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The effect of continuous positive airway pressure treatment on the systemic immune-inflammation index in obstructive sleep apnea syndrome

Obstrüktif uyku apne sendromunda sürekli pozitif hava yolu basıncı tedavisinin sistemik immün-inflamasyon indeksi üzerine etkisi

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ABSTRACT

Objectives: This study aims to investigate the effect of continuous positive airway pressure (CPAP) treatment on the systemic immune-inflammation index (SII) in patients with obstructive sleep apnea syndrome (OSAS).

Patients and Methods: In this retrospective cohort study, records of 197 OSAS patients (132 males, 65 females; median age: 55 years; range, 26 to 85 years) who underwent polysomnography and hemogram testing and were recommended CPAP therapy between January 2020 and April 2022 were analyzed. Forty-nine healthy volunteers (32 males, 17 females; median age: 31 years; range, 18 to 64 years) without OSAS-related complaints were included as controls. Hemogram-derived neutrophil, lymphocyte, and platelet counts were used to calculate neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and SII. These indices were compared between groups, and pre- and posttreatment values in OSAS patients. Correlations between CPAP duration and inflammatory indices were also examined.

Results: The moderate OSAS group (n=45) showed a nonsignificant decrease in SII after CPAP (p=0.173), whereas the severe OSAS group (n=152) demonstrated a significant increase (p=0.041). Duration of CPAP use was positively correlated with changes in platelet-to-lymphocyte ratio (r=0.151, p=0.034) and SII (r=0.157, p=0.028).

Conclusion: Treatment with CPAP was associated with a nonsignificant reduction in systemic inflammation in moderate OSAS but paradoxically increased SII in severe OSAS. These findings suggest that CPAP alone may be insufficient to normalize systemic inflammation in advanced OSAS, and additional interventions such as weight loss or adjunctive therapies may be required.

Keywords: Continuous positive airway pressure, hemogram, obstructive sleep apnea syndrome, systemic immune inflammation index.

ÖZ

Amaç: Bu çalışmada, obstrüktif uyku apne sendromu (OUAS) olan hastalarda sürekli pozitif hava yolu basıncı (CPAP) tedavisinin sistemik immün-inflamasyon indeksi (Sİİ) üzerine etkisini araştırıldı.

Hastalar ve Yöntemler: Bu retrospektif kohort çalışmada, Ocak 2020 - Nisan 2022 tarihleri arasında polisomnografi ve hemogram testi yapılan ve CPAP tedavisi önerilen 197 OUAS hastasının (132 erkek, 65 kadın; medyan yaş: 55 yıl; dağılım, 26-85 yıl) kayıtları incelendi. Obstrüktif uyku apne sendromu ile ilişkili şikayetleri olmayan 49 sağlıklı gönüllü (32 erkek, 17 kadın; medyan yaş: 31 yıl; dağılım, 18-64 yıl) kontrol olarak çalışmaya dahil edildi. Hemogramdan elde edilen nötrofil, lenfosit ve trombosit sayıları kullanılarak nötrofil-lenfosit oranı, trombosit-lenfosit oranı ve Sİİ hesaplandı. Bu indeksler gruplar arasında karşılaştırıldı ve OUAS hastalarında tedavi öncesi ve sonrası değerler analiz edildi. Ayrıca CPAP süresi ile inflamasyon indeksleri arasındaki korelasyonlar da incelendi.

Bulgular: Orta şiddette OUAS grubunda (n=45) CPAP sonrası SII'de anlamlı olmayan bir azalma görüldü (p=0.173), buna karşın şiddetli OUAS grubunda (n=152) anlamlı bir artış görüldü (p=0.041). Sürekli pozitif hava yolu basıncı kullanım süresi trombosit-lenfosit oranındaki (r=0.151, p=0.034) ve Sİİ'deki (r=0.157, p=0.028) değişikliklerle pozitif korelasyon gösterdi.

