RESEARCH ARTICLE

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Mean Platelet Volume (MPV) in Obstructive Sleep Apnea (OSA) and Effect of Continuous Positive Airway Pressure (CPAP) Treatment on MPV in OSA

ABSTRACT

Objective: In this study, our objective was to evaluate mean platelet volume (MPV), an indirect marker of platelet activation, in patients with obstructive sleep apnea (OSA), and assess the effect of OSA treatment with continuous positive airway pressure (CPAP) on MPV.

Materials and Methods: In this study, records of consecutive patients who underwent polysomnographic evaluation for OSA symptoms in the Sleep Disorders Laboratory during a one-year period were reviewed retrospectively. Patients who had both complete blood count and MPV measurements were included in the study.

Results: A total of 158 patients, including 51 females (32.3%) and 107 males (67.7%), were included in the study. The mean age of the patients was 51±13 (min-18, max-82) years. OSA was detected in 74.1% (117/158) of the patients. It was determined that as the severity of OSA increased, hemoglobin and hematocrit values increased significantly. There was no significant difference in platelet count according to the presence and severity of OSA. The MPV was significantly lower in severe OSA cases compared to those without OSA and mild OSA cases. A negative correlation was observed between MPV and the apnea-hypopnea index, desaturation index, and the amount of oxygen saturation below 90% during sleep. There was no significant difference in median erythrocyte and thrombocyte counts, hematocrit percentage and hemoglobin values before and after treatment in OSA patients who used CPAP therapy. However, a significant decrease in MPV was observed after OSA treatment compared to pre-treatment. (p=0.021).

Conclusions: The results of the study do not support an increase in MPV and hence platelet activation in severe OSA patients compared with those without OSA. However, the results suggest that one month of CPAP treatment reduces MPV and thus platelet activation in severe OSA patients. Further controlled, prospective studies including treatment outcomes are needed on this subject.

Keywords: Sleep Apnea, Mean Platelet Volume, Obstructive Sleep Apnea, Platelets.

Obstrüktif Uyku Apnede (OUA) Ortalama Trombosit Hacmi (OTH) ve OUA'da Sürekli Pozitif Hava Yolu Basıncı (CPAP) Tedavisinin OTH Üzerine Etkisi

ÖZET

Amaç: Bu çalışmada amacımız, obstrüktif uyku apnesi (OUA) olan hastalarda trombosit aktivasyonunun dolaylı bir belirteci olan ortalama trombosit hacmini (OTH) değerlendirmek ve sürekli pozitif hava yolu basıncı (CPAP) ile OUA tedavisinin OTH üzerindeki etkisini değerlendirmektir.

Gereç ve Yöntem: Bu çalışmada, Uyku Bozuklukları Laboratuvarı'nda bir yıl boyunca OSA semptomları nedeniyle polisomnografik değerlendirme yapılan ardışık hastaların kayıtları retrospektif olarak incelendi. Çalışmaya hem tam kan sayımı hem de MPV ölçümü yapılan hastalar dahil edildi.

Bulgular: Çalışmaya 51 kadın (%32.3) ve 107 erkek (%67.7) olmak üzere toplam 158 hasta dahil edildi. Hastaların yaş ortalaması 51±13 (min-18, maks-82) yıldı. Hastaların %74,1'inde (117/158) OSA saptandı. OSA şiddeti arttıkça hemoglobin ve hematokrit değerlerinin anlamlı olarak arttığı belirlendi. Trombosit sayısında OSA varlığı ve şiddetine göre anlamlı bir fark yoktu. MPV, ağır OSA olgularında OSA olmayanlara ve hafif OSA olgularına kıyasla anlamlı derecede düşüktü. OTH ile apne-hipopne indeksi, desatürasyon indeksi ve uyku sırasında %90'ın altındaki oksijen satürasyonu miktarı arasında negatif bir korelasyon gözlendi. CPAP tedavisi kullanan OSA hastalarında tedavi öncesi ve sonrası medyan eritrosit ve trombosit sayıları, hematokrit yüzdesi ve hemoglobin değerlerinde anlamlı bir fark bulunmadı. Bununla birlikte, OSA tedavisi sonrasında tedavi öncesine kıyasla MPV'de anlamlı bir düşüş gözlendi. (p=0.021).

Bulgular: Çalışmaya dahil edilen 2920 hastanın 15'inde (%0,51) RSLVN saptandı. Beş hastada birden fazla RSLVN gözlendi ve dolayısıyla on beş hastada toplam 23 RSLVN tanımlandı. Nodüllerin sekizi (%34,8) lateral ventrikül tavanında, on iki tanesi (%52,2) ön boynuzda, üçü ise septum pellucidum'da yerleşmişti. 23 RSLVN'den 6'sı (%26,1) 1 cm'den büyüktü. Tüm RSLVN'ler T1W ve T2W'de izointens, FLAIR sekansında ise hiperintensti. DAG'de 23 RSLVN'den 20'sinde izointens sinyal vardı, geri kalan 3 lezyon ise hiperintens idi. Ortalama ADC değeri ve nADC oranı sırasıyla 1,42 ± 0,29 × 10-3mm2 ve 1,87 ± 0,31 idi.

Sonuç: Çalışmanın sonuçları, OSA'sı olmayanlara kıyasla ağır OSA hastalarında MPV'de ve dolayısıyla trombosit aktivasyonunda bir artışı desteklememektedir. Ancak, sonuçlar bir aylık CPAP tedavisinin ağır OUA hastalarında MPV'yi ve dolayısıyla trombosit aktivasyonunu azalttığını düşündürmektedir. Bu konuda tedavi sonuçlarını içeren daha ileri kontrollü, prospektif çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Uyku Apne, Ortalama Trombosit Hacmi, Obstruktif Uyku Apne, Trombositler.

INTRODUCTION

Obstructive sleep apnea (OSA) is a common worldwide condition, estimated to affect approximately 1 billion people globally, with a prevalence exceeding 50% in some countries (1-3).

