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The Correlation between Red Blood Cell Distribution Width Levels with the Severity of Obstructive Sleep Apnea and Carotid Intima Media Thickness

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Background: Obstructive sleep apnea syndrome (OSAS) is characterized by repetitive collapse of the upper airway during sleep. Red blood cell distribution width (RDW) increases platelet activation and has been reported as an independent predictor of adverse outcomes in the general population and is believed to be associated with cardiovascular morbidity and mortality. We evaluated RDW, mean platelet volume (MPV), and platelet distribution width (PDW) as a severity index in OSAS and the relationship between carotid intima media thickness and pulmonary hypertension.

Material/Methods: The study population consisted of 99 patients who were admitted to the sleep laboratory. Based on the apnea-hypopnea index, patients were grouped into 3 OSAS severity categories. Morning blood samples were withdrawn from patients after a 12-hour fasting period. MPV, PDW, and RDW were measured in a blood sample. Bilateral common carotid arteries of the patients were scanned.

Results: Ninety-nine patients – 73 with OSAS and 26 simple snoring control cases – were included. Mean values of MPV, PDW, and RDW were similar in patients compared to simple snoring subjects in the control group (p=0.162, p=0.656, p=0.091). RDW showed an inverse correlation with mean desaturation and lowest desaturation (p<0.01). Body mass index, apnea-hypopnea index, pulmonary artery pressure, and desaturation time under 90% were positively correlated with RDW (p<0.05). MPV, PDW, and carotid intima media thickness had no correlation with any other parameters.

Conclusions: The study showed a positive relationship between RDW and the apnea-hypopnea index and systolic pulmonary hypertension in patients with OSAS.

MeSH Keywords: Carotid Intima-Media Thickness • Erythrocyte Indices • Sleep Apnea, Obstructive

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Background

Obstructive sleep apnea syndrome (OSAS) is characterized by collapse of the upper airway during sleep, recurring apnea, intermittent hypoxemia, and daytime sleepiness, associated with a decreased daytime performance and impaired quality of life [1]. It is a common disorder of middle-aged adults, affecting 4% of men and 2% of women [2]. OSAS is related with cardiac mortality and morbidity.

OSAS is associated with several cardiovascular diseases, such as congestive heart failure, hypertension, atrial fibrillation, nocturnal arrhythmias, stroke, pulmonary hypertension, and atherosclerosis [3,4]. Carotid intima-media thickness is a useful marker of early endothelial defect and atherosclerosis development. Recent studies have indicated that OSAS is associated with endothelial disfunction [5]. There is increasing evidence that systemic inflammation markers such as high sensitive C-reactive protein, interleukin (IL)-6, tumor necrosis factor-α, and pentraxin-3 are increased in OSA patients with cardiovascular complications [6,7].

Red blood cell distribution width (RDW) is a numerical measure of the size variability of circulating erythrocytes. Disorders related to ineffective erythropoiesis or increased red blood cell destruction cause heterogeneity in size and a higher RDW [8,9]. RDW has been reported as an independent predictor of adverse outcomes in the general population and is believed to be associated with cardiovascular morbidity and mortality in patients with a previous myocardial infarction [10–12]. Increased platelet activation plays an important role in the development of cardiovascular complications [13]. Several studies have reported increased platelet activation and aggregation in patients with OSAS [14–16]. Increased platelet activity is associated with increased platelet volume, which can be measured by larger mean platelet volume (MPV) and platelet distribution width (PDW). Large platelets are more adhesive and tend to aggregate more than smaller ones [17]. This increase in platelet volume increases the tendency for coronary thrombus formation in acute coronary syndrome patients [18].

A few studies have examined the relationship between RDW, PDW, MPV, and AHI in OSAS, but their relationship with CIMT in OSAS is unclear. Considering the association between OSAS and cardiovascular disease and the overlapping risk factors, we evaluated RDW, MPV, and PDW as a severity index in OSAS and the relationship of carotid intima media thickness as endothelial damage with AHI and other sleep parameters.

