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The use of the CT90 value in predicting anxiety in OSA: could it be a useful parameter?

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Abstract. – OBJECTIVE: Obstructive sleep apnea (OSA) is characterized by recurrent episodes of complete or partial obstruction of the upper airway leading to episodic desaturation. OSA patients often show symptoms of anxiety. Our study aimed to examine the presence and levels of anxiety in OSA and simple snoring relative to control subjects and to investigate the correlation between anxiety scores and polysomnographic, demographic, and sleepiness parameters.

SUBJECTS AND METHODS: **The study included 80 OSA, 30 simple snoring, and 98 control cases. Demographic, anxiety, and sleepiness data of all subjects were acquired. The Beck Anxiety Inventory (BAI) was used to determine the level of anxiety. The Epworth Sleepiness Scale (ESS) was used to evaluate the sleepiness level of participants. In addition, polysomnography recordings of those in the OSA and the simple snoring group were acquired.**

RESULTS: **Significantly higher anxiety scores were found in patients with obstructive sleep apnea and simple snoring compared to the control group ($p<0.01$, $p<0.01$, respectively). From the polysomnographic data obtained from OSA and simple snoring subjects, the CT90 values (cumulative percentage of the time spent at saturations below 90%) and the AHI showed a weak positive correlation between the level of anxiety ($p=0.004$, r=0.271; $p=0.04$, r=0.196, respectively).**

CONCLUSIONS: **Our study concluded that polysomnographic data showing the depth and duration of hypoxia may be more reliable in showing neuropsychological disorder and hypoxia-related comorbidities in OSA. The CT90 value can be used as a measure in the assessment of anxiety in OSA. Its advantage is that it can be measured with overnight pulse oximetry along with in-laboratory PSG and HSAT (home sleep apnea test).**

Key Words:
OSA, Snoring, Anxiety, AHI, CT90.

Introduction

Obstructive sleep apnea syndrome (OSAS) is a syndrome characterized by recurrent episodes of complete or partial upper respiratory tract obstruction and desaturation in mostly arterial blood during sleep[1]. OSAS is one of the most common sleep disorders that can be observed in both genders and all races, ages, socioeconomic stratum, and ethnic groups[2]. Obstructive sleep apnea is a common condition affecting 10% of the population[3].

The most frequently encountered application complaints include snoring, excessive sleepiness, and a feeling of being out of breath during sleep[4]. In addition to these complaints, neuropsychiatric symptoms such as psychomotor slowing, cognitive impairments, memory weakness, attention deficit, lack of concentration, loss of interest and desire, poor professional performance, and sexual problems can be seen[5,6]. Although there is no definitive diagnostic finding in a physical examination, patients should be examined with a multidisciplinary approach since most of the comorbidities occur together[7]. Polysomnography (PSG), which is the gold standard method for the diagnosis of OSAS, is an examination that allows the detailed evaluation of sleep stages and many vital parameters[8]. Sleep interruptions due to the course of the disease in OSAS patients are the main cause of excessive daytime sleepiness[9].

Anxiety and depression in OSAS patients are closely related to the severity of excessive daytime sleepiness. Severe and mild-to-moderate OSAS patients with excessive daytime sleepiness have worse anxiety and depression scores[10]. Although studies are showing that the prevalence of depression and anxiety disorders in OSAS is higher than in the general healthy population, conflicting results have also been reported in the literature, and a definite consensus on the subject could not be reached[11]. Various studies[12-15] on the

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relationship between OSAS in neuropsychiatric disorders have been made in the literature; in particular, Fidan et al[12], Ehi et al[13], Inanç et al[14], and Salepci et al[15] investigated the relationship between OSAS and anxiety. These studies achieved quite different results from each other.

In our study, the aim was to determine the anxiety levels of patients diagnosed with OSA by performing a polysomnographic examination in the sleep laboratory of Kocaeli University Training and Research Hospital. The duration of respiratory events during sleep has a significant impact on OSA outcomes, but the AHI does not take this important factor into account. The CT90 value can be used as a measurement in the evaluation of anxiety in OSA since it shows the duration and depth of respiratory events during sleep and can be easily obtained with measurements such as in-laboratory PSG, HSAT, and overnight pulse oximetry. Therefore, we hypothesized that the CT90 value could better reflect anxiety in patients with OSA and be of more practical use.