Cardiovascular complications are the most significant issues associated with OSA (4-8). The development of cardiovascular diseases in OSA involves a multifactorial process, including fluctuations in negative intrathoracic pressure, intermittent hypoxia and hypercapnia, increased sympathetic nervous system activity, vascular endothelial dysfunction, oxidative stress, systemic inflammation, excessive platelet activation, and metabolic dysregulation (5).

Epidemiological data support the notion that OSA is an independent risk factor for cardiovascular diseases. These observations have prompted research into the role of OSA in the pathogenesis of cardiovascular diseases. Platelets play a key role in cardiovascular diseases, and increased platelet activation is suggested to be a significant contributor to the frequent cardiovascular complications in OSA patients (9). Mean platelet volume (MPV) is a parameter that reflects platelet function and activity (10). Increased MPV indicates larger platelet size (11). Larger platelets are metabolically more active and more prone to adhesion and aggregation compared to smaller platelets (10, 12). They contain more alpha granules and platelet-derived substances. The increased activity of larger platelets may be attributed to higher thromboxane A2 production compared to smaller platelets (10). Increased platelet volume is associated with indicators of platelet activation, including increased aggregation, TxA2 synthesis, serotonin levels, release of platelet factor-4 and β-thromboglobulin, and expression of adhesion molecules (13,14). MPV, measured as part of a complete blood count, can safely estimate potential platelet activity and aggregation (10, 15).

In this study, our objective was to evaluate MPV, an indirect marker of platelet activation, in OSA patients, and assess the effect of OSA treatment with continuous positive airway pressure (CPAP) on MPV.

MATERIAL AND METHODS

Study Population: In this study, we retrospectively analyzed the records of consecutive patients admitted to the Sleep Respiratory Disorders Laboratory of the Chest Diseases Clinic of Duzce University Faculty of Medicine within one year (2012) with OSA symptoms. Consecutive patients who underwent a complete polysomnography test with both complete blood count (CBC) and mean platelet volume (MPV) measurements were included in the study. The study was approved by the Non-Invasive Clinical Research Ethics Committee of Düzce University Faculty of Medicine (Decision Number: 2012/309).

Evaluation of Blood Samples: On the morning following the polysomnography, 3 mL of blood was collected for a complete blood count (CBC). The blood samples were collected in K3 EDTA tubes and measured within 2 hours using Pentra DX 120-Pentra XL 80 devices at the Microbiology-CBC Laboratory.

Sleep Study: Patients were questioned about symptoms of snoring and witnessed apnea. Daytime sleepiness was evaluated using the Epworth Sleepiness Scale. Full-night polysomnography (SomnoMedics: Model: Somnoscreen PSG, Germany) was performed on all patients in the laboratory setting. The recorded parameters included three channels of electroencephalography (EEG), two channels of electrooculography (EOG), one channels of chin electromyography (EMG), oral and nasal airflow (thermistor and nasal cannula), thoracic and abdominal movements, body position, snoring, electrocardiography (ECG), and pulse oximetry (recorded for >6 hours). All recordings were manually scored in a computerized environment. Apnea was defined as a complete cessation of airflow in the mouth and nose for 10 seconds or longer, while hypopnea was defined as a decrease of airflow by more than 30% for 10 seconds or longer, accompanied by a 3% desaturation or aurasol. Patients with an apnea-hypopnea index (AHI) ≥ 5 were considered to have OSA

Evaluation of Patients: Based on the full-night polysomnography (PSG) data, patients were classified into groups according to the apnea-hypopnea index (AHI) as follows: no OSA (AHI < 5), mild OSA (AHI 5-15), moderate OSA (AHI 16-30), and severe OSA (AHI > 30). The groups were compared in terms of demographic and clinical characteristics, polysomnographic data, hemogram parameters, and MPV. Additionally, the changes in MPV were investigated in severe OSA patients who received regular CPAP treatment for one month and underwent hemogram follow-up (20 cases) to demonstrate the effect of OSA treatment on MPV.

Statistical Analysis: Demographic, clinical, and hemogram characteristics of patients were compared with the polysomnographic results using SPSS 21 software package. The chi-square test was used for the comparison of categorical data among the groups determined by polysomnography, while the Kruskal-Wallis test was used for the comparison of numerical data. Pairwise comparisons were performed using the Mann-Whitney U test with Bonferroni correction. Correlation analyses were conducted using Spearman's test. Comparisons before and after CPAP treatment in severe OSA patients were performed using the Wilcoxon test. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 158 patients, including 51 females (32.3%) and 107 males (67.7%), were included in the study. The mean age of the patients was 51±13 (min-18, max-82) years. OSA was detected in 74.1% (117/158) of the patients (Figure 1). The comparison of some clinical characteristics according to the presence and severity of OSA is summarized in Table 1 and 2. Aspirin use was higher in moderate and severe OSA cases. The percentage of OSA symptoms such as snoring, habitual snoring, and witnessed apnea increased significantly with the severity of OSA.