Material and Methods

Patients

This prospective study consisted of 99 patients who were admitted to the sleep laboratory of our hospital with complaints of snoring, apnea, or daytime sleepiness and in whom polysomnography (PSG) had been performed between January 2013 and August 2013. Patients were selected consecutively. Demographic and health behavior-related data, including age, sex, body mass index (BMI), Epworth sleepiness scale scores, and medical histories regarding sleep habits and cardiovascular disease were collected from patient records. A respiratory function test, posteroanterior chest x-ray, and electrocardiography performed before PSG were evaluated, and complete blood counts were analyzed. Echocardiography and ultrasound examination of the carotid arteries were performed.

Patients known to have cardiovascular, renal, or hepatic diseases were excluded. Based on the AHI, patients were grouped into 3 OSAS severity categories: mild (AHI 5–15), moderate (AHI 15–30), and severe (AHI >30). As a control group, 26 individuals (ages 20 and 67) diagnosed with simple snoring were chosen. Patients were also grouped by BMI according to the WHO classification. Obesity, severity of AHI, and recurrent hypoxemia are the cardiovascular risk factors in the OSAS population. The study protocol was approved by the local ethics committee and all patients gave written informed consent.

Measurement of laboratory parameters

Morning blood samples were drawn from patients after a 12-hour fasting period. MPV, PDW, and RDW were measured in a blood sample collected in dipotassium EDTA tubes. They were determined using an ABX Pentra 120 analyzer. The biochemical analysis CRP, ast, alt, urea, lipid parameters, and glucose were measured at the same time (Architect plus ci16200Abbott Illinois USA).

Polysomnography

Overnight polysomnography was performed with 16-channel Embla (Medcare Inc, Iceland) continuous sleep technician monitoring. The system consists of 4 channels of EEG (with electrode placements at C4-A1, C3-A2, O2-A1, and O1-A2), 2 channels of EOG, submental EMG, oronasal air flow, thoracic and abdominal movements, pulse oximeter oxygen saturation, tibial EMG, body position detector, electrocardiogram, and tracheal sound. Apnea was defined as the complete cessation of airflow lasting more than 10 seconds. Hypopnea was defined as a >30% reduction in airflow lasting more than 10 seconds accompanied by >4% desaturation and/or arousal. The average number of episodes of apnea and hypopnea per hour of

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Table 1. Demographical, anthropometric characteristics of OSAS patients and controls.

	Patients	Control	P
Age (year)	50.8±11.7	41.3±11.0	<0.05
BMI (kg/m^2)	32.9±5.0	27.3±4.5	<0.05
AHI	33.2±26.8	2.58±1.39	<0.05
Lowest desaturation (%)	73.6±10.3		
Duration of desaturation (min)	59.9±76.6		
Average desaturation (%)	85.9±11.6		

BMI – body mass index; AHI – apnea-hypopnea index.

sleep were measured as AHI. The OSAS diagnosis was made on the basis of an apnea/hypopnea index (AHI) >5. Sleep stages were scored following standard criteria with 30-second epochs and were reviewed and verified by a certified sleep physician.

Determination of CIMT

Bilateral common carotid arteries of the patients were scanned longitudinally with a 7-MHz transducer attached to the available machine (Vivid 3, General Electric). Images were obtained from the distal portion of the common carotid artery, 1–2 cm proximal to the carotid bulb. The 2 bright echogenic lines in the arterial wall were identified as the intima and media lines. The intima media thickness was measured as the distance from the main edge of the first echogenic line to the main edge of the second. All examinations were performed by the same physician. Images showing the maximum intima media thickness were digitally stored and CIMT measurements were made offline. The intima media thickness of the distal wall of the right common carotid artery on the lengthwise axis was calculated according to the method described by Pignoli et al. [19]. Each measurement was repeated 3 times and the mean of the left and right common carotid arteries was used for analysis. Plaques, defined as >50% localized thickening of the intima compared to the rest of the wall or as an endoluminal protrusion of the arterial lumen of >0.5 mm, were not included in the measurement of CIMT.

