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Evaluation of Nocturia Frequency and Post- CPAP Nocturia in Patients with Obstructive Sleep Apnea Syndrome

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Keywords

- Obstructive Sleep Apnea Syndrome;
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- Oksygen Desaturation Index;
- Continuous Positive Airway Pressure

Abstract

Introduction: The aim of our study is to contribute to the elucidation of the nocturia mechanism in patients with Obstructive Sleep Apnea Syndrome (OSAS) by investigating the frequency of nocturia, evaluation of polysomnography parameters, and examining whether there is improvement in nocturia after Continuous Positive Airway Pressure (CPAP) treatment.

Material and Method: 100 male patients were included in the study. The relationship between patients' age, Body-Mass Index (BMI), neck circumference, CPAP values, comorbidities and nocturia were examined. Patients with nocturia were re-evaluated for nocturia at 12 weeks after CPAP.

Results: A total of 100 male patients with a mean age of 49 (min 31-max 76) were included in the study. Nocturia was present in 41 of the patients included in the study. When we grouped the patients as BMI > 35 and ≤ 35 and as > 43 cm and ≤ 43 cm in neck circumferences, there was a significant difference in the presence of nocturia in those with BMI > 35 and neck circumferences > 43 cm.

Conclusion: It was observed that the frequency of nocturia was 41% in our study group, and there was a significant relationship between BMI and neck circumference measurements and nocturia. There was a significant difference between the number of nighttime urination before and after CPAP. It is important to consider OSAS in the differential diagnosis, especially in patients who do not have a history of uncontrolled Diaebetes Mellitus (DM), Benign Prostatic Hyperplasia (BPH), HF, diuretic use for the etiology of nocturia, since OSAS treatment improved nocturia in our patients.

ABBREVIATIONS

AASM: American Academy of Sleep Medicine; AHI: Apnea Hypopnea Index; AI: Apnea Index; ANP: Atrial Natriuretic Peptide; BMI: Body-mass index; BPH: Benign Prostatic Hyperplasia; CAD: Coronary Artery Disease; CHF: Congestive Heart Failure ; COPD: Chronic Obstructive Pulmonary Disease; CPAP: Continuous Positive Airway Pressure; CVD: Cardiovascular Disease; DM: Diabetes Mellitus; EDS: Excessive Daytime Sleepiness; EEG: Electroencefalography; EKG: Electrocardiography; EMG: Electromyography; EOG: Electrooculography; ESS: Epworth Sleepiness Scale; HT: Hypertension; ICS: International Continence Society; ICSD: International Classification of Sleep Disorders; IPSS: International Prostate Symptom Score; NREM: Non-Rapid Eye Movements; ODI: Oksygen Desaturation Index; OSAS: Obstructive Sleep Apnea Syndrome; PHT: Pulmonary Hypertension; PSG: Polysomnography; REM: Rapid Eye Movements

BRIEF SUMMARY

OSAS is a syndrome that is accompanied by many comorbidities, reduces the quality of life, and in addition to its major symptoms, nocturia, one of the lower urinary system symptoms, is also common. In our study, we aimed to examine the frequency of nocturia in patients with OSAS, the relationship of nocturia with Polysomnography (PSG) data and demographic data, and to evaluate the nocturia status after CPAP treatment. We thought that the significant improvement in nocturia status in patients after CPAP, the consideration of OSAS diagnosis in applications for nocturia with multifactorial etiology, may prevent unnecessary examination and treatment in these patients.

INTRODUCTION

Obstructive Sleep Apnea Syndrome (OSAS); It is characterized by recurrent episodes of complete (apnea) or partial (hypopnea) upper airway obstruction during sleep and mostly by symptoms of decreased blood oxygen saturation and daytime sleepiness [1]. OSAS prevalence; It varies according to the Apnea-Hypopnea Index (AHI) value used to determine the severity of the disease. The prevalence of OSAS was reported to be 24% in men and

9% in women when AHI ≥ 5 was used in studies. However, in addition to sleepiness in people between the ages of 30-60, the rate of OSAS diagnosis by PSG in the laboratory was found to be 4% in men and 2% in women [2].