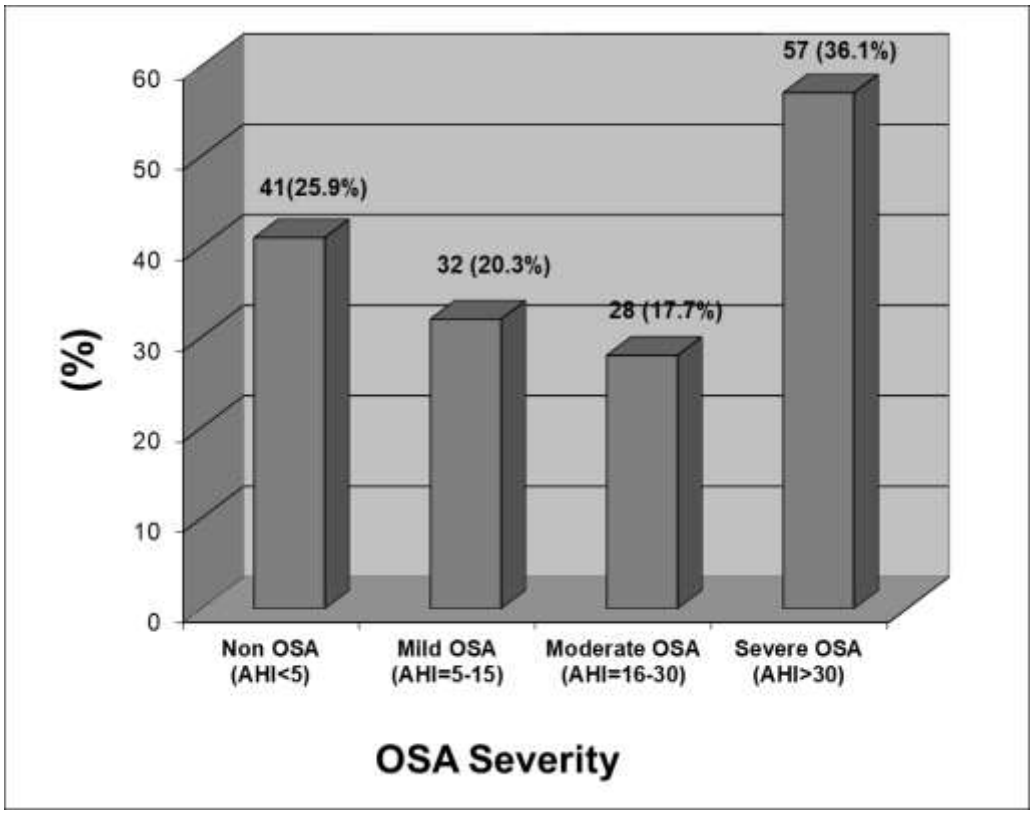

Figure 1. Polysomnographic results of the cases included in the study

Table 1. The comparison of some clinical characteristics (gender, smoking, alcohol use, diabetes mellitus, hypercholesterolemia, drugs used and OSA symptoms) according to the presence and severity of OSA

	N	Non OSA AHİ < 5	mild OSA AHİ=5-15	moderate OSA AHİ=16-30	Severe OSAS AHİ > 30	*p*
Gender *(Male/Female)*	158	22/19	24/8	20/8	41/16	*0.163*
Smoking						
Yes / quit / no	135	14/1/24	13/7/11	13/1/13	20/2/16	-
Alcohol use *n (%)*	134	4 (10.5%)	5(16.1%)	3(11.1%)	4(10.5%)	*0.878*
Diabetes Mellitus *n (%)*	133	6 (15.4%)	8(25.0%)	3(11.5%)	4(11.1%)	*0.393*
Hypercholesterolemia *n (%)*	130	6 (15.4%)	5(16.7%)	10(38.5%)	11(31.4%)	*0.095*
Drugs Used						
ACE inhibitor *n (%)*	120	3 (8.3%)	3 (10.7%)	6 (24.0%)	7 (22.6%)	*0.223*
Beta blocker *n (%)*	119	2 (5.7%)	1 (3.6%)	1 (4.0%)	4 (12.9%)	*0.443*
Ca channel blocker *n (%)*	119	1 (2.8%)	- (-)	1 (4.2%)	3 (9.7%)	*0.293*
Diuretic *n (%)*	120	1 (2.8%)	3 (10.7%)	6 (24.0%)	5 (16.1%)	*0.086*
Antiaggregant *n (%)*	120	1 (2.8%)	1 (3.6%)	6 (24.0%)	6 (19.4%)	-*
OSA Symptoms						
Habitual snoring *n (%)*	135	29 (72.5%)	23 (74.2%)	24 (92.3%)	36 (94.7%)	***0.018***
Witnessed apnea *n (%)*	132	20 (52.6%)	23 (76.7%)	20 (76.9%)	31(81.6%)	***0.026***

Ca: calcium; ACE: angiotensin converting enzyme; *p value was not shown due to expected value issue in Chi square test.

Table 2. Comparison of age, BMI, hemogram and some polysomnographic findings according to OSA severity

	Median (min-max)				*p*
	Non OSA (AHI < 5) N=41	**mild OSA (AHI=5-15) N=32**	**moderate OSA (AHI=16-30) N=28**	**Severe OSA (AHI > 30) N=57**	
Age *(years)*	47 (18-81)	53 (23-70)	53 (32-80)	52 (29-82)	*0.278*
BMI *(kg/m²)*	28.7 (19.7-47.5)	29.6 (22.2-62.2)	32.8 (25.0-50.3)	36.0 (25.4-71.2)	***<0.001***
Neck circumference *(cm)*	40 (24-48)	41 (37-45)	40 (37-46)	44 (36-51)	***0.005***
Epworth sleepiness scale	8 (0-22)	7 (0-22)	10 (1-24)	13 (1-24)	***0.014***
Polysomnographic findings					
Sleep efficiency *(%)*	87 (42-95)	88 (28-99)	90 (69-96)	89 (32-97)	*0.304*
Sleeping snoring *(%)*	22 (0 -70)	42 (0-87)	44 (2-88)	37 (2-81)	***0.007***
Sleep desaturation *(<%90 %)*	0 (0-84)	1 (0-14)	8 (3-67)	30 (0-99)	***<0.001***
Desaturation index *(hourly)*	1 (0-22)	7 (0-18)	20 (9-44)	55 (5-108)	***<0.001***
Complete blood count					
Hematocrit *(%)*	40.4 (28.6-46.3)	42.1 (27.6-53.6)	42.6 (36.8-51.9)	43.8 (32.1-54.4)	***0.001***
Hemoglobin *(g/dl)*	13.3 (9.1-16.8)	13.8 (8.2-17.9)	14.4 (12.5-17.0)	14.3 (9.9-17.1)	***0.024***
Platelets *(mm3'de bin)*	223 (102-344)	244 (150-423)	254 (99-354)	253 (117-524)	*0.283*
Mean platelet volume *(fL)*	10.30 (7.23-12.50)	10.50 (6.71-13.20)	10.10 (7.96-12.10)	9.30 (6.41-12.40)	***<0.001***

OSA; obstructive sleep apnea BMI; body mass index; AHI; apnea hypopnea index

The hemoglobin and hematocrit values from the hemogram parameters were found to increase parallel to the severity of OSA. There was no significant difference in platelet count according to the presence and severity of OSA. The mean platelet volume (MPV) was significantly lower in severe OSA cases compared to those without OSA and mild OSA cases (Figure 2).