Statistical analysis

Statistical analyses were performed using SPSS 16 software. Continuous data are expressed as means ± standard deviation (SD). Statistical comparisons were performed using a 1-way ANOVA and chi-square test. Analysis of variance followed by Duncan's test was used to determine the different groups. To determine the relationships between these variables in each group separately, Pearson's correlation coefficients were calculated. PAP, CIMT, PDW, RDW, and MPV variables in patient and control groups were assessed and used in separating the cut-off value ROC analysis. Results were considered statistically significant when p value was <0.05.

Results

Patient characteristics

We included a total of 99 patients – 73 with OSAS [5 patients 6.9% mild, 18 patients 24.7% moderate, and 50 patients 68.5% severe] and 26 simple snoring control cases.

The mean age of the OSAS patients was 50.84±11.0 years and 61.6% (45) were male. There were statistically significant differences between the 2 groups regarding age, BMI, and Epworth sleep score, but there was no statistically significant difference in sex distribution.

Clinical characteristics of the patients and controls are shown in Table 1. The parameters in OSAS and patient groups are shown in Table 2.

Controls were overweight (BMI 25–30) and patients were obese (BMI >30). There was no lung disease despite the history of heavy smoking in both groups. Patients more often had a history of hypertension (p<0.05).

There was a positive correlation between body mass index and Epworth scale. Mean values of MPV, PDW, and RDW were similar in patients compared to simple snoring persons in the control group (p>0.05).

In the patient population, mean RDW was 14.4 (±2.05) and RDW was not correlated with age or sex. Among other hematological variables, RDW showed an inverse correlation with mean desaturation and lowest desaturation. Body mass index, ahi, pulmonary artery pressure (pap), and desaturation time under 90% were positively correlated with RDW.

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Table 2. Parameters of biochemical analysis of OSAS patients and controls.

	Patients	Control	P
AST (U/L)	22.3	23.1	>0.05
ALT (U/L)	26.6	25.8	>0.05
CRP (mg/l)	2.62	3.25	>0.05
Glucose (mg/dl)	105.9	91.9	>0.05
LDL (mg/dl)	117.8	118.3	>0.05
Colesterol (mg/dl)	194.1	191.1	>0.05
HDL (mg/dl)	41.4	40.0	>0.05
RDW (mg/dl)	14.4±2.0	13.6±1.4	>0.05
PDW	16.3±1.8	16.1±1.7	>0.05
MPV	8.6±0.9	9.07±1.5	>0.05
CIMT	0.75±0.11	0.74±0.09	>0.05

Variables expressed as mean ±SD; RDW – red cell distribution width; PDW – platelet distribution width; MPV – mean platelet volume; CIMT – carotis intima media thicknes.

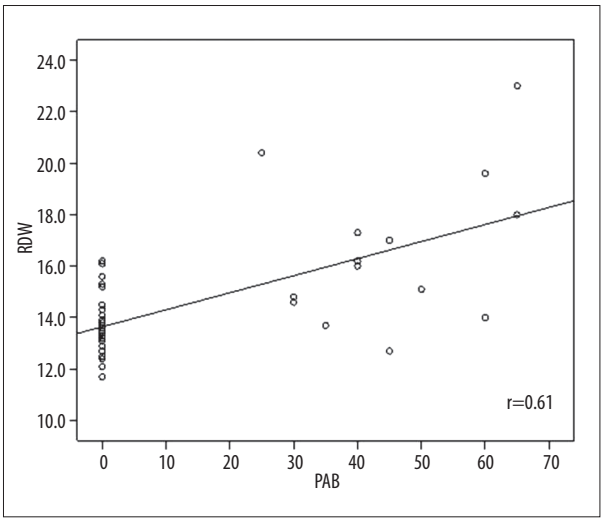

Figure 1. The correlation between RDW and PAB.

MPV, PDW, and CIM had no correlation with any other parameters.

PAP had a positive correlation with RDW and negative correlation with the lowest saturation (Figure 1).