Although a definite diagnosis cannot be made with physical examination findings, OSAS has systemic consequences and therefore it is important to perform a standard systemic examination. Upper respiratory tract examination should be given priority in terms of detecting risk factors. During this examination, the teeth should also be evaluated (bruxism, missing teeth, etc.). Symptoms in OSAS vary and affect the daily lives of patients and their performance in work life. Physiopathological changes due to recurrent apnea and arousal cause cardiovascular, pulmonary, metabolic, endocrine and neurological diseases [3]. Clinical complaints in OSAS can be classified as those during sleep (snoring, witnessed apnea, night sweats) and those while awake (sleepiness, depression, attention deficit), as stated in the ICSD-3 in the Turkish Thoracic Society OSAS consensus report published in 2012.

Snoring is the most common complaint in OSAS and the most common reason for patients to apply to the clinic. Clinically significant snoring; 4 or more nights in a week. Rarely, OSAS may occur without snoring (6%) [4]. The most common cognitive consequence of OSAS; is Excessive Daytime Sleepiness (EDS). While it is seen in 8-30% of the society, results reaching 50% in OSAS have been reported [5]. As the severity of OSAS increases, the frequency of EDS also increases. Witnessed apnea is determined by the spouses of the patients. It has a frequency of 3.8-6% in the society. It is detected at a rate of 24.4% in OSAS with AHI >15 [6]. In addition to these three main symptoms in cases with OSAS, almost half of the patients get up to urinate at least once a night [7]. Nocturia has also been associated with cardiovascular changes in sleep and many mechanisms have been suggested.

Although nocturia was previously thought to be only a sign of the lower urinary tract, it has now been understood that it can be a symptom of many systemic diseases, and nocturia has become a common urological problem rather than being defined as a clinical symptom [8]. Nocturia burden was identified as the most common urinary irritant [9]. Nocturia is defined by the Continence Society (ICS) as one or more awakenings during the night to urinate [8]. There are 4 factors that play a role in the pathophysiology of nocturia. These; nocturnal polyuria, small bladder capacity, 24 hour polyuria and sleep disturbance. These factors show a synergistic effect [10,11]. Nocturia may occur in response to excessive fluid intake. In addition, diseases that cause deterioration in fluid homeostasis, bladder dysfunction, diuretic or excessive caffeine intake may also cause increased frequency of urination at night. Diabetes Mellitus (DM), Congestive Heart Failure (CHF) and OSAS are the main conditions in which nocturia is seen [12].

The aim of this study is to determine the frequency of nocturia in patients diagnosed with moderate and severe OSAS in the sleep laboratory of our hospital, to determine the relationship between OSAS severity and nocturia, and to evaluate whether there is an improvement in nocturia after 3 months of CPAP treatment.

MATERIALS AND METHODS

Research Population

Male patients who applied to Kocaeli University Practice and Research Hospital Sleep laboratory between February 2019 and March 2022 and whose PSG results were compatible with moderate-severe OSAS were included in our study. The PSG device we used in the study is the GRAEL-Compumedics E series. Among the patients who came to receive the PSG report, International Prostate Symptom Score (IPSS) scoring was applied to those who met the appropriate criteria for the study, except for the data in the sleep outpatient clinic application form. Patients with an IPSS score of > 7 were referred to the urology outpatient clinic.

The study was approved by Kocaeli University Ethics Committee (KÜ GOKAEK GOKAEK 2018/20.16). The information form describing the procedures to be performed during the study was read to the patients included in the study and their written consent was obtained.

Inclusion Criteria in the Study

1) Patients over 18 years old
2) Male patients diagnosed with moderate-severe OSAS with PSG
3) Patients who agreed to participate in the study

Exclusion Criteria

1) Using diuretics
2) Uncontrolled diabetes mellitus
3) Symptomatic heart failure
4) Kidney failure
5) Urinary infection
6) Known prostate-related disease

RESEARCH PLAN AND METHODS

PSG results and sleep laboratory outpatient forms of 200 patients diagnosed with moderate and severe OSAS in the sleep laboratory were evaluated. Of 200 patients with moderate and severe OSAS, 17 were not included in the study because they used diuretics, 36 did not provide CPAP due to its cost, 4 were diagnosed with BPH, and 43 patients could not be reached for the evaluation of nocturia at the 12th week. Epworth and STOP-BANG scores were made by informing other patients about the study, their nocturia status was questioned, and contact information was obtained from patients with nocturia at the 12th week of CPAP

treatment to reevaluate their nocturia status. IPSS questionnaire was also applied to patients with nocturia.