Sonuç: Sürekli pozitif hava yolu basıncı tedavisi, orta şiddette OUAS'ta sistemik inflamasyonda anlamlı olmayan bir azalma ile ilişkilendirilirken, şiddetli OUAS'ta paradoksal olarak Sİİ'yi artırdı. Bu bulgular, ileri OUAS'ta sistemik inflamasyonu normalleştirmek için CPAP'ın tek başına yeterli olmayabileceğini ve kilo verme veya yardımcı tedaviler gibi ek müdahalelerin gerekebileceğini düşündürmektedir.

Anahtar sözcükler: Sürekli pozitif hava yolu basıncı, hemogram, obstrüktif uyku apnesi sendromu, sistemik immün enflamasyon indeksi.

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Obstructive sleep apnea syndrome (OSAS) is a condition in which recurrent apnea or hypopnea episodes during sleep cause temporary decreases in the oxygen level. The global prevalence of OSAS is extremely high, ranging from 9 to 38%.[1,2] Intermittent attacks of hypoxia and reoxygenation observed in OSAS can activate the expression of proinflammatory cytokines. Consequently, OSAS causes a status of chronic low-level inflammation.[3,4]

Continuous positive airway pressure (CPAP) treatment is the method for the first step of treatment for OSAS. Compared to other nonsurgical treatments for OSAS, CPAP has shown the greatest improvement in quality of life measurements and the apnea-hypopnea index (AHI).[5] Treatment with CPAP has a positive effect on oxygen desaturation and reduces chronic inflammation by improving symptoms such as snoring and excessive daytime sleepiness.[6,7]

In recent years, the systemic immune-inflammation index (SII), the neutrophil-lymphocyte ratio (NLR), and the platelet-to-lymphocyte ratio (PLR), which can be obtained from neutrophil, platelet, and lymphocyte counts, have been used as inflammatory biomarkers for many diseases. The SII has been determined to be associated with a worse prognosis in solid tumors, pulmonary emboli, and cardiovascular diseases.[8,9]

In a meta-analysis of OSAS patients, small decreases were observed in some inflammation biomarkers (C-reactive protein, interleukin [IL]-6, IL-8, and tumor necrosis factor-alpha) following CPAP.[4] Moreover, the use of CPAP has been determined to cause a significant decrease in the NLR.[10] It has also been determined that CPAP treatment causes a decrease in platelet activation in OSAS.[11] However, the effect of CPAP treatment on the SII is unknown.

Therefore, this study aimed to investigate the effect on the SII of CPAP used in the treatment of patients diagnosed with OSAS.

PATIENTS AND METHODS

The retrospective study was conducted with 197 patients (132 males, 65 females; median age: 55 years; range, 26 to 85 years) who presented to the Neurology or Ear, Nose, and Throat Clinics of the Kütahya Health Sciences University Evliya Çelebi Training and Research Hospital with complaints of sleep apnea/snoring between January 2020 and April 2022. All patients underwent polysomnography (PSG). A record was made of the PSG findings (Apnea-Hypopnea Index [AHI] score and mean oxygen saturation), body mass index, hemogram results, and the use and duration of CPAP. The control group consisted of 49 healthy volunteers (32 males, 17 females; median age: 31 years; range, 18 to 64 years) who were referred to our clinic and had no complaints related to OSAS, such as excessive daytime sleepiness, snoring, and nasal obstruction. The exclusion criteria were a history of hematological disease, chronic inflammatory disease such as systemic lupus erythematosus, the presence of infection, previous treatment for sleep apnea, or alcohol dependence. Patients were also excluded from the study if they were diagnosed with central sleep apnea, narcolepsy, upper airway resistance syndrome, or movement disorders using PSG, if they were using drugs that could affect platelet functions such as aspirin, clopidogrel, dipyridamole, heparin, aminophylline, verapamil, steroids, or furosemide, if they had any pulmonary disease that could cause hypoxemia such as asthma, chronic obstructive lung disease, or interstitial lung disease, if they did not undergo either PSG or complete blood count, or if they were recommended to use CPAP but did not use it regularly. Continuous positive airway pressure adherence was defined as use for more than 4 h in at least 70% of the last 30 consecutive nights.[12] Written informed consent was obtained from all participants. The study protocol was approved by the Clinical Research Ethics Committee of Kütahya Health Sciences University Ethics Committee (Date 25.05.2022, No: 2022/06-36). The study was conducted in accordance with the principles of the Declaration of Helsinki.