Subjects and Methods

Subjects

We recruited 80 newly diagnosed, treatment-naive OSA subjects and 30 simple snoring subjects from the Sleep Disorders Laboratory at the Kocaeli University Training and Research Hospital and 98 age- and gender-comparable healthy controls. The study was conducted prospectively between September 2019 and March 2020. The inclusion of participants in the study can be seen in the flowchart in Figure 1.

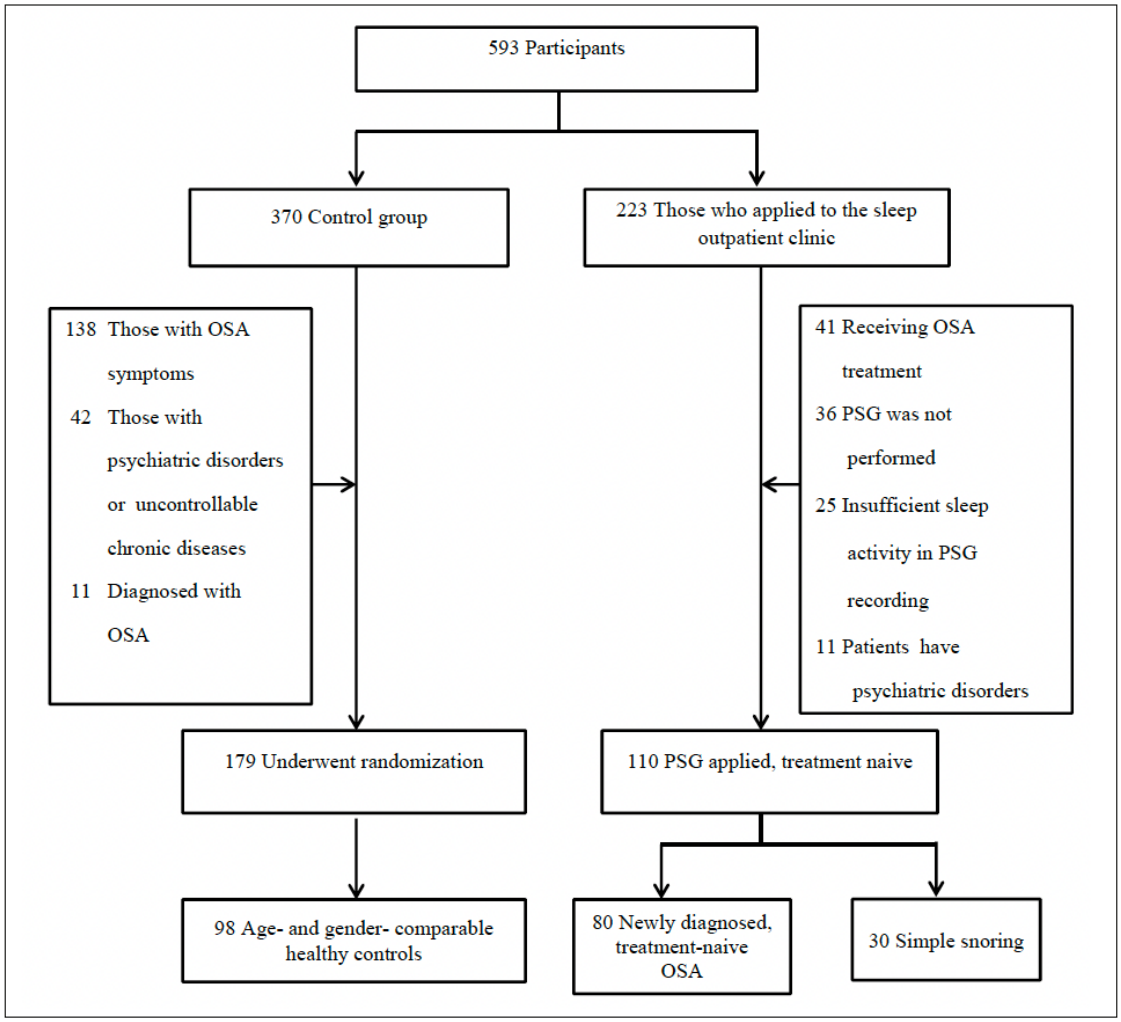

Figure 1. Flowchart of Participant Enrollment.