The age, height, weight, body mass index [weight (kg)/height squared (m^2)] and neck circumference data of the participants were recorded. BMI was calculated separately for each patient and BMI > 35, which is one of the STOP-BANG criteria, was considered significant. Demographic data, occupation, comorbidities, drugs used, alcohol use, departments for which consultation was requested, smoking status, Epworth Sleepiness Scale (ESS) and STOP-BANG data were recorded from the sleep laboratory outpatient form.

Research Measures

EEG (electroencephalography), EOG (electrooculography), chin and leg EMG (electromyography), ECG (electrocardiography), chest and abdominal respiratory movements, body position, oronasal cannula airflow, SaO_2 with fingertip pulse oximeter and snoring with a tracheal microphone placed on the neck were recorded in PSG. The number of apneas + hypopneas per hour of sleep was defined as the Apnea-Hypopnea Index (AHI). According to the patients' AHI; simple snoring (AHI < 5), mild OSAS (AHI = 5-15), moderate OSAS (AHI = 15-30), and severe OSAS (AHI > 30). Moderate and severe patients with AHI ≥ 15 were included in the study. ESS consisting of 8 questions was applied to each patient (**Appendix-1**). The answers for each question were scored between 0 and 3, and a total score above 10 was used to define increased sleepiness.

STOP-BANG scoring was applied to each patient. This scoring; snoring, fatigue, witnessed apnea, high blood pressure, BMI, age, neck circumference and gender data of the patients. In this scoring, if 2 questions were answered "YES", it was considered as low-level OSA risk, if 3-4 questions were answered "YES", it was considered as moderate OSA risk, if 5-8 questions were answered "YES", it was considered as high-level OSA risk. In addition, if 2 of the first 4 questions (STOP), i.e. snoring, fatigue, witnessed apnea and presence of Hypertension (HT), are present, in addition to male gender or BMI > 35 kg/m^2 or neck circumference > 43 cm, if there is one of the criteria, it was considered as high risk for OSAS.

Statistical Analysis

Statistical analysis was done with IBM SPSS 20.0 (IBM Corp., Armonk, NY, USA) package program. Normal distribution was evaluated with the Kolmogorov-Smirnov test. Normally distributed numerical variables are given as mean±standard deviation, non-normally distributed numerical variables are given as median (25^{th} -75^{th} percentile), and categorical variables are given as frequency (percentage). The difference between the two groups was determined by Student's t test for normally distributed numerical variables and by Mann Whitney U test for non-normally distributed numerical variables. Relationships between categorical variables were determined by Pearson Chi-Square and Fisher Exact tests. In the testing of two-sided hypotheses, $p < 0.05$ was accepted as sufficient for statistical significance.

RESULTS

All of the patients included in the study were male. A total of 100 patients with a mean age of 49 years (min: 31 and max: 76) and a mean BMI of 32.7 kg/m^2 (min22.1 and max: 53.9) were included in our study. Demographic variables and PSG data of the patients are shown in (Table 1). Considering the smoking habits of the patients; It was observed that 23 of them had never smoked, 44 of them were active smokers, and 33 of them had ex-smoker. The consultation rates of the patients, respectively; ear nose throat diseases outpatient clinic (41%), urology outpatient clinic (22%) and neurology outpatient clinic (10%). It was observed that the patients for whom urology consultation was requested were patients with nocturia at night 2 or more.

In 37 of the patients included in the study, AHI was between 15-30, moderate OSAS, and 63 patients had AHI > 30 and severe OSAS was detected. While the mean BMI of patients with moderate OSAS was 31, the mean BMI of patients with severe OSAS was 33.5 (p : 0.02). The mean neck circumferences of moderate and severe OSAS patients were 42 cm and 43 cm, respectively (p : 0.03). While the mean CPAP pressure of moderate OSAS patients was 6 cmH_2O, the mean CPAP pressure of severe OSAS patients was 8 cmH_2O (p : 0.001). A significant difference was found between patients with moderate and severe OSAS in terms of BMI, neck circumference and CPAP pressures (Figure 1). When the major symptoms of OSAS were questioned; All patients had snoring, 90% had fatigue, and 77% had witnessed apnea (p : 1). In addition to major symptoms, when other STOP-BANG criteria were examined, 33 patients had a diagnosis of HT, 28 patients had a BMI above 35, 46 patients were over 50 years old, and 58 patients had a neck circumference of 43 cm. Since all of our patients were male, all of them received 1 point in terms of gender. According to the STOP-BANG results, 97 patients were at high risk for OSAS, 1 patient was at medium risk and 2 patients were at low risk.