Discussion

This prospective study is one of a few studies examining the relationship between RDW, PDW, MPV, and AHI in OSAS. The main finding of the present study was that PDW, RDW, MPV, and CIM were similar in the OSAS and simple snoring control group. There was no statistically significant difference between control and OSAS groups. Among the patients there was a correlation between RDW and the severity of OSAS and pulmonary hypertension.

Our results revealed a positive association between RDW and AHI. Our study demonstrates a relationship between severity of OSAS and RDW that is dependent on inflammation and intermittent hypoxia, and independent of anemia.

We also found a negative association of RDW with average minimum oxygen saturation and desaturation time under 90% during sleep, which could be explained by the effect of hypoxia on RDW. Intermittent hypoxia is a trigger for the cardiovascular and metabolic modifications associated with OSAS [20]. A positive relationship between RDW and the oxygen desaturation index may also indicate the severity of OSAS. Sokucu et al. found similar results about RDW and OSAS severity [21]. In agreement with their results, we found a positive correlation between pulmonary artery pressure and RDW, and a relationship between OSAS severity and pulmonary hypertension. RDW could be used in sleep laboratories as an indicator of pulmonary hypertension in further investigations.

Varol et al. and Nena et al. reported that levels of MPV were significantly greater in patients with severe OSAS than in patients in the control group and patients with mild-to-moderate OSAS [22,23]. In contrast, Beyan et al. concluded that platelet markers should not be used alone as direct indicators of platelet activation [24]. According to their results, large platelets did not show stronger activation in the aggregometer. Also, platelets shape and volume are variable, even in healthy persons. Our results indicate that patients with severe OSAS do

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not have significantly higher MPV values compared with controls and mild-to-moderate OSAS. The lack of difference between OSAS groups reduces the importance of platelet markers. Due to contradictory results on this subject, further investigations are needed.

Thickness of the common carotid intima media (CIMT) has been used in the assessment of endothelial function [7,25–27]. Increased CIMT is correlated with cardiovascular risk factors [28] and severity of coronary atherosclerosis [29] and predicts cardiovascular events in populations [30].

According to European Society of Cardiology (ESC) comments, a common carotid artery IMT >0.9 mm can be considered as a measured estimate of actual abnormalities [31]. Many hypotheses have been recommended to explain endothelial disfunction: Oxidative stress seems to be a cause of endothelial deterioration in OSAS patients [32,33]. Hypoxia is a part of the illness and causes real damage to the endothelium. OSAS leads to sympathetic nervous system hyperactivity, a condition that can stimulate early alterations in the vascular morphology and countering the atherosclerotic process. Literature data suggest that carotis intima media thickness is evidence of early alterations in vascular morphology [34]. This is not synonymous with atherosclerosis, but because the underlying pathophysiological mechanisms are similar, the 2 conditions have been associated [35]. Ciccone et al. found a positive relationship between IMT and OSAS duration [36]. In the present study we did not find any difference between patients and control groups regarding CIMT, probably because the duration of osas symptoms was short.

Many studies suggest that OSAS originates from pulmonary hypertension. A major cause of PHT and cor pulmonale is chronic hypoxia, which leads to pulmonary arterial vasoconstriction and a cascade of molecular and biochemical events resulting in vascular smooth muscle hypertrophy, and intimal and adventitial thickening. In the present study, the average saturation and the lowest saturation were negative correlated with PAP. The time under 90% saturation was not correlated with PAP. There is evidence that CV homeostatic mechanisms in subjects with OSA are disrupted, as demonstrated by daytime abnormalities in sympathetic nervous system function and heart rate variability [37]. This means that at the lowest saturation, the sympathetic system is more active; thus the length of desaturation is not as effective as the lowest saturation on PAP.

Ages and BMI's were different between the study subjects and the controls. There was no correlation with age and all parameters, so this condition did not affect the results. One of the weaknesses of our study is that we did not have markers of inflammation, which could affect RDW values. Also, RDW could not be used as a screening tool in the general population according to our results because it could be affected by various independent variables.