The PSG recordings were performed in the sleep laboratory under the supervision of a sleep technician using a PSG device with at least 16 channels. The PSG device had the features of six electroencephalography (F4-M1, C4-M1, O2-M1, F3-M2, C3-M2, and O2-M2), two electrooculography, three mentalis/submentalis electromyography, oximeter, snoring signal, body position sensor, nasal pressure/flow signal (thermistor and nasal cannula), respiratory effort (thorax-abdomen bands), two electromyography (tibialis anterior), and electrocardiography recordings.

Apnea is defined as the termination of airflow from the mouth and nose of 10 sec or more.[1] Hypopnea is a reduction of 30% or more in airflow for longer than 10 sec and desaturation or waking accompanying a decrease in respiratory depth. The AHI is calculated as the mean number of apnea or hypopnea episodes per hour determined during sleep.

The PSG results of all the patients were evaluated by the same researcher according to the American Sleep Academy scoring rules. According to the PSG results, the patients were separated into four groups based on the AHI score: simple snoring/normal (AHI <5), mild (AHI 5-15), moderate (AHI 16-30), and severe (AHI >30).[13]

This study enrolled patients with moderate (AHI 16-30) and severe (AHI >30) obstructive sleep apnea syndrome (OSAS) who had been using continuous positive airway pressure (CPAP) therapy for at least one month. Eligible patients were those able to tolerate CPAP and expected to adhere to the treatment. Exclusion criteria included cranial malformations or any condition preventing CPAP use, malignancy with intolerance to CPAP, ineffectiveness of CPAP therapy, or anticipated insufficient adherence due to distance or lack of patient confidence. Adherence to CPAP treatment was defined as usage for more than 4 h on at least 70% of nights over the most recent consecutive month.[12] Titration throughout the night for AHI to be ≤10 was accepted as good titration according to the American Academy of Sleep Medicine Positive Airway Pressure Titration Task Force.[14]

On the day before the PSG test and after at least one month of CPAP use, evaluations were made with venous blood samples taken from the patients after 8 to 12 h of overnight fasting. In the control group, venous blood samples were taken after 8 to 12 h of overnight fasting. The patients' blood was taken to investigate infection findings. The patients with active infection were not included in the study.

The blood samples were withdrawn into tubes containing ethylenediaminetetraacetic acid (EDTA) and were analyzed in the Kütahya Sağlık Bilimleri Üniversitesi Medical Faculty Biochemistry Department using an LH780 Beckman Coulter automated blood count device (Beckman Coulter Ireland Inc,. Mervue, Galway, Ireland).

In the hemogram analyses, the NLR was defined as the simple ratio between absolute neutrophil count and absolute lymphocyte count. The PLR was defined as the simple ratio between absolute platelet count and absolute lymphocyte count. The SII was calculated by multiplying the neutrophil count (μL) by the platelet count (μL) and dividing by the lymphocyte count (μL).

Statistical analyses

Data obtained in the study were analyzed with IBM SPSS version 23.0 software (IBM Corp., Armonk, NY, USA). The Shapiro-Wilk test and the Kolmogorov-Smirnov test were used to assess the conformity of the data to normal distribution. Independent samples t-test was used to compare the data conforming to normal distribution in paired groups. The Mann-Whitney U test was used to compare the data that did not conform the normal distribution in paired groups. Pearson's chi-square test was used to examine the relationship between categorical data. Paired samples t-test was used for the comparison of data conforming to normal distribution in paired groups, and the Wilcoxon signed-rank test was used for the comparison of data not conforming to normal distribution. The Kruskal-Wallis H test was used to analyze nonnormally distributed data in groups of three or more. One-way analysis of variance was used to analyze normally distributed data in three or more groups. The relationship between quantitative data that were nonnormally distributed was analyzed with Spearman's rho correlation coefficient (r). In the evaluation of r, a value of 0-0.25 was accepted as very weak, 0.26-0.49 as weak, 0.50-0.69 as moderate, 0.70-0.89 as strong, and 0.90-1.00 as a very strong correlation.[15] Analysis results were presented as mean ± standard deviation (SD) and median (min-max) for quantitative data. Frequency and percentage were used to represent categorical data. A value of $p<0.05$ was accepted as statistically significant.