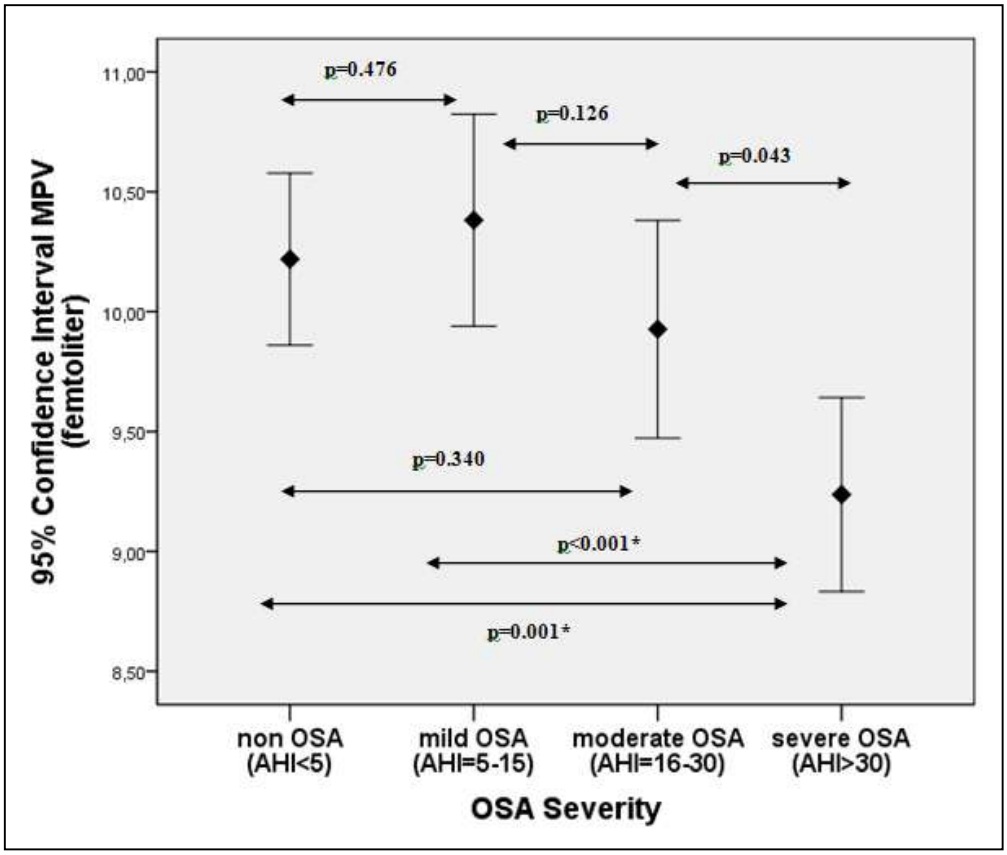

Figure 2. Comparison of mean platelet volume according to OSA severity. (Pairwise comparisons were made with Mann Whitney U test, and p significance value was determined as (0.05/6) < 0.0083 by applying Bonferroni correction)

When examining the correlation between patient characteristics and MPV, a negative correlation was observed between MPV and the apnea-hypopnea index (AHI), desaturation index, and the amount of oxygen saturation below 90% during sleep. On the other hand, a positive correlation was found between MPV and sleep efficiency and lactate dehydrogenase (LDH) levels.

As AHI increased, MPV significantly decreased (r=-0.241, p=0.003) (Figure 3). MPV significantly increased with increased sleep efficiency and LDH levels (r=0.207, p=0.015 and r=0.373, p=0.003, respectively). Additionally, MPV significantly decreased with an increase in the desaturation index and the amount of oxygen desaturation during sleep below 90% (r=-0.251, p=0.004 and r=-0.174, p=0.045, respectively).

Median MPV values were not statistically different according to gender, smoking, alcohol use, comorbidities and use of drug. However, the median MPV was found to be significantly lower in severe OSA cases. (Table 3 and Figure 2).

There were no significant differences between groups in terms of median red blood cell and platelet count, hematocrit percentage, and hemoglobin values before and after OSA treatment (Table 4). However, a significant decrease in MPV was observed after OSA treatment compared to before treatment (p=0.021, Figure 4).