The OSA and simple snoring subjects were diagnosed based on overnight polysomnography (PSG). The PSG data were obtained with PSG system (Compumedics E series, Australia). The polysomnography records were scored manually by an experienced sleep laboratory specialist. EEG, EOG, chin and leg EMG, ECG, thorax and abdominal breathing movements, body position, oronasal cannula airflow, SpO_2 with a fingertip pulse oximeter, and snoring with a tracheal microphone placed in the neck were recorded in PSG.

We used the standardized scoring criteria recommended by the American Academy of Sleep Medicine (AASM)[2] to define OSA severity based on the apnea-hypopnea index (AHI), which is derived by dividing the number of apnea and hypopnea events by the total sleep time. Based on these criteria, the OSA subjects were categorized as follows: mild OSA, AHI of 5 or more but fewer than 15 events/hr; moderate OSA, AHI of 15 or more but fewer than 30 events/hr; and severe OSA, AHI of 30 or more events/hr. To score a respiratory event as hypopnea in an adult patient, the following listed rules were observed: 1) the respiratory signal during sleep (obtained with the nasal cannula in the diagnostic test) decreased by ≥30% from the baseline, 2) the signal loss of ≥30% lasted for ≥10 seconds, 3) the pre-event baseline oxygen saturation was ≥3% reduction or the event ended with arousal. If all the listed rules were satisfied, OSAS was diagnosed according to AASM criteria[16].

The lowest saturation and average saturation values evaluating oxygenation during sleep and the times where there was less than 90% saturation were recorded. To calculate the ODI and CT90 values, the number of SpO_2 decreased by 3% and the times below 90% of saturation were recorded. According to these recorded parameters, the ODI and CT90 parameters were calculated manually. In the calculation of ODI, the index was calculated by finding the hourly amount of 3% reduction numbers. For the CT90 parameter, it was found by proportioning the time elapsed below 90% of the saturation to the total sleep time.

Polysomnography was performed on 110 people in the study. According to AHI, 30 simple snoring, 28 mild OSA, 20 moderate OSA, and 32 severe OSA were diagnosed. Inclusion criteria for all participants were: age >18 years old; no previous diagnosis of sleep apnea, psychiatric disorders, or mood disorders; and the absence of underlying diabetes or cardiovascular diseases including coronary artery disease, stroke or peripheral vascular disease, as assessed by a review of the subjects past medical history and medication list.

Exclusion criteria included: pregnancy, current or previous treatment for sleep apnea, alcohol abuse, and use of supplemental oxygen. Subjects taking prescription or over-the-counter sedatives, respiratory suppressants, medications for cardiovascular disease, and psychiatric drugs were also excluded.

The healthy control subjects were recruited from among volunteers at the Kocaeli University campus and the Kocaeli area. We interviewed control subject, as well as their sleep partners when available, to determine the potential for sleep disordered breathing, and subjects suspected of having such disturbed patterns based on symptoms of snoring and gasping or with abnormal Epworth Sleepiness Scale (ESS) scores. Those with a potential for sleep-disordered breathing were excluded. All participants gave written informed consent, and the study protocol was approved by the Institutional Review Board at Kocaeli University.

Assessment of Sleep and Mood

We assessed sleep quality and daytime sleepiness in all OSA and the simple snoring and control subjects using the Epworth Sleepiness Scale (ESS), and anxiety symptoms using the Beck Anxiety Inventory (BAI) in all participants included in this study. Major symptoms of OSAS, such as snoring, excessive daytime sleepiness, witnessed apnea, and ENT diseases, if any, were recorded. The BAI self-administered questionnaires include 21 questions (each question score ranges from 0 to 3) with total scores ranging from 0 to 63 based on mood or anxiety symptoms[17].