RESULTS

The distribution of sex was similar between the groups ($p=0.895$). The median age was comparable between the OSAS groups, whereas the median age of the control group was significantly lower (31 years; range, 18 to 64 years; $p<0.001$; Table 1). Among patients included in the study, CPAP adherence was 52.8%. This rate falls within the range reported in previous studies (30 to 60%), underscoring the persistent challenge of ensuring long-term treatment compliance in clinical practice.[12,16]

For the whole patient group, the median AHI score was 44.65 (range, 15.1 to 132), and the median oxygen saturation was 92 (range, 65 to 96). The patients were separated into four groups according to the AHI scores determined in the American Sleep Academy scores.[13] The study included a moderate OSAS group (AHI 15-30) and severe OSAS group (AHI >30). The median AHI score was 21.8 (range, 15.1 to 29.7) in the moderate OSAS group and 54.05 (range, 30.1 to 132) in the severe OSAS group. The demographic data of the participants in the study are shown in Table 1.

Table 1
The demographic data of the participants in the study

	Moderate OSAS (AHI: 15-30) (n=45)				Severe OSAS (AHI: >30) (n=152)				Control group (n=49)				
	n	%	Median	Min-Max	n	%	Median	Min-Max	n	%	Median	Min-Max	*p*
AHI			21.80	15.1-29.7			54.05	30.1-132			-	-	**<0.001†**
BMI (kg/m^2)			29.60	21.9-45.7			32.70	21.3-51.9			-	-	**0.001†**
REM AHI			29	0-120			52.10	0-120			-	-	**<0.001†**
Arousal index (h)			13.80	0-84.7			19.40	1.3-117.4			-	-	**0.005†**
Mean O_2 saturation (%)			92.9	87-96			91.45	65-95			-	-	**0.012†**
Mean CPAP use (mo)			14	1-72			17	1-108			-	-	0.852†
Sex													0.895‡
Male	29	64.4			103	67.8			32	65.3			
Female	16	35.6			49	32.2			17	34.7			
Age (year)			55	26-79*			54	28-85[a]			31	18-64[b]	**<0.001***

OSAS: Obstructive sleep apnea syndrome; AHI: Apnea-Hypopnea Index; BMI: Body mass index; REM: Rapid eye movement; CPAP: Continuous positive airway pressure; † Mann Whitney U test; ‡ Pearson Chi-Square test; * Kruskal Wallis H test; [a,b] There is no difference between groups with the same letter.

The median AHI, body mass index, rapid eye movement AHI, and Arousal index values of the moderate and severe OSAS groups statistically significant increased as the severity of OSAS increased (p<0.001, p=0.001, p<0.001, p=0.005, respectively). The median saturation value significantly decreased as the severity of OSAS increased (p=0.012). The median duration of CPAP use was similar in the moderate and severe OSAS groups (p=0.852; Table 1).

In the moderate and severe OSAS group, NLR, PLR, and SII values at pretreatment were similar to the control group (0.334, 0.431, and 0.626, respectively). In the moderate and severe OSAS group, NLR, PLR, and SII values at posttreatment were similar to the control group (0.235, 0.640, and 0.665, respectively; Table 2).

In the moderate OSAS group (AHI 15-30), a statistically significant difference was not determined in the mean NLR, PLR, and SII values from before CPAP treatment to posttreatment (p=0.424, p=0.2, and p=0.173 respectively; Table 3).

In the severe OSAS group, a statistically significant was determined in the NLR, PLR, and SII values from before CPAP treatment to posttreatment (p=0.005, p=0.008, and p=0.041 respectively). A statistically significant decrease was observed in lymphocyte values (p=0.009; Table 4).

Spearman's correlation was performed to further define the relationships between changes in neutrophil, lymphocyte, platelet, NLR, PLR, SII parameters and duration of CPAP use. As shown in Table 5, changes in PLR (r=0.151, p=0.034) and SII (r=0.157, p=0.028) were significantly positively correlated with the duration of CPAP use.