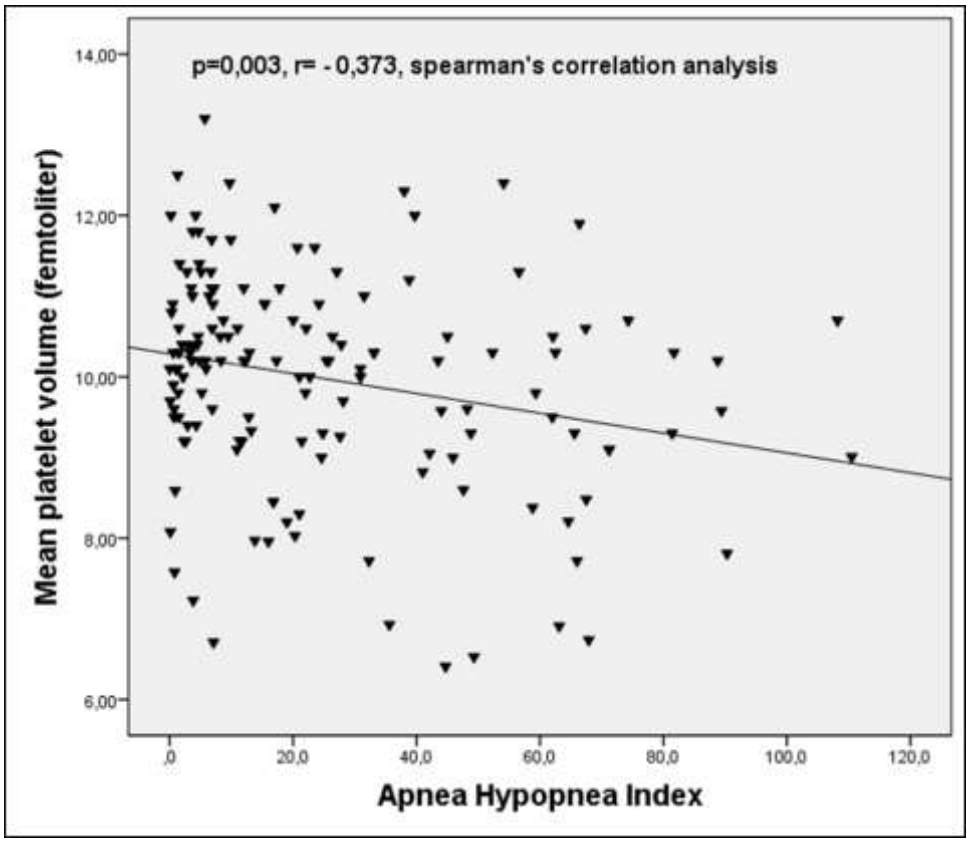

Figure 3. Correlation between MPV and apnea-hypopnea index

DISCUSSION

Contrary to the literature, study findings suggest that MPV decreases as AHI and desaturation index increase, and MPV is lower in cases with severe OSA (AHI>30) than in cases without OSA and with mild OSA (AHI<15). However, other results of this study are consistent with the literature and indicate that continuous positive airway pressure (CPAP) treatment applied to severe OSA patients significantly reduces MPV.

In many studies evaluating MPV from hemogram parameters according to the presence and severity of OSA, MPV was found to be significantly higher in patients with severe OSA compared to the control group (16-21). The common feature of these studies is that conditions such as diabetes and cardiovascular diseases, which have the potential to affect MPV, were used as exclusion criteria. On the other hand, some other studies concluded that MPV was not associated with the severity of OSA (22-24). In some of these studies, a healthy control group was used, while in others, as in our study, patients who underwent polysomnography test and had AHI<5 were included as the control group. Considering the differences in polysomnography indications, it can be said that the control group representing the non-OSA population in all these studies is quite heterogeneous.

Table 3. Comparison of MPV level according to some clinical features

	N	Mean Platelet Volume *(fL)* median (min-max)	*p*
Gender			
Male	107	10.10(6.41-13.20)	*0.224*
Female	51	10.20(7.58-12.50)	
Sigara			
No	64	10.25(6.41-12.50)	
Quit	11	10.10(6.71-13.20)	*0.631*
Yes	60	10.20(6.53-12.40)	
Alcohol use			
No	118	10.20(6.41-12.50)	*0.711*
Yes	16	10.15(8.48-13.20)	
Diabetes Mellitus			
No	112	10.20(6.41-12.50)	*0.287*
Yes	21	10.50(7.23-13.20)	
Hypercholesterolemia			
No	98	10.25(6.41-13.20)	*0.912*
Yes	32	10.20(7.72-12.50)	
ACE inhibitor			
No	101	10.20(6.41-13.20)	*0.487*
Yes	19	10.20(6.71-12.10)	
Ca channel blocker			
No	114	10.25(6.41-13.20)	*0.657*
Yes	5	10.20(7.71-10.70)	
Beta blocker			
No	111	10.30(6.41-13.20)	*0.147*
Yes	8	9.95(6.71-10.70)	
Diuretic			
No	105	10.30(6.41-13.20)	*0.243*
Yes	15	10.10(6.71-12.10)	
Antiaggregant			
No	106	10.25(6.41-13.20)	*0.134*
Yes	14	10.05(6.71-10.90)	
OSA severity			
Non (AHİ<5)	41	10.30(7.23-12.50)	
Mild (AHİ=5-15)	32	10.50(6.71-13.20)	***<0.001***
Moderate (AHİ=16-30)	28	10.10(7.96-12.10)	
Severe (AHİ>30)	57	9.30(6.41-12.40)	

Ca: calcium; ACE: angiotensin converting enzyme;

Table 4. Comparison of pre- and post-CPAP treatment hemogram parameters in severe OSA

	Median (min-max)		*p*
	Before Treatment N=20	**After Treatment N=20**	
Number of erythrocytes *(million per mm^3)*	5.15 (4.00-5.93)	4.94 (3.16-6.19)	*0.086*
Hematocrit *(%)*	44.1 (37.5-54.4)	43.6 (29.7-59.7)	*0.305*
Hemoglobin *(g/dl)*	14.4 (11.8-17.1)	14.3 (10.0-18.8)	*0.765*
Platelets *(thousand in mm^3)*	248 (176-317)	251 (169-386)	*0.513*
Mean Platelet Volume *(fL)*	8.31 (6.44-9.60)	7.92 (5.99-9.50)	***0.021***