Statistical Analysis

The statistical evaluation was made with the IBM SPSS 26.0 (IBM Corp., Armonk, NY, USA) package. Normal distribution was evaluated by the Kolmogorov-Smirnov and Shapiro-Wilk tests. Numerical variables were given as mean±standard deviation or median (25^{th}-75^{th} percentile). Categorical variables were expressed as frequency (percentage). Differences between groups were analyzed using one-way analysis of variance (ANOVA) when the assumption of normal distribution was provided and the Mann-Whitney U test and the Kruskal-Wallis' test when the assumption of normal distribution was not provided. The LSD and Dunn tests were used for multiple comparisons. The relationships between numerical variables were evaluated using Spearman correlation analysis, and relationships between categorical variables were evaluated using Chi-square analysis. In testing the two-sided hypotheses, $p<0.05$ was considered sufficient for statistical significance.

Table I. Sleep, mood, and demographic variables of OSA, simple snoring, and control subjects.

Variables	OSA (n=80)	Simple Snoring (n=30)	Controls (n=98)	*p*-value
Age range (yrs)	24-73	25-66	24-59	-
Mean age (yrs)	45.18±11.17	44.87±9.11	42.53±7.36	0.23
Gender (male-female)	60:20	23:7	60:38	0.08
BMI (kg/m^2)	31.47±5.43	29.25±3.64	27.25±3.24	**<0.01**
AHI (events/h)	30.57±2.76	2.99±0.25	-	-
BAI	14.08±10.94	9.47±8.83	5.05±6.20	**<0.01**
ESS	9.51±6.14	7.43±5.95	5.00±3.29	**<0.01**

BMI, body mass index; yrs, years; AHI, apnea-hypopnea index; BAI, Beck anxiety inventory; ESS, Epworth sleepiness scale.

Results

The total study included 65 women (31.2%) and 143 men (68.8%) with a mean age of 43.88±9.29 years and a mean BMI of 29.16±4.66 kg/m^2. A total of 208 people were included. There was no significant relationship between age for gender and The Beck anxiety score. Sleep, mood, OSA demographic and physiologic data, simple snoring, and control subjects are summarized in Table I. Detailed PSG data and the sleep records of OSA subjects are provided in Table II.

In the study, the mean total ESS score for females was 5.46±4.39 and for males, 7.83±5.61. The mean ESS score for males was found to be significantly higher than that of females (p<0.01). Of the participants included in the study, 114 (54.8%) stated that they had never smoked, 47 (22.6%) still smoked, and 47 (22.6%) had quit smoking (Table III).

The mean BAI scores of the control group (5.05±6.20) were found to be significantly lower than both the newly diagnosed OSAS patients (14.08±10.94) and the simple snoring group (9.47±8.83). No significant difference was found between the newly diagnosed OSAS patients and the simple snoring group in terms of the mean BAI scores.

Table II. Detailed PSG data and sleep records of OSA subjects.

PSG Variables	Mean	SD
Total recording time (mins)	472.01	40.12
Total sleep time (mins)	398.70	87.40
Sleep efficiency index (%)	84.83	14.24
Latency of sleep onset (mins)	27.58	41.10
REM sleep (%)	15.56	15.88
Latency of REM onset (mins)	130.18	95.75
Stage N1 (%)	4.50	3.28
Stage N2 (%)	51.95	14.20
Stage N3 (%)	29.66	17.94
Number of obstructive apneas	74.25	137.86
Number of central apneas	11.38	33.96
Number of mixed apneas	6.36	34.50
Number of apneas	92.41	156.97
Number of hypopneas	86.42	70.54
Supin AHI	16.77	27.40
Non-supine AHI	31.06	69.36
REM AHI	25.77	26.23
Non-REM AHI	25.77	26.23
Lowest SpO2	79.41	11.09
Average SpO2	91.51	4.07
ODI (3%)	25.30	25.24
ODI (4%)	18.73	23.35
CT90	0.08	0.13
Time below 90% saturation	35.76	54.88

OSA, obstructive sleep apnea; PSG, polysomnography; REM, rapid eye movement sleep; SpO_2, peripheral oxygen saturation; ODI, oxygen desaturation index; N1, N2, and N3 sleep, non-rapid eye movement sleep stages stage; CT90, the cumulative percentage of time spent at saturations below 90%; AHI, apnea-hypopnea index.