DISCUSSION

In this study, CPAP treatment led to a nonsignificant decrease in SII among patients with moderate OSAS. However, unexpectedly, a significant increase in SII was observed in the severe OSAS group. To our knowledge, this is the first study to evaluate the effect of CPAP therapy on SII in OSAS patients.

Several factors may explain these divergent outcomes. First, obesity and metabolic syndrome, which were more prevalent in the severe OSAS group, are well-known drivers of systemic inflammation and may counteract the anti-inflammatory effects of CPAP. Second, CPAP therapy effectively reduces hypoxia and improves sleep quality, but it may not fully reverse underlying inflammatory dysregulation

Table 2
Neutrophils, lymphocytes, platelets, NLR, PLR, SII values of the control group and the patient group before and after treatment

	Moderate OSAS (AHI: 15-30) (n=45)			Severe OSAS (AHI: >30) (n=152)			Control group (n=49)				
	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	Test statistic	*p*
Pretreatment											
Neutrophils		4.18	2.09-7.49		4.18	1.8-9.3		4.06	2.13-8.7	0.152	0.927†
Lymphocytes		2.29	1.24-4.34		2.49	0.98-5.05		2.32	1.37-4.91	4.888	0.087†
Platelets	244.9±52.3		156-369	256±60.7		127-437	261.2±50.7		149-382	1.170	0.312‡
NLR		1.72	0.86-3.52		1.67	0.62-4.88		1.67	0.67-3.47	2.196	0.334†
PLR		107.58	60.62-214.53		104.8	52.86-204.47		106.11	51.12-207.85	1.685	0.431†
SII		473.50	164.05-977.46		405.47	161.41-1553.87		459	141.68- 1073.22	0.937	0.626†
Posttreatment											
Neutrophils		4.18	2.18-8.63		4.33	1.9-6.26		4.06	2.13-8.7	0.671	0.715†
Lymphocytes		2.26	0.77-4.27		2.39	0.82-4.97		2.32	1.37-4.91	1.941	0.379†
Platelets		243	145-473		251	122-480		254	149-382	1.064	0.588†
NLR		1.94	0.97-5.52		1.84	0.82-5.05		1.67	0.67-3.47	2.895	0.235†
PLR		111.15	58.78-285.34		105.77	51.90-256.52		106.11	51.12-207.85	0.893	0.640†
SII		454.10	176.72-1360.18		451.33	152.57-1482.69		459	141.68- 1073.22	0.815	0.665†

NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SII: Systemic immune-inflammation index; OSAS: Obstructive sleep apnea syndrome; AHI: Apnea-Hypopnea Index; SD: Standard deviation; † Kruskall Wallis H test; ‡ One-way analysis of variance.

Table 3
The NLR, PLR, and SII values before and after treatment in the moderate OSAS group

	Pretreatment moderate OSAS (AHI: 15-30) (n=45)			Posttreatment moderate OSAS (AHI: 15-30) (n=45)			
	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	*p*
Neutrophil	4.21±1.23			4.34±1.22			0.568†
Lymphocyte	2.29±0.66			2.25±0.7			0.884†
Platelets		246.5	156-369		254.5	145-473	0.054‡
NLR		1.72	0.86-3.52		1.94	0.97-5.52	0.424‡
PLR		107.58	60.62-214.53		111.15	58.78-285.34	0.200‡
SII		473.50	164.05-977.46		454.10	176.72-1360.18	0.173‡

NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SII: Systemic immune-inflammation index; OSAS: Obstructive sleep apnea syndrome; AHI: Apnea-Hypopnea Index; SD: Standard deviation; † Paired student t test; ‡ Wilcoxon signed ranks test.

Table 4
The NLR, PLR, and SII values before and after treatment in the severe OSAS group

	Pretreatment severe OSAS (AHI: >30) (n=152)			Posttreatment severe OSAS (AHI: >30) (n=152)			
	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	*p*
Neutrophil	4.33±1.22			4.32±1.02			0.711†
Lymphocyte	2.53±0.72			2.42±0.71			**0.009†**
Platelets	256±60.71			253.81±58.54			0.506†
NLR		1.67	0.62-4.88		1.84	0.82-5.05	**0.005‡**
PLR		104.8	52.86-204.47		105.77	51.90- 256.52	**0.008‡**
SII		405.47	161.41-1553.87		451.33	152.57-1482.69	**0.041‡**

NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SII: Systemic immune-inflammation index; OSAS: Obstructive sleep apnea syndrome; AHI: Apnea-Hypopnea Index; SD: Standard deviation; † Paired student t test; ‡ Wilcoxon signed ranks test.