Conclusions

Our study showed a positive relationship between RDW and the AHI and systolic pulmonary hypertension in patients with OSAS. The association between elevated RDW and the severity of OSAS in the study suggests the clinical utility of values. We showed that average saturation and lowest saturation were negative correlated with PAP, although the time under 90% saturation was no correlated with PAP. Patients with prominent low saturation should be considered for further investigation for pulmonary hypertension. Prospective, randomized, controlled studies are needed to assess the association between these parameters and OSAS.

Conflicts of interest

All authors have no conflicts of interest to disclose.

References:

1. Young T, Palta M, Dempsey J et al: The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med, 1993; 328(17): 1230–35
2. Lattimore JD, Celermajer DS, Wilcox I: Obstructive sleep apnea and cardiovascular disease. J Am Coll Cardiol, 2003; 41(9): 1429–37
3. Dempsey JA, Veasey SC, Morgan BJ, O'Donnell CP: Pathophysiology of sleep apnea. Physiol Rev, 2010; 90(1): 47–112
4. Drager LF, Togeiro SM, Polotsky VY, Lorenzi-Filho G: Obstructive sleep apnea: A cardiometabolic risk in obesity and the metabolic syndrome. J Am Coll Cardiol, 2013; 62(7): 569–76
5. Brunetti L, Francavilla R, Scicchitano P et al: Impact of respiratory disorders on endothelial function in children. Scientific World Journal, 2013; 2013: 719456
6. O'Leary DH, Polak JF: Intima-media thickness: A tool for atherosclerosis imaging and event prediction. Am J Cardiol, 2002; 90(10C): 18–21
7. Ciccone MM, Scicchitano P, Zito A et al: Correlation between Inflammatory Markers of Atherosclerosis and Carotid Intima-Media Thickness in Obstructive Sleep Apnea. Molecules, 2014; 19(2): 1651–62
8. Romero AJ, Carbia CD, Ceballo MF, Diaz NB: [Red cell distribution width (RDW): its use in the characterization of microcytic and hypochromic anemias]. Medicina (B Aires), 1999; 59(1): 17–22
9. Tonelli M, Sacks F, Arnold M et al: Relation between red blood cell distribution width and cardiovascular event rate in people with coronary disease. Circulation, 2008; 117(2): 163–68
10. Perlstein TS, Weuve J, Pfeffer MA et al: Red blood cell distribution width and mortality risk in a community-based prospective cohort. Arch Intern Med, 2009; 169(6): 588–94
11. Patel KV, Ferrucci L, Ershler WB et al: Red blood cell distribution width and the risk of death in middle-aged and older adults. Arch Intern Med, 2009; 169(5): 515–23
12. Felker GM, Allen LA, Pocock SJ et al: Red cell distribution width as a novel prognostic marker in heart failure: data from the CHARM Program and the Duke Databank. J Am Coll Cardiol, 2007; 50(1): 40–47
13. Tsiara S, Elisaf M, Jagroop IA, Mikhailidis DP: Platelets as predictors of vascular risk: is there a practical index of platelet activity? Clin Appl Thromb Hemost, 2003; 9(3): 177–90