Table III. Correlation between total BAI score and total ESS score and demographic data.

	BAI		ESS	
	R	*p*-value	R	*p*-value
Age	0.154*	0.027	0.047	0.502
Height (cm)	-0.164*	0.018	0.065	0.354
Weight (kg)	0.070	0.313	0.238	**0.001****
BMI	**0.215****	**0.002**	0.206	**0.003****
Cigarette smoking (pack-year)	-0.116	0.272	-0.187	0.076

BMI, body mass index; BAI, Beck anxiety inventory; ESS, Epworth sleepiness scale. *The correlation is significant at p-value = 0.05. **The correlation is significant at p-value = 0.01.

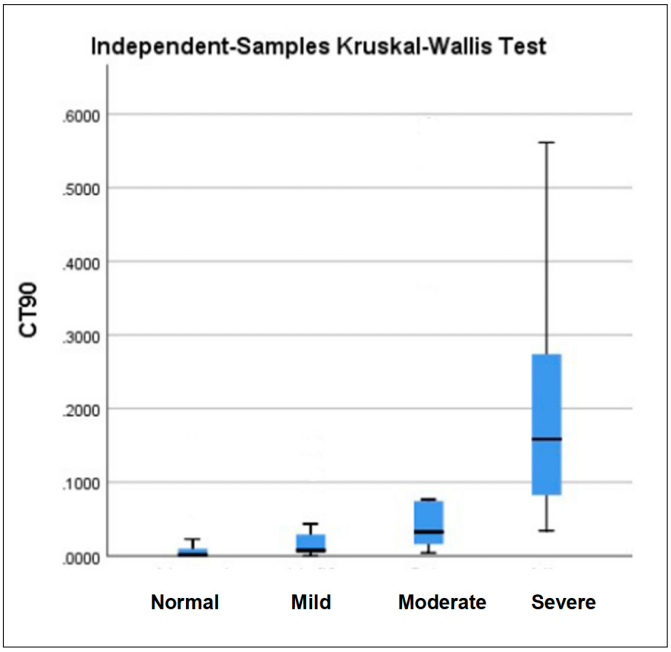

Figure 2. The Kruskal-Wallis' test was performed in terms of CT90 data among the categories separated according to AHI in OSAS. There was a significant difference between some groups. Severe OSA was found to be significantly higher than all other groups in terms of CT90. There was a significant increase in favor of "moderate" between the "normal" and "moderate" OSAS groups. (p<0.01) However, there was no significant difference in CT90 value between "normal" and "mild" and between "mild" and "moderate" (p>0.05).

There was a significant difference between the groups in terms of mean ESS scores (p<0.01). The source of this difference was found to be significantly lower in the control group (5.00±3.29) than both newly diagnosed OSAS patients (9.51±6.14) and the simple snoring group (7.43±5.95). There was no significant difference in mean ESS scores between the simple snoring and newly diagnosed OSAS groups. CT90 values were compared between groups separated by AHI in OSAS (Figure 2). There was a significant difference between some groups (p<0.01).

Statistics were correlated between the data of those who underwent a PSG examination and total BAI and total ESS scores (Table IV). There was a negative correlation between the total BAI score and mean saturation (r=-0.293, p<0.01). A weak positive correlation was found with the total BAI score, AHI (r=0.196, p=0.04), and CT90 (r=0.271, p<0.01).