The Epworth questionnaire results of the patients were found to have a total score of 0-21. Nocturia was detected in

Table 1: Demographic variables and polysomnography data.

Mean ± Standard Deviation	
Age	49 ± 9.76
Height(cm)	174 ± 7.47
Weight (kg)	97 ± 16.43
BMI	32.7 ± 5.27
AHI	40.2 ± 22.3
Obstructive apnea	179.7 ± 91
Mean O2	91 ± 4.9
Minimum O2	76 ± 11.7
ODI3	41.6 ± 23.2
ODI4	31.3 ± 24.3
Time under Sat90 (min)	93 ± 45,5
NonREM Stage1	4,6 ± 4,3
NonREM Stage 2	55,2 ± 15,5
NonREM Stage 3	27,1 ± 16,9
REM	11,25 ± 7,5
Total sleep time	428 ± 60,2

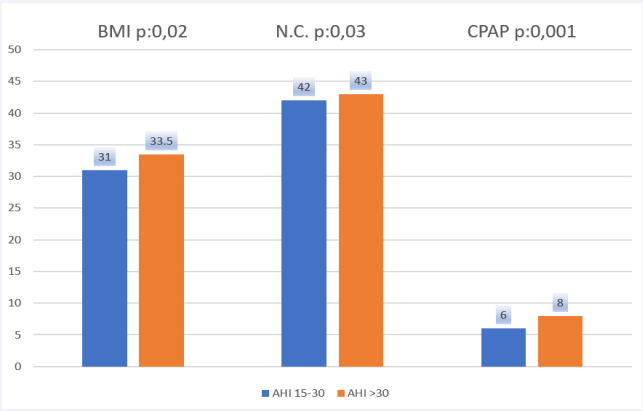

Figure 1 Comparison of BMI, Neck Circumference (NC) and CPAP pressures of moderate and severe obstructive sleep apnea patients.

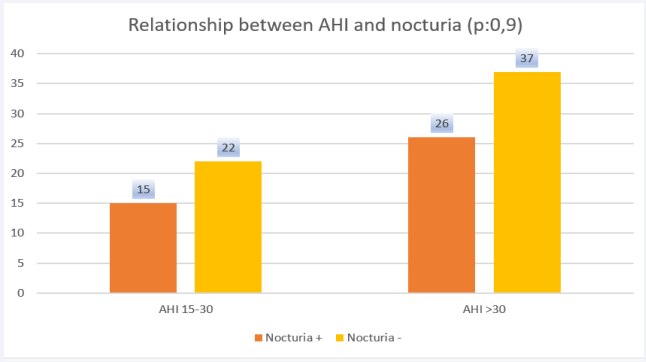

Figure 2 Comparison of the presence of nocturia between moderate and severe OSAS groups.

Table 2: Comparison of moderate and severe OSAS groups with ODI3-ODI4-90% saturation time.

	ODI3	ODI4	Time under Sat90 (min)
AHI 15-30	23	14.4	19
AHI > 30	59	51.3	80
p	0,00	0,00	0.00

