in OSA patients.

## Methods

### Subjects

This study design was cross sectional. Participants were adult patients who visited sleep laboratories for evaluation of suspected OSA between 2009 and 2011. Their chief complaints were OSA-related symptoms such as snoring, stopping breathing during sleep, choking, gasping during sleep, or excessive daytime sleepiness (EDS). They were recruited from a single tertiary hospital in Korea. Basic demographic information, medical comorbidity, and medication information were obtained from the self-reported checklist for medical history and the patient's electronic medical record. The inclusion criteria were as follows: aged above 18 years, undertook an overnight polysomnography (PSG) for suspected OSA, and diagnosed with OSA [apnea–hypopnea index (AHI)  $\geq 5/h$ ]. Patients were excluded if they had a periodic limb movement arousal index  $\geq 5/h$ , if they had psychiatric or medical disorders based on the self-reported checklist for medical history and the patient's electronic medical record, if they were previously diagnosed with and treated for OSA, or if they filled out questionnaires incompletely. We did not exclude patients whose Beck Depression Inventory (BDI) or State-Trait Anxiety Inventory (STAI)–State Scale (STAI-S) scores were over the threshold of depression or anxiety disorder if they had not been previously diagnosed with a psychiatric disorder or were taking medication for the treatment of their condition. The study was reviewed and approved by the Institutional Review Board of the Asan Medical Center.

### Polysomnography

OSA was diagnosed using the standard PSG. Apnea, hypopnea, and respiratory effort-related arousal were scored according to the American Academy of Sleep Medicine guidelines [15]. An apnea was defined as a drop in the peak thermal sensor excursion of  $\geq 90\%$  of the baseline value for at least 10 s. A hypopnea was defined as a nasal pressure signal excursion drop of  $\geq 30\%$  of the baseline value for at least 10 s, accompanied by a  $\geq 4\%$  reduction in  $O_2$  saturation from the pre-event baseline. AHI was defined as the average number of episodes of apnea and hypopnea per hour. The respiratory distress index (RDI) was defined as the average number of episodes of apnea, hypopnea, and respiratory effort-related arousal per hour.

### Instruments

On the night of the PSG, patients completed a battery of questionnaires that was routinely administered to all patients undergoing PSG at our sleep laboratory.

The presence and severity of current symptoms of anxiety (state-anxiety level) was assessed using State Scale of the STAI [16]. The Trait Scale of the STAI evaluating a generalized propensity to be anxious (trait-anxiety level) was not used in this study. For anxiety assessment, individuals rate themselves on each statement using a Likert scale, with responses from 1 (not at all) to 4 (very much so) based on how they feel at that moment. The range of scores is between 20 and 80; the higher the score, the higher the level of anxiety. Because a cutoff point of  $\geq 40$  for the STAI-S has been suggested to detect clinically significant symptoms [17], anxiety was defined as high level of anxiety symptoms (STAI-S score  $\geq 40$ ). We used the Korean version of the STAI-S [18].

Daytime sleepiness was evaluated using the Epworth Sleepiness Scale (ESS). The ESS is a self-report, 8-item questionnaire for measuring EDS in everyday situations. The Korean version of the ESS was recently validated [19]. Higher scores indicate greater sleepiness during daily activities.

The BDI is a 21-item, self-report measure assessing the patient's current level of depression. Each item is rated on four-point scale (0–3), with a total possible score range of 0 to 63. Higher scores represent higher levels of depression. In this study, depression was defined as high level of depressive symptoms (BDI  $\geq 10$ ). The Korean version of the BDI has also been validated [20].

QoL was assessed using the Medical Outcomes Study Short Form Health Survey (SF-36) [21]. The SF-36 is a multipurpose, self-administered, and non-disease-specific health survey consisting of 36 questions divided into eight individual domains. All domain scores are transformed, resulting in scale scores from 0 (lowest level of functioning) to 100 (highest level of functioning). A higher score indicates a better health-related QoL. The Korean version of the SF-36 was recently validated [21].

### Statistical analysis

Several continuous variables such as STAI-S, BDI, ESS, and AHI were dichotomized and analyses were conducted in terms of group differences rather than individual differences because the severity of OSA was not found in previous investigations to be related to accompanying anxiety and depression [5,7,10]. The dependent variable was the presence or absence of anxiety in OSA patients. We dichotomized OSA patients into two groups according to the STAI-S: the presence (STAI-S score  $\geq 40$ ) and the absence (STAI-S score  $< 40$ ) of anxiety. The relationship between independent variables and anxiety status was evaluated by univariate and multivariate analyses. The independent variables included in the analysis were age, sex, body mass index (BMI), educational level (university vs. high or middle school), marital status (married vs. single), employment status (employed vs. unemployed), AHI (mild, moderate, and severe), and the presence or absence of EDS (ESS scores  $\geq 10$  vs.  $< 10$ ). For univariate analysis, a Student's *t*-test was used for numeric variables, and a chi-square test was used for nominal variables. Multivariate analysis using binary logistic regression was performed to further assess variables with  $p < 0.05$  according to the univariate analysis.

To determine whether a relationship between anxiety and QoL measured by the SF-36 is independent of the depressive mood in OSA patients, we used linear regression analysis. The confounding variables included in the analysis were age, sex, BMI, educational level (university vs. high or middle school), EDS (ESS  $\geq 10$  vs.  $< 10$ ), and the status of depression (BDI scores  $\geq 10$  vs.  $< 10$ ). The significance level was set at  $p < 0.05$ . Data were analyzed using SPSS version 21.0 (SPSS Inc., Chicago, IL).

## Results

### Patient characteristics

Of 863 consecutive patients who underwent overnight PSG for suspected OSA, 774 were diagnosed with OSA (AHI  $\geq 5/h$ ). Of these, 119 patients were excluded, due to medical problems (cardiac disease,  $n = 13$ ; pulmonary disease,  $n = 9$ ; cancer,  $n = 6$ ; thyroid problems,  $n = 5$ ; gastrointestinal disorder,  $n = 4$ ; and other problems,  $n = 3$ ), neurologic disease ( $n = 15$ ), psychiatric disease (major depression,  $n = 5$ ; panic disorder,  $n = 2$ ; bipolar disorder,  $n = 1$ ; and schizophrenia,  $n = 1$ ), sleep disorder ( $n = 4$ ), previous diagnosis with and treatment for OSA ( $n = 6$ ), a periodic limb movement arousal index  $\geq 5/h$  ( $n = 30$ ), and incomplete data ( $n = 15$ ). The remaining 655 OSA subjects (569 men and 86 women) participated in the study (Table 1). The average age was 49.8 years (SD = 11.7 years). The mean AHI was 28.5/h (SD = 20.1/h). Of these patients, 205 (31.3%) were classified as having mild OSA ( $5/h \leq \text{AHI} < 15/h$ ), 199 (30.4%) as having moderate OSA ( $15/h \leq \text{AHI} < 30/h$ ), and 251 (38.3%) as having severe OSA (AHI  $\geq 30/h$ ).

The mean STAI-S score was 34.0 (SD = 16.9). The prevalence of clinically significant anxiety (STAI-S  $\geq 40$ ) in the whole group was 48.4%. Severe anxiety (STAI-S  $\geq 55$ ) was identified in 7.5% of OSA patients. The mean BDI score was 10.1 (SD = 7.2). The prevalence

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