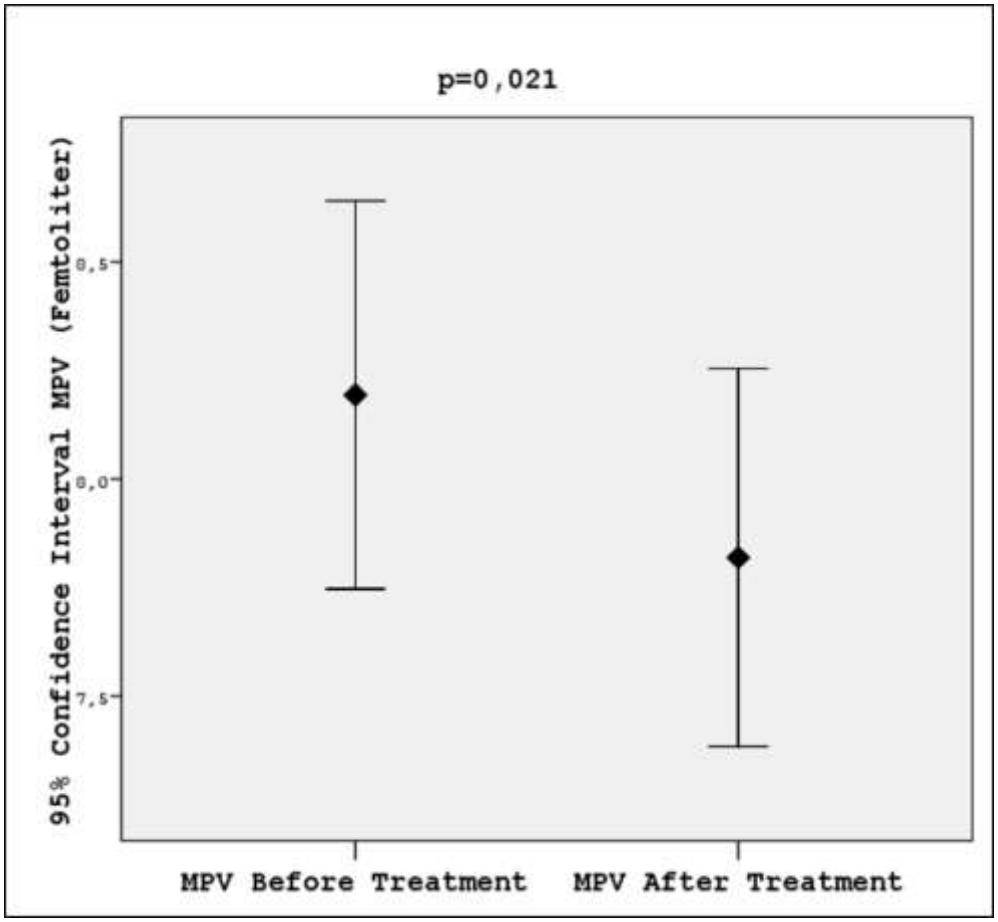

Figure 4. Comparison of MPV before and after treatment in severe OSA cases

In our study, we unexpectedly found significantly lower MPV values in the severe OSA group. The control group in our study did not consist of healthy volunteers, but rather of subjects with OSA symptoms, clinically thought to have OSA but with AHI < 5. In addition, some clinical conditions that have been shown to increase MPV in previous studies (diabetes, cardiovascular diseases, etc.) were not used as exclusion criteria in our study. Moreover, in studies related to this topic, patients taking antiaggregants were not included in the study because of the potential effect on MPV value, but in our study, all patients taking antiaggregants and other drugs were included without exception. In our study, the rates of antiaggregant use in the moderate and severe OSA groups (24% and 19.4%, respectively) were much higher than in the nonOSA and mild OSA groups (2.8% and 3.6%, respectively). Statistical evaluation could not be performed optimally because the number of subjects using antiaggregants was insufficient in the NonOSA and mild OSA groups (p value was not shown due to expected value issue in Chi square test - table 2). In addition, even though it did not reach statistical significance, median MPV values were lower in antiaggregant users compared to non-users in our study (10.05 fL vs. 10.25 fL, p=0.134, table 3). All these factors may explain the possible reasons why we paradoxically found lower MPV levels in the moderate and severe OSA group in our study.

Another reason for the conflicting results in the literature may be the differences in the methods and techniques used for MPV measurements. Platelet volume parameters are objective parameters in evaluating platelet size and can be examined during automated complete blood count without additional cost (15). Platelet shape and ultrastructure vary depending on the anticoagulant used, ambient temperature, and the method employed (25). Normal MPV values are measured as 4.5-8.5 fL (femtoliters) when sodium citrate is used as an anticoagulant, whereas when Ethylenediaminetetraacetic acid (EDTA) is used, this value is measured as 7-13 fL (26). Platelets collected with EDTA are spherical in shape, while those collected with citrate are discoid. EDTA causes platelets to swell over time. MPV can be measured using impedance or optical methods. When impedance measurement is performed using EDTA, MPV increases over 24 hours, with a maximum value reached after 2 hours. When an optical system is used, MPV decreases by 10% within 2 hours when EDTA is used (27). When citrate is used as an anticoagulant, MPV remains stable over time. At 37°C, OTH changes by 3% in 3 hours, while at room temperature, MPV increases by 20% (22). Dastjerdi et al., measurements using

EDTA and sodium citrate and showed no significant difference (28). Bath et al., considering that MPV measurements were previously performed using EDTA, which causes platelet swelling, measured MPV using sodium citrate. In this study, no difference was found between hypertensive patients and healthy control group (29). In our study, MPV were measured using the impedance measurement method in the Microbiology-CBC Laboratory within 2 hours after collecting 3 ml of blood in a K3 EDTA tube in the morning following polysomnography. In the studies conducted by Karakaş and Varol, the method used for MPV measurement, anticoagulant (EDTA), and the duration of blood collection were the same as the method, anticoagulant, and duration we used in our study (16, 18).

When impedance measurement is performed using EDTA, MPV increases over time. The lack of attention to the time interval between blood collection and MPV measurement in MPV-related studies may be another important reason for confusing results.

It would be more valuable to evaluate the same cases with the same method before and after treatment (self-control) rather than comparing with an insufficiently matched control group to reveal a causal relationship between MPV and OSA.

Varol et al. found that MPV values were significantly higher in severe OSA patients compared to the control group. They also showed that 6 months of CPAP treatment led to a significant decrease in MPV values in severe OSA patients (30). In our study, although MPV values did not show a positive correlation with OSA severity, it was shown that 1-month CPAP treatment significantly reduced MPV in severe OSA patients. In our study, platelet counts in OSA patients before and after CPAP treatment were statistically similar. Considering that the platelet life is 10 days, 1 month of CPAP treatment was considered sufficient. The results support the idea that CPAP therapy improves possible increased platelet activation in OSA.