Discussion

Contrary to studies[18] showing that the incidence of OSA increases with age, no significant age-related difference was found in the newly diagnosed OSA patients in our study. Obesity poses a significant risk for OSA[19]. The relationship between

Table IV. Correlation between total BAI score, total ESS score, and PSG parameters.

PSG parameter	BAI		ESS	
	R	*p*-value	R	*p*-value
AHI	**0.196***	**0.040**	0.163	0.089
Lowest saturation (%)	-0.168	0.079	-0.121	0.206
Average Saturation (%)	**-0.293****	**0.002**	-0.190*	0.047
Time under 90% saturation	**0.273****	**0.004**	0.129	0.179
ODI (3%)	**0.192***	**0.045**	0.160	0.096
ODI (4%)	0.182	0.057	0.156	0.105
CT90	**0.271****	**0.004**	0.120	0.210

BAI, Beck anxiety inventory; ESS, Epworth sleepiness scale; PSG, polysomnography; ODI, oxygen desaturation index; CT90, the cumulative percentage of time spent at saturations below 90%. *The correlation is significant at p-value = 0.05. **The correlation is significant at p-value = 0.01.

the AHI and weight loss has been the subject of various studies[20,21], and weight loss is important in the treatment of OSA. In our study, the weight and body mass indexes of the newly diagnosed OSA and the simple snoring group were found to be significantly higher than those of the control group. In this case, it is important for those with OSA and simple snoring to maintain a healthy, controlled weight within the scope of general precautions.

Excessive daytime sleepiness is a symptom that disrupts the daily functions of OSAS patients, affects their quality of life, and may cause accidents[22,23]. Similar to the literature, the ESS scores of newly diagnosed OSA and simple snoring groups were significantly higher than those of the control group in our study (Table V).

OSAS patients often show cognitive deficits, depression, and anxiety symptoms[24]. Several studies[25,26] have shown that OSAS causes cognitive and mood decline and affects 17-47% of adult patients with OSAS. In our study, the mean scores of those with newly diagnosed OSAS and the BAI scores of those in the simple snoring group were found to be significantly higher than those of the control group (Table V). However, no significant correlation was found between the newly diagnosed OSAS patients and the simple snoring group in terms of mean BAI scores.

Although the pathological basis of the underlying neuropsychological comorbidities in OSAS is not fully understood, various mechanisms have been suggested[27-30]. Some of those include brain tissue damage caused by intermittent hypoxia or ischemia which is an emotion-related network dysfunction caused by insomnia and fragmented sleep[27,28]. Intermittent hypoxia and episodic hypoxemia accompany OSA, and this may directly affect neurons, axons, and glia[29,30]. In our study, it was shown that the difference in anxiety levels between study groups was associated with an increase in the newly diagnosed OSAS and simple snoring groups. The BAI scores had a weak positive correlation with body mass index, time under 90% SpO_2, CT90, and negatively correlated with mean oxygen saturation. Also, a weak positive correlation was found between BAI scores, AHI, and ODI (3%) (Table IV).

Similarly, in a study conducted on patients with anxiety, depression scales were applied, and no correlation could be found between them and AHI[13]. However, the role of AHI in detecting intermittent hypoxia and episodic hypoxemia, which is implicated in neuropsychological pathologies in OSAS, is questionable. Similarly, there was no significant relationship between the ODI and BAI scores. Both parameters are used to determine the frequency of desaturation decreases in polysomnography. The CT90 parameter, which is used to determine the desaturation time, suggests that this parameter can provide more accurate information about hypoxia which is the basis of the neuropsychological pathologies of OSAS.

A positive correlation was found between BAI and ESS scores. This situation shows an increase in the anxiety levels of people with an increase in sleepiness. The worsening of sleepiness can be explained by the anxiety caused by this situation since it affects the quality of life and cognitive status of individuals and causes various accidents.

Limitations

In this study, although the newly diagnosed OSA, simple snoring, and control groups were similar in terms of age and gender, there was a significant difference in terms of BMI. This match was not balanced because obesity is in the general character of OSA. However, one study found that functional brain changes that lead to neuropsychological differentiation are directly related to OSA rather than obesity[31].