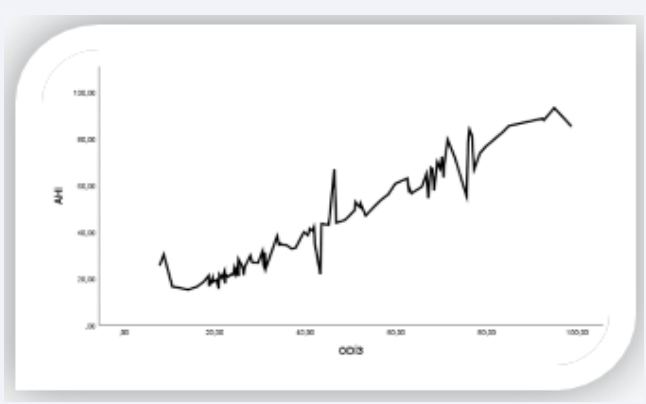

Figure 3 AHI-ODI3 and AHI-ODI4 correlation chart

20 (44.4%) of 45 patients with an ESS of ≥ 10, while nocturia was found in 21 (38.2%) of 55 patients with an ESS of <10. No significant correlation was found between ESS and the presence of nocturia (p : 0.5). While nocturia was detected in 41 of the patients. While the mean age of patients with nocturia was 48, the mean age of patients without nocturia was 50, and there was no significant difference between the groups in terms of mean age. While nocturia was found in 26 (41.3%) of 63 patients with severe OSAS, nocturia was found in 15 (40.5%) of 37 patients with moderate OSAS, and no significant difference was observed between the groups (Figure 2).

There was no significant difference between the moderate and severe OSAS groups in terms of comorbidity and drug use rates (p : 0.7). A significant difference was observed between the moderate and severe OSAS groups in terms of ODI3 (3% desaturation number per hour), ODI4 (4% desaturation number per hour), and saturation time below 90% (Table 2). A linear correlation was found between AHI and ODI3 (Figure 3), ODI4 (Figure 4) values (p : 0.001). While nocturia was found in 17 (51.5%) of 33 patients with HT, nocturia was found in 24 (35.8%) of 67 patients without HT, and there was no significant relationship between HT and nocturia (p : 0.1).

Nocturia was found in 18 (64.3%) of 28 patients with a BMI > 35, while 23 (31.9%) of 72 patients with a BMI ≤ 35 had nocturia (p : 0.003). A significant difference was found between patients with BMI > 35 and ≤ 35 in terms of ODI3, ODI4 and below 90% saturation time (p : 0.009, p : 0.004, p : 0.016). Nocturia was detected in 30 of 58 patients with a neck circumference of 43 cm and above, while nocturia was found in 11 of 42 patients with a neck circumference of less than 43 cm. There was a significant difference between neck circumference and nocturia (p : 0.02) (Figure 5).

When additional diseases are examined one by one according to the presence of nocturia; No significant difference was found between patients with and without nocturia in terms of DM, HT, Coronary Artery Disease (CAD), asthma, Chronic Obstructive Pulmonary Disease (COPD), and arrhythmia. PSG data of patients with and without nocturia were compared. The patients' total sleep duration, NREM stage 1, NREM stage 2, NREM stage 3, REM times were compared. There was no significant difference between the groups in terms of PSG data. Although the mean oxygen and minimum oxygen values of patients with nocturia were lower than those without nocturia, there was no significant difference. AHI, ODI3, ODI4 and below 90% saturation times were also higher in those with nocturia than those without nocturia, but the difference was not significant (Table 3).

Comparisons were made between those aged < 50 and ≥ 50 in terms of the presence of nocturia. Nocturia was detected in 18 (39.1%) of 46 patients aged 50 and over and 23 (42.6%) of 54 patients under 50 years of age and no significant difference was found between the groups (p : 0.7). When the groups according to age were compared, AHI, ODI3, BMI, neck circumference were higher in those < 50 years old, but no significant difference was found. Again, no significant difference was found between the