In studies conducted on pediatric patient groups, high MPV levels were found in OSA patients, and decreases in MPV values were demonstrated after treatments such as adenotonsillectomy (31, 32). In recent studies, Ulusoy and colleagues found that MPV values were significantly higher in OSA patients. However, in this study, contrary to our study, a 1-month PAP treatment was insufficient to decrease elevated MPV values (20). In a study investigating the changes in MPV values in OSA patients who underwent uvulopalatal flap (UPF) surgery, a significant decrease in platelet volume was observed in OSA patients after UPF surgery (33). In another study by Özdemir and colleagues (34), contrary to all other studies, a 3-month CPAP treatment in OSA patients resulted in a statistically significant increase in MPV (before treatment 9.25±1.55, after 3-month CPAP treatment 9.66 ±1.22, p=0.010).

In another study by Kutlucan et al., which included a large population of 2298 individuals, the correlation between metabolic syndrome and its components with MPV was investigated in obese individuals. The presence of metabolic syndrome and its components did not make a significant difference in MPV values in obese patients with a BMI ≥ 30 kg/m2 (35). In our study, there was no statistically significant difference between MPV and BMI, but a statistically significant higher BMI was found in the severe OSA group.

In a retrospective study conducted by Binita et al., the relationship between platelet activity measured by MPV, metabolic syndrome, and diabetes was examined. A total of 13,021 patients between 1999 and 2004 were included in the study. In this study, MPV was found to be statistically significantly higher in diabetic patients compared to non-diabetic individuals and in abdominal obesity, indicating a strong and independent association between MPV and the presence and severity of diabetes (36). In our study, the presence of diabetes did not affect MPV in OSAS patients.

Although there is no study specifically related to LDH and OTH in the literature, it has been reported that LDH increases in diseases associated with thrombocytosis (37, 38). In our study, platelet counts were similar between the pre- and post-treatment groups, and it was observed that MPV statistically significantly increased as LDH levels increased (r=0.373; p=0.003). Further studies are needed to investigate the correlation between LDH and MPV in OSAS patients.

The most powerful aspect of our study compared to other studies is that the control group included all consecutive patients who underwent full PSG, whose clinical and demographic characteristics were similar to those of OSA patients but who were proven not to have OSA by PSG. Another important advantage of the study is the good methodological standardization in MPV measurements. The most significant limitation of this study is the relatively small number of cases in the follow-up after CPAP treatment.

CONCLUSION

The results of the study do not support an increase in MPV and hence platelet activation in severe OSA patients compared with those without OSA. However, the results suggest that one month of CPAP treatment reduces MPV and thus platelet activation in severe OSA patients. Further controlled, prospective studies including treatment outcomes are needed on this subject.

Compliance with Ethical Standards

Funding: This study received no funding.

Conflict of Interest: The authors declared no potential conflict of interest with respect to the

research, authorship, and/or publication of this article

Ethical Approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by Duzce University Medical Faculty Non-Invasive Clinical Trials Ethics Committee (Decision Number: 2012/309).

Informed Consent: Informed consent was obtained from all individual participants included in the study.

REFERENCES

1. Ralls F, Cutchen L. A contemporary review of obstructive sleep apnea. Curr Opin Pulm Med. 2019 Nov;25(6):578-593.
2. Partinen M, Jamieson A, Guilleminault C. Long-term outcome for obstructive sleep apnea syndrome patients. Mortality. Chest. 1988 Dec;94(6):1200-4.
3. Benjafield AV, Ayas NT, Eastwood PR, Heinzer R, Ip MSM, Morrell MJ, Nunez CM, Patel SR, Penzel T, Pépin JL, Peppard PE, Sinha S, Tufik S, Valentine K, Malhotra A. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. Lancet Respir Med. 2019 Aug;7(8):687-698.
4. Dredla BK, Castillo PR. Cardiovascular Consequences of Obstructive Sleep Apnea. Curr Cardiol Rep. 2019 Nov 9;21(11):137.
5. Arnaud C, Bochaton T, Pépin JL, Belaidi E. Obstructive sleep apnoea and cardiovascular consequences: Pathophysiological mechanisms. Arch Cardiovasc Dis. 2020 May;113(5):350-358.
6. Phillips B. Sleep-disordered breathing and cardiovascular disease. Sleep Med Rev. 2005 Apr;9(2):131-40.
7. Calvin AD, Somers VK. Obstructive sleep apnea and cardiovascular disease. Curr Opin Cardiol. 2009 Nov;24(6):516-20.
8. Roux F, D'Ambrosio C, Mohsenin V. Sleep-related breathing disorders and cardiovascular disease. Am J Med. 2000 Apr 1;108(5):396-402.
9. Henning BF, Zidek W, Linder B, Tepel M. Mean platelet volume and coronary heart disease in hemodialysis patients. Kidney Blood Press Res. 2002;25(2):103-8.
10. Hekimsoy Z, Payzin B, Ornek T, Kandoğan G. Mean platelet volume in Type 2 diabetic patients. J Diabetes Complications. 2004 May-Jun;18(3):173-6.
11. Dindar S, Cinemre H, Sengul E, Annakkaya AN. Mean platelet volume is associated with glycaemic control and retinopathy in patients with type 2 diabetes mellitus. West Indian Med J. 2013 Jul;62(6):519-23.
12. Park Y, Schoene N, Harris W. Mean platelet volume as an indicator of platelet activation: methodological issues. Platelets. 2002 Aug-Sep;13(5-6):301-6.
13. Norgaz T, Hobikoglu G, Aksu H, Bolca O, Uyarel H, Eren M, Narin A. The relationship between preprocedural platelet size and subsequent in-stent restenosis. Acta Cardiol. 2004 Aug;59(4):391-5.
14. Bath P, Algert C, Chapman N, Neal B; PROGRESS Collaborative Group. Association of mean platelet volume with risk of stroke among 3134 individuals with history of cerebrovascular disease. Stroke. 2004 Mar;35(3):622-6.
15. Noris P, Melazzini F, Balduini CL. New roles for mean platelet volume measurement in the clinical practice? Platelets. 2016 Nov;27(7):607-12.
16. Varol E, Ozturk O, Gonca T, Has M, Ozaydin M, Erdogan D, et al. Mean platelet volume is increased in patients with severe obstructive sleep apnea. Scand J Clin Lab Invest. 2010 Nov;70(7):497-502.
17. Nena E, Papanas N, Steiropoulos P, Zikidou P, Zarogoulidis P, Pita E, et al. Mean Platelet Volume and Platelet Distribution Width in non-diabetic subjects with obstructive sleep apnoea syndrome: new indices of severity? Platelets. 2012;23(6):447-54.
18. Karakaş MS, Altekin RE, Baktır AO, Küçük M, Cilli A, Yalçınkaya S. Association between mean platelet volume and severity of disease in patients with obstructive sleep apnea syndrome without risk factors for cardiovascular disease. Turk Kardiyol Dern Ars. 2013;41(1):14-20.
19. Akyol S, Çörtük M, Baykan AO, Kiraz K, Börekçi A, Şeker T, et al. Mean platelet volume is associated with disease severity in patients with obstructive sleep apnea syndrome. Clinics (Sao Paulo). 2015;70(7):481-5.
20. Ulusoy B, Oğuzhan T, Akyol M, Bozdemir K, Çiftçi B, Korkmaz MH. Insufficiency of positive airway pressure treatment on increased mean platelet volume: a prospective controlled study in patients with obstructive sleep apnea syndrome. Sleep Breath. 2020 Sep;24(3):885-91.
21. Rahangdale S, Yeh SY, Novack V, Stevenson K, Barnard MR, Furman MI, et al. The influence of intermittent hypoxemia on platelet activation in obese patients with obstructive sleep apnea. J Clin Sleep Med. 2011;7(2):172-8.
22. Sökücü SN, Ozdemir C, Dalar L, Karasulu L, Aydın S, Altın S. Is mean platelet volume really a severity marker for obstructive sleep apnea syndrome without comorbidities? Pulm Med. 2014;2014:754839.
23. Kurt OK, Yildiz N. The importance of laboratory parameters in patients with obstructive sleep apnea syndrome. Blood Coagul Fibrinolysis. 2013;24(4):371-4.