Table V. Data of study groups and ıntergroup significance value.

	OSA		Simple snoring		Control group		
	Mean	SD	Mean	SD	Mean	SD	*p*-value
Age	45.18	11.17	44.87	9.11	42.53	7.36	0.23
Height (cm)	172.40	9.60	171.33	9.04	170.59	8.32	0.34
Weight (kg)	93.54	17.38	85.53	9.57	79.49	12.10	**<0.01**
BMI	31.47	5.43	29.25	3.64	27.25	3.24	**<0.01**
BAI	14.08	10.94	9.47	8.83	5.05	6.20	**<0.01**
ESS	9.51	6.14	7.43	5.95	5.00	3.29	**<0.01**

BMI, body mass index; BAI, Beck anxiety inventory; ESS, Epworth sleepiness scale. The correlation is significant at *p*-value = 0.01.

While designing the control group for this study, attention was paid to the ESS scores of the participants. Snoring, awakening with choking or gasping, daytime sleepiness, and witnessed apneas by the bed partner were questioned. Those without potential sleep-disordered breathing were included. The study has a sensitivity of 80-90% in the diagnosis of OSA even for snoring complaints[32]. Thus, the control group consisted of individuals with a very low probability of OSA. However, these people were not given polysomnography. Stronger studies can be planned by applying PSG to the control group. This part constitutes the weak side of our study.

Conclusions

In our study, the anxiety scores of the OSAS and simple snoring groups were found to be significantly higher than those of the control group. In many studies in literature, while measuring the anxiety scores of patients with OSAS, patients are divided into groups according to AHI. Thus, individuals with AHI<5 on PSG were put in a control group and compared with OSAS patients in terms of anxiety scores, and it was shown that there were no significant differences. However, in our study, the anxiety scores of those who applied to the sleep clinic because of their symptoms, who were suspected of having OSAS, and who were in the normal category according to AHI, were found to have higher scores than the control group.

In other studies[31] measuring the anxiety level in OSAS patients, the correlation between the anxiety level and the AHI of the OSAS patients was examined. In our study, in addition to AHI, ODI, and CT90, which are not routinely expressed in PSG reports in many places, were also examined. In addition, the lowest oxygen saturation, average oxygen saturation, time under 90% of saturation, 3% SpO_2 decline, and 4% SpO_2 decline numbers were recorded in PSGs. In statistical analyses performed with all these parameters, a weak positive significant correlation was found between the mean BAI score and the CT90.

According to our study, the CT90 value may more practically reflect hypoxemia and intermittent hypoxia, which play an important role in the pathophysiology of OSAS. The CT90 value can be used as a more practical measure compared to AHI in the evaluation of anxiety in OSAS. The advantage of the CT90 value is that it can be measured with overnight pulse oximetry along with in-laboratory PSG and HSAT (Home Sleep Apnea Test). In this context, the possibility that people who are in the normal category, according to AHI, and have a high CT90 parameter are affected by hypoxia should be evaluated, and more comprehensive treatment may be required. Research is needed to determine whether CT90 can be used in the diagnosis algorithm, treatment, and follow-up.

Conflict of Interest
The Authors declare that they have no conflict of interests.

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Authors' Contributions
Study conception and design: E. Alkilinc and A. H. Ilgazli. Data collection and input: E. Alkilinc, A.H. Ilgazli, H. Boyaci, I. Basyigit, S. Argun Baris, S. Ozgun. Analysis and interpretation of the results: E. Alkilinc, A.H. Ilgazli, H. Boyaci, I. Basyigit, S. Argun Baris, S. Ozgun. Draft manuscript and preparation: E. Alkilinc and A.H. Ilgazli. All authors gave their final approval and agreed to be accountable for all aspects of the work.

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Ethics Approval
The study was approved by the Kocaeli University Ethical Committee of Clinical Research (2019/294). All procedures performed in the study were by the 1964 Helsinki Declaration and its later amendments.

Informed Consent
Written informed consent was obtained from all patients.

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