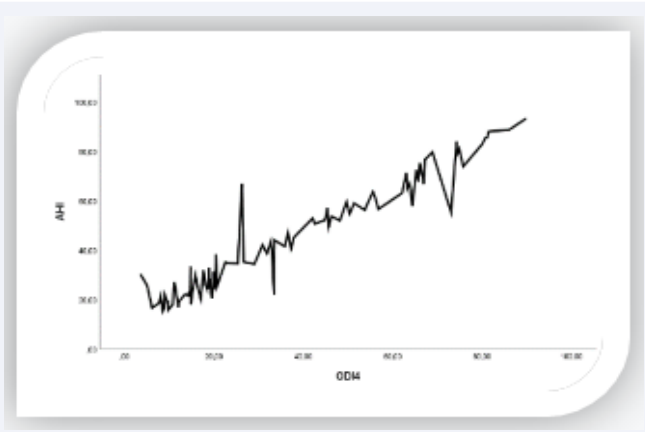

Figure 4 AHI-ODI3 and AHI-ODI4 correlation chart

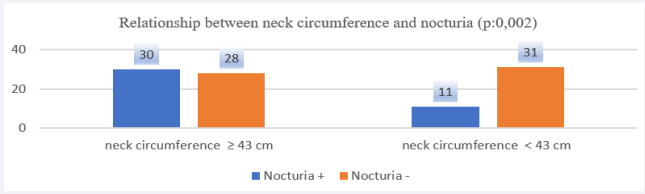

Figure 5 Relationship between neck circumference and nocturia

Table 3: Comparison of polysomnography data of patients with and without nocturia.

	Nocturia +	Nokturia -	*p*
Mean O_2	91	92	0.1
Minimum O_2	73	79	0.1
ODI3	45.1	37.8	0.2
ODI4	33.4	26,6	0.2
Time under Sat90 (min)	69	36	0.5
AHI	43	35	0.4
Total sleep time	416	429	0.2
Stage 1	4.9	4.6	0.3
Stage 2	55	53	0.5
Stage 3	27	29	0.4
REM	10	11	0.3

groups in terms of the presence of HT (p : 0.1). In addition, when patients with and without nocturia were divided into groups under 50 years of age and above; While the mean CPAP pressure was 8 cmH2O in those aged < 50 years with nocturia, it was found to be 7 cmH_2O in those aged ≥ 50 years (Table 4). In those without nocturia, the mean CPAP pressure of patients < 50 years and ≥ 50 years was 7 cmH_2O, and there was no significant difference between the groups.

When the number of nocturia before and after CPAP was examined, when urination even once less than once a night was considered an improvement in the initial number of nocturia, it was found that while there was improvement in 35 of the patients, there was no improvement in 6 of them. There was a significant difference between the number of baseline and control nocturia (p : 0.001). While the mean AHI value of the

Table 4: Comparison of variables by age.

	< 5 0 age	≥ 50 age	*p*
BMI	33.4	31.5	0.06
AHI	46.1	34.8	0.2
Neck circumference	43.5	43	0.08
ODI3	47.9	38.7	0.3
Patients with nocturia	23	18	0.7

patients with improvement in nocturia was 45, the mean ODI3 was 49, and the saturation time below 90% was 69 minutes, the mean AHI value of the patients who did not improve was 25, the mean ODI3 was 48, and the saturation time below 90% was 55 minutes. There was no significant correlation between AHI, ODI3, ODI4 values and presence of HT between those with and without improvement in nocturia. IPSS scoring was applied to patients with nocturia and 21 patients with an IPSS score of ≥ 7 were referred to the urology outpatient clinic. Medical treatment was started in 3 of the patients referred to the urology outpatient clinic, pathology was not considered in 9, and follow-up was planned by urology for 9 patients.

DISCUSSION

The frequency of OSAS increases in proportion to age and is seen at the highest rate between 40-65 years [13]. In the study of Fidan, et al. the mean age was found to be 48.4 [14]. The relationship between age and OSAS risk has been examined in many studies and it has been shown that the incidence of OSAS increases with age. The mean age of the patients included in our study was 49 (ss ± 9.76), which was consistent with the literature. Although the strongest relationship between OSAS and Cardiovascular Disease (CVD) was found with systemic HT, many CVD risks such as HF, Pulmonary Hypertension (PHT), cardiac arrhythmias, CAD, sudden cardiac death were increased. HT was the most common comorbidity in our study.

In studies, the frequency of OSAS was found to be 25% in patients with HT, and the frequency of HT in patients with OSAS was found to be 50% [15,16]. While 33% of our patients had HT, 4% had arrhythmia and 7% had CAD. Many common risk factors in the development of both diseases; age, increased BMI, family history, and male gender. Obesity is the most important risk factor for OSAS. OSAS risk increased 8-12 times in those with a Body Mass Index (BMI) > 29 kg/m^2 [17]. BMI > 29 was found in 72% of the patients included in our study. In our study, a significant relationship was found between AHI and BMI. The BMI of the moderate and severe OSAS groups were respectively 31 and 33.5 (p : 0.02). Neck circumference greater than 43 cm in men and 38 cm in women is risky for OSAS [18]. In our patients, the mean neck circumferences of the moderate and severe OSAS groups were 42 cm and 43 cm, respectively, and a significant difference was found (p : 0.03).