24. Bülbül Y, Aydın Özgür E, Örem A. Platelet indices in obstructive sleep apnea: the role of mean platelet volume, platelet distribution widht and plateletcrit. Tuberk Toraks. 2016;64(3):206-10.
25. Jackson SR, Carter JM. Platelet volume: laboratory measurement and clinical application. Blood Rev. 1993;7(2):104-13.
26. McShine RL, Sibinga S, Brozovic B. Differences between the effects of EDTA and citrate anticoagulants on platelet count and mean platelet volume. Clin Lab Haematol. 1990;12(3):277-85.
27. Macey M, Azam U, McCarthy D, Webb L, Chapman ES, Okrongly D, Zelmanovic D, Newland A. Evaluation of the anticoagulants EDTA and citrate, theophylline, adenosine, and dipyridamole (CTAD) for assessing platelet activation on the ADVIA 120 hematology system. Clin Chem. 2002;48(6 Pt 1):891-9.
28. Dastjerdi MS, Emami T, Najafian A, Amini M. Mean platelet volume measurement, EDTA or citrate? Hematology. 2006;11(5):317-9.
29. Bath PM, Carney C, Markandu ND, MacGregor GA. Platelet volume is not increased in essential hypertension. J Hum Hypertens. 1994;8(6):457-9.
30. Varol E, Ozturk O, Yucel H, Gonca T, Has M, Dogan A, Akkaya A. The effects of continuous positive airway pressure therapy on mean platelet volume in patients with obstructive sleep apnea. Platelets. 2011;22(7):552-6.
31. Chang WD, Tseng CH, Tsou YA. Mean platelet volume levels in children with sleep-disordered breathing: a meta-analysis. BMC Pediatr. 2020 May 11;20(1):204.
32. Zeng GH, Xu G, Liu HY, Gao Z. Association between mean platelet volume and obstructive sleep apnea-hypopnea syndrome in children. Medicine (Baltimore). 2022;101(43):e31505
33. Simsek G, Haytoglu S, Muluk NB, Arikan OK, Cortuk M, Kiraz K. Mean Platelet Volume Decreases in Adult Patients With Obstructive Sleep Apnea After Uvulopalatal Flap Surgery. J Craniofac Surg. 2015;26(7):2152-4.
34. Özdemir C, Sökücü S, Aydın Ş, Önür ST, Kara K. Response of Blood Parameters to PAP Treatment in Patients with Obstructive Sleep Apnea. Noro Psikiyatr Ars. 2018;56(3):182-5.
35. Kutlucan A, Bulur S, Kır S, Bulur S, Önder E, Aslantaş Y, Ekinözü İ, Aydn Y, Özhan H. The relationship between mean platelet volume with metabolic syndrome in obese individuals. Blood Coagul Fibrinolysis. 2012;23(5):388-90.
36. Shah B, Sha D, Xie D, Mohler ER 3rd, Berger JS. The relationship between diabetes, metabolic syndrome, and platelet activity as measured by mean platelet volume: the National Health And Nutrition Examination Survey, 1999-2004. Diabetes Care. 2012;35(5):1074-8.
37. Kabutomori O, Kanakura Y, Iwatani Y. Characteristic changes in platelet-large cell ratio, lactate dehydrogenase and C-reactive protein in thrombocytosis-related diseases. Acta Haematol. 2007;118(2):84-7.
38. Zhang KJ, Lu QY, Li P, Zhang P, Niu XQ. [Significance of platelet parameters and lactate dehydrogenase level in differential diagnosis for thrombocytosis]. Zhongguo Shi Yan Xue Ye Xue Za Zhi. 2010;18(4):972-5.