Table 5
Correlation analysis between duration of CPAP use and neutrophils, lymphocytes, platelets, NLR, PLR, and SII

	Spearman correlation coefficient (r)	*p*
Neutrophil changed of the data pre- and posttreatment	0.082†	0.251
Lymphocyte changed of the data pre- and posttreatment	–0.082†	0.251
Platelet changed of the data pre- and posttreatment	0.120†	0.095
NLR changed of the data pre- and posttreatment	0.093†	0.193
PLR changed of the data pre- and posttreatment	0.151†	**0.034**
SII changed of the data pre- and posttreatment	0.157†	**0.028**

CPAP: Continuous positive airway pressure; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SII: Systemic immune-inflammation index; † Spearman's rho correlation.

in patients with long-standing or severe disease. Third, adherence to CPAP was moderate (52.8%), which may have further limited the therapeutic effect.

Our findings differ from prior studies reporting reductions in NLR or C-reactive protein following CPAP, suggesting that SII may capture a broader inflammatory burden not fully addressed by CPAP. These results indicate that CPAP, while essential for controlling apneic events, may be insufficient to normalize systemic immune activation in severe OSAS. Consequently, combined treatment approaches, including lifestyle modification, weight

loss, or surgical options, should be considered in selected patients.

Treatment with CPAP caused a nonsignificant decrease in the SII of the moderate OSAS group (AHI 15-30, n=45; p=0.173), while the increase in SII in the severe OSAS group (AHI >30, n=152) was determined to be statistically significant (p=0.041). To the best of our knowledge, this is the first study in the literature to have examined the effect on SII of CPAP treatment in OSAS. Furthermore, duration of CPAP use was associated with changes in PLR (r=0.151, p=0.034) and SII (r=0.157, p=0.028).

The two most important factors in the pathophysiology of OSAS and associated comorbidities are chronic systemic inflammation and oxidative stress. Increased neutrophils and decreased lymphocytes have been shown in chronic systemic inflammation.[17,18] Chronic intermittent hypoxia increases sympathetic activity and causes an increase in the number of lymphocytes.[19,20] Apnea and hypoxia have been reported to cause systemic inflammation in OSAS in previous studies.[21] The SII, which can be easily obtained from neutrophil, platelet, and lymphocyte counts, has recently been determined to be an inflammatory marker associated with a poor prognosis in solid tumors, pulmonary emboli, and cardiovascular diseases.[8,9] There has been increasing interest in the relationship between SII and OSAS. In a study of 8505 patients, Kadier et al.[22] showed a positive relationship between patients with OSAS symptoms and a high SII value (beta=23,088, 95% confidence interval 0.441-45.735). Topuz et al.[23] also found a positive correlation between SII and OSAS severity in a retrospective study. These results were supported by Kim et al.,[24] who showed a significant relationship between SII and the AHI score in a severe OSAS group. This was not consistent with the results of our study (Table 2). Moreover, this result was similar to the results of Gölen et al.[25] However, there are no data related to the effect on SII of CPAP treatment in OSAS patients. This relationship was investigated in the current study, and while CPAP treatment did not cause a significant decrease in SII in moderate OSAS patients (p=0.173; Table 3), a statistically significant increase was observed after CPAP treatment in severe OSAS patients (p=0.041; Table 4). These findings represent the first evidence on the effect of CPAP treatment on the SII. The reasons for the different trends in SII among the subgroups are not clear but may be due to the effect of obesity on chronic inflammation, as the body mass index was relatively high (32.70 kg/m^2) in the severe OSAS group. In addition, the increase in SII in the severe OSAS group may be due to the dominant effects of other risk factors (metabolic syndrome) on systemic inflammation. Therefore, CPAP therapy may need to be combined with additional treatments (weight loss and surgery), particularly in the severe OSAS group. However, further studies are needed to clarify this point.