Smoking history is an important risk factor in the etiology of OSAS. The risk of snoring and witnessed apnea is approximately 2.5 times higher in smokers [19,20]. Examined the relationship between sleep-disordered breathing and smoking in 811 people in the USA and found that the frequency of simple snoring and

moderate-to-severe sleep-disordered sleep was significantly higher in smokers. All of the patients included in our study had a complaint of snoring. While 44% of the patients included in the study were still smoking, 33% had a history of smoking cessation. In other words, 77% of the patients had a history of smoking. While 46.3% of patients with nocturia were active smokers, 42.4% of patients without nocturia were active smokers, but there was no significant difference in smoking status between the groups.

In a meta-analysis including 13 studies investigating the relationship between nocturia and OSAS; in subgroup analysis classified according to OSA severity (mild: Apnea-Hypopnea Index (AHI) ≥ 5 and < 15), moderate (AHI ≥ 15 and < 30), severe (AHI ≥ 30); severe OSA had a higher incidence of nocturia than mild or moderate OSA [21]. In our study, 37 of the patients had moderate OSAS and 40.5% of these patients had nocturia, while 63 of the patients had severe OSAS and 41.3% of them had nocturia. There was no significant difference in the frequency of nocturia between the moderate and severe OSAS groups (p : 0.9). Miyauchi, et al. found a significant reduction in the frequency of getting up to urinate at night and in nocturnal urine volume after continuous CPAP therapy in 51 patients with OSAS [22]. In patients with nocturia included in our study, when their nocturia status was questioned after 3 months of effective CPAP treatment, a decrease was observed in the number of nighttime urination before and after CPAP, and a statistically significant difference was found (p : 0.001).

In a study conducted in the USA involving a large patient population, a significant dose-dependent relationship was found between BMI and nocturia [23]. This result was consistent with those reported in previous studies in Taiwan, Korea, and Finland. One of the strongest aspects of the study conducted in the USA is that various subgroup analyzes were made. In subgroup analyzes according to age classification, a significant correlation was found between obesity and nocturia in both young and old subgroups. In our study, a significant difference was found between patients with BMI >35 and ≤ 35 in terms of the presence of nocturia (p : 0.003). The frequency of nocturia was significantly higher in patients with BMI > 35. Similarly, study conducted in the USA, although the mean BMI was higher in younger patients, there was no significant difference in age among the groups separated according to BMI.

The relationship between BMI and OSAS has also been shown in many studies. Obesity is one of the most important risk factors for OSAS. Mild to moderate obesity has been associated with a significantly increased prevalence of sleep apnea [24]. Showed in a population-based cohort of middle-aged patients that a one unit increase in BMI was associated with a fourfold increased risk for sleep apnea. In severe obesity (BMI > 40 kg/m^2), the prevalence of sleep apnea has been estimated to range from 40% to 90% and the severity of sleep apnea is generally higher than that found in leaner populations [24-26]. In our study, the mean BMI of patients with moderate OSAS was 31, while the mean BMI of patients with severe OSAS was 33.5 and a significant difference was found between the groups in terms of BMI (p : 0.02).

In one study, a moderately significant relationship was observed between OSAS and nocturia in young and middle-aged men, but no such relationship was found in older men. In the same study, no relationship was found between nocturia and OSAS in the elderly [27]. These findings in the study by Hajduk et al; It is also consistent with the conclusion that sleep apnea symptoms are more associated with pathological nocturia in young men than in older men [28]. In addition, the study by Moriyama et al. found that obstructive sleep apnea was significantly associated with nocturia in men younger than 50 years of age but not in men older than 50 years. It was observed that AHI did not differ significantly in men with and without nocturia [29]. In our study, when patients were grouped as < 50 years and ≥ 50 years, no significant difference was observed between the groups in terms of nocturia frequency and AHI value. The mean age of patients with nocturia was 48 and the mean age of patients without nocturia was 50. Although the mean age of those with nocturia was younger, no significant difference was found. While the BMI of patients < 50 years of age with nocturia was 34.7, the BMI of patients ≥ 50 years of age was 33. Young patients had a higher BMI, and a significant correlation was found between BMI and nocturia.