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14. Hui DS, Ko FW, Fok JP et al: The effects of nasal continuous positive airway pressure on platelet activation in obstructive sleep apnea syndrome. Chest, 2004; 125(5): 1768–75
15. Minoguchi K, Yokoe T, Tazaki T et al: Silent brain infarction and platelet activation in obstructive sleep apnea. Am J Respir Crit Care Med, 2007; 175(6): 612–17
16. Varol E, Ozturk O, Gonca T et al: Mean platelet volume is increased in patients with severe obstructive sleep apnea. Scand J Clin Lab Invest, 2010; 70(7): 497–502
17. Schoene NW: Design criteria: tests used to assess platelet function. Am J Clin Nutr, 1997; 65(5 Suppl.): 1665–85
18. Huczek Z, Filipiak KJ, Kochman J et al: Baseline platelet size is increased in patients with acute coronary syndromes developing early stent thrombosis and predicts future residual platelet reactivity. A case-control study. Thromb Res, 2010; 125(5): 406–12
19. Pign P, Tremoli E, Poli A et al: Intimal plus medial thickness of the arterial wall: A direct measurement with ultrasound imaging. Circulation, 1986; 74(6): 1399–406
20. Ryan S, Taylor CT, McNicholas WT: Systemic inflammation: a key factor in the pathogenesis of cardiovascular complications in obstructive sleep apnoea syndrome? Thorax, 2009; 64(7): 631–36
21. Sokucu NS, Karasulu L, Dalar L et al: Can Red Blood Cell Distribution Width Predict Severity of Obstructive Sleep Apnea Syndrome? J Clin Sleep Med, 2013; 8(5): 521–25
22. Varol E, Ozturk O, Gonca T et al: Mean platelet volume is increased in patients with severe obstructive sleep apnea. Scand J Clin Lab Invest, 2010; 70(7): 497–502
23. Nena E, Papanas N, Steiropoulos P 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
24. Beyan C, Kaptan K, Ifran A: Platelet count, mean platelet volume, platelet distribution width, and plateletcrit do not correlate with optical platelet aggregation responses in healthy volunteers. J Thromb Thrombolysis, 2006; 22(3): 161–64
25. Corretti MC, Anderson TJ, Benjamin EJ et al: Guidelines for the ultrasound assessment of endothelial-dependent flow-mediated vasodilation of the brachial artery: a report of the International Brachial Artery Reactivity Task Force. J Am Coll Cardiol, 2002; 39(2): 257–65
26. Gullu H, Erdogan D, Caliskan M et al: Interrelationship between noninvasive predictors of atherosclerosis: transthoracic coronary flow reserve, flow-mediated dilation, carotid intima-media thickness, aortic stiffness, aortic distensibility, elastic modulus, and brachial artery diameter. Echocardiography, 2006; 23(10): 835–42
27. Raitakari OT, Juonala M, Kahonen M et al: Cardiovascular risk factors in childhood and carotid artery intima-media thickness in adulthood: the Cardiovascular Risk in Young Finns Study. JAMA, 2003; 290(17): 2277–83
28. Burke GL, Evans GW, Riley WA et al: Arterial wall thickness is associated with prevalent cardiovascular disease in middle-aged adults. The Atherosclerosis Risk in Communities (ARIC) Study. Stroke. 1995; 26(3): 386–91
29. O'Leary DH, Polak JF, Kronmal RA et al: Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. Cardiovascular Health Study Collaborative Research Group. N Engl J Med, 1999; 340(1): 14–22
30. Eren M, Gorgulu S, Uslu N et al: Relation between aortic stiffness and left ventricular diastolic function in patients with hypertension, diabetes, or both. Heart, 2004; 90(1): 37–43
31. Mancia G, de Backer G, Dominiczak A et al: 2007 Guidelines for the management of arterial hypertension. The Task Force for the management of arterial hypertension of the European Society of hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens, 2007; 25(6): 1105–87
32. Garvey JF, Taylor CT, McNicholas WT: Cardiovascular disease in obstructive sleep apnoea syndrome: the role of intermittent hypoxia and inflammation. Eur Respir J, 2009; 33(5): 1195–205
33. Kohler M, Stradling JR: Mechanisms of vascular damage in obstructive sleep apnea. Nat Rev Cardio, 2010; 7(12): 677–85
34. Lorenz MW, Markus HS, Bots ML et al: Prediction of clinical cardiovascular events with carotid intima-media thickness. A systematic review and meta-analysis. Circulation, 2007; 115(4): 459–67
35. Pignoli P, Tremoli E, Poli A et al: Intimal plus medial thickness of the arterial wall: a direct measurement with ultrasound imaging. Circulation, 1986; 74(6): 1399–406
36. Ciccone MM, Scicchitano P, Mitacchione G et al: Is there a correlation between OSAS duration/severity and carotid intima-media thickness? Respir Med, 2012; 106(5): 740–46
37. Somers VK, Dyken ME, Clary MP, Abboud FM: Sympathetic neural mechanisms in obstructive sleep apnea. J Clin Invest, 1995; 96(4): 1897–904

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