Recent studies have suggested that NLR used as a marker of general inflammation could be a more effective measurement reflecting the stress burden than the leukocyte parameter alone.[26,27] In a meta-analysis, there was observed to be a significant tendency for NLR to gradually increase from mild OSAS to severe OSAS (weighted mean difference =0.90, 95% confidence interval 0.04-1.76, p=0.04).[17] However, in our study, no significant difference was observed in the moderate and severe group compared to the control group (Table 2). Oyama et al.[10] showed a significant decrease in the NLR value following three months of CPAP treatment. However, in a study of 36 patients with OSAS, Ulusoy et al.[27] reported that no significant difference was observed in the NLR value from before to after treatment after at least one month of CPAP treatment (p=0.844). In our study, the NLR value did not significantly change in the moderate group, while the NLR value increased statistically significantly in the severe group OSAS (Tables 3, 4). The reason for this difference may be the high rate of comorbidity among the patients included in the studies, as comorbidity can trigger chronic inflammation. Consequently, the effect of CPAP treatment on NLR is not consistent; therefore, there is a need for further studies to be able to better understand this difference.

The platelet count, which is a key factor in tissue repair, increases during inflammatory response.[28] A high platelet-lymphocyte complex level in circulation may be a sign of platelet activation, and therefore, the PLR is valuable in OSAS patients.[29] Increased platelet activation plays a significant role in the onset and progression of atherosclerosis.[30] This was proven in an animal study by Gautier-Veyret et al.,[30] in which an increase was shown in atherosclerotic plaque in rats exposed to intermittent hypoxia. In a recent study by Koseoglu et al.,[31] a significant correlation was reported between the AHI score of OSAS patients and the severity of hypoxia and the PLR. However, Dikbaş et al.[32] reported that the PLR was lower in OSAS patients than in a healthy control group, and therefore, a significant relationship between OSAS and PLR remains debatable. In a meta-analysis by Wu et al.,[17] OSAS was determined to be associated with a higher PLR value, and there

was shown to be a tendency for a gradual increase from mild to severe in the OSAS group. However, no significant relationship was observed between the control groups and OSAS subgroups in terms of PLR values in our study (Table 2). Nevertheless, there are very few data on the effect on PLR of CPAP treatment in OSAS patients. In another study, it was determined that PAP treatment did not lead to any statistically significant differences in the mean PLR values of moderate and severe OSAS groups (p=0.643).[33] In our study, a significant increase in the PLR value was observed in the severe OSAS group (pretreatment: 104.8 (52.86-204.47); posttreatment: 105.77 (51.90-256.52); p=0.008; Table 4). These results highlight the inconsistency of PLR values. However, it was reported that surgery in the severe OSAS group led to a significant decrease in the PLR value (preoperative: 118.3±38.9; postoperative: 108.7±34.0; p<0.001).[34] In the severe OSAS group, additional treatments to CPAP therapy should be given to the patient as an option.

The results of the present study revealed a significant positive association between PLR, SII, and the duration of CPAP use (Table 5). Continuous positive airway pressure is considered the first-line treatment for OSAS. It has been hypothesized that CPAP may reduce inflammatory markers and improve vascular load in OSAS patients. However, in this study, inflammatory markers showed a different trend with CPAP use. Randomized controlled trials are needed to determine the reasons.

There were some limitations to this study. First, this was a retrospective study with inherent selection bias. Second, systemic inflammation status of an individual may have been affected by many variables that could not be controlled. A third limitation was that patients in the moderate and severe OSAS groups were not homogeneous. Importantly, the control group did not undergo PSG, so undiagnosed OSAS could not be fully excluded. Furthermore, the control group was significantly younger than the patient group, which may have influenced inflammatory indices. These limitations should be considered when interpreting the results. Future randomized controlled studies with age- and PSG-matched controls are warranted to confirm our findings.

In conclusion, CPAP treatment was associated with a nonsignificant reduction in inflammation in moderate OSAS, but paradoxically increased SII in severe OSAS, suggesting that additional treatments such as weight loss or adjunctive therapies may be necessary.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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