Although the relationship between OSAS and nocturia has not been fully clarified, 3 mechanisms have been suggested. The first mechanism; it is right atrial distension and ANP (atrial natriuretic peptide) release from atrial myocytes as a result of increased intrathoracic negative pressure due to airway obstruction and then increased venous return to the right atrium [30,31]. The second mechanism is right ventricular enlargement caused by right atrial distension, causing the interventricular septum to shift to the left, impairing left ventricular filling and reducing stroke volume [32]. As a result, the heart perceives this as fluid overload and ANP secretion from the atrium is stimulated [33]. Third, hypoxia and hypercapnia caused by apnea sympathetic nerve system, which causes vasoconstriction, increase in blood pressure and increase in left ventricular afterload, which reduces cardiac output and the heart perceives this as fluid overload and ANP secretion from the atria is stimulated [31]. Based on the above mechanisms, the ANP release occurring in OSAS, can cause nocturia. ANP, aldosterone and arginine may cause nocturia by inhibiting vasopressin secretion as well as increasing glomerular filtration [34-36].

In a study investigating the relationship between nocturia and oxygen desaturation index, the mean O_2 saturation and T90 and ODI4 values were found to be significantly lower and significantly higher in the nocturia group compared to the control group [37]. In our study, the mean O_2 saturation of patients with nocturia was lower, ODI3 and ODI4 values, the time under 90% was higher than those without nocturia. However, there was no significant difference between those with and without nocturia in terms of mean O_2, minimum O_2, ODI3, ODI4, and less than 90% saturation time. In addition, patients with improved nocturia after CPAP had a mean AHI value of 45, a mean ODI3 of 49 and a saturation time below 90% of 69 minutes, while those who did not improve had a mean AHI of 25, an average of ODI3 of

48 and a saturation time of less than 90% was 55 minutes. This result suggested that nocturia was associated with OSAS in the severe OSAS group and in patients with a longer saturation time below 90% in proportion to AHI and that evaluation and follow-up should be performed in terms of other nocturia etiologies in patients who did not improve.

In OSAS patients, nocturia is subjectively associated with sleep disturbance, decreased sleep quality due to sleep fragmentation, EDS and has also been shown to cause adverse objective changes in sleep patterns as measured by polysomnography [38]. In addition to its effect on quality of life, nocturia is associated with sleep apnea comorbidities. Various mechanisms have been suggested between recurrent nocturnal hypoxia/reoxygenation cycles and OSAS-associated HT. Sleep apnea triggers oxidative stress and low-grade inflammation, which are initiators of a pathophysiological cascade leading to sympathetic overactivity.

Sympathetic system activation in OSAS patients causes an increase in systemic resistance and therefore an increase in blood pressure. Also, sympathetic activation; stimulates renal renin release and leads to elevated circulating levels of angiotensin II and aldosterone; this suggests that the renin-angiotensin system is involved in OSAS-associated HT [39]. This study clearly demonstrated that nocturia is also strongly associated with OSAS-related HT, after adjusting for confounding factors. Nocturia is a symptom that has no cause-effect relationship with HT, but it has been shown that it can trigger a specific mechanical pathway for the formation of HT in OSAS patients [40]. In our study, the frequency of HT in patients with nocturia was higher than those without nocturia, but no statistically significant difference was found.

In conclusion, in our study group, the frequency of nocturia was found to be 41% and the BMI and neck circumference values of patients with nocturia were higher than those without nocturia. When PSG data of patients with nocturia were analyzed, mean O_2 and minimum O_2 values were lower than those without nocturia and saturation time below 90% AHI-ODI3-ODI4 was higher, but no statistically significant difference was found. In our study, moderate and severe OSAS cases were included. Thus, significant results can be obtained in terms of the mechanism that starts with sympathetic activation, which is examined by hypoxia, by making comparisons between all groups of OSAS mild, moderate, and severe. In addition, in terms of ANP release, which is another mechanism, the mechanism of isolated nocturia in OSAS patients can be elucidated by making ANP measurements before and after CPAP and comparing the improvement of nocturia with objective data such as uroflowmetry.

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