

Original Article

The Importance of Red Cell Distribution width value in Obstructive Sleep Apnea

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ABSTRACT

Background: Obstructive sleep apnea (OSA) is a very common condition among sleep disorders. The relationship between inflammation and OSA has been described and inflammation was found to have a role in the development of the disease. Hematologic parameters have been found as inflammatory biomarkers in various diseases. **Aim:** To evaluate the association of OSA and red blood cell distribution width (RDW) value, and the association of RDW value in OSA patients with hypertension (HT) and without HT. **Method:** A retrospective and cross-sectional evaluation of the complete records of 412 patients, who were presented to our sleep center and underwent polysomnography. Polysomnographic parameters and RDW-CV values for these patients were evaluated. **Result:** Total 372 patients with obstructive sleep apnea syndrome and 40 people as a control group were included in the study. There was no significant difference between the OSA and control group regarding the mean RDW value ($p>0.05$). No statistically significant association was detected between RDW and apnea hypopnea index (AHI) in the evaluation of the OSA group. There was a negatively significant correlation between RDW and minimum oxygen saturation and mean oxygen saturation values in the OSA patients ($p=0.002$; $r=-0.159$, $p=0.004$, $r=-0.148$; respectively). A statistically significant difference was found in the mean RDW value based on the presence of HT in all OSA groups ($p=0.031$). The mean RDW of the group with HT was higher than group without HT. **Conclusion:** RDW must be taken into consideration during follow-up in severe OSA, and in the presence of HT.

Key words: red cell distribution width; obstructive sleep apnea; hypertension

Obstructive sleep apnea (OSA) is a very common condition among sleep disorders. OSA is characterized by repetitive partial or complete obstructions of the upper respiratory tract that results in hypoxia-reoxygenation cycles and arousals. Many factors have a role in the pathophysiology of OSA. The contributing roles of the factors vary between individuals who are diagnosed as having OSA [1-3]. Obstructive sleep apnea causes high cardiac risk due to its hemodynamic complications such as hypoxemia, increased pulmonary and systemic arterial pressure, and changes in heart rate during apnea. It has a significant association with cardiovascular morbidity and mortality such as systemic and pulmonary hypertension, heart failure, coronary heart

disease, arrhythmia, sudden death, and cerebrovascular disease [4]. Neurohumoral and hemodynamic incidents that develop in OSA cause functional and structural changes in the cardiovascular system. General characteristics of patients with OSA as obesity, high blood pressure, advanced age, and male sex are the known risk factors for cardiovascular diseases.

The relationship between inflammation and OSA has been described and inflammation was found to be a risk factor in the development of the disease. It increases the risk of cardiovascular disease, which is accompanied by repetitive airway obstructions [5]. Recently, several hematologic parameters were found as inflammatory

biomarkers in various diseases, and increased levels were reported in many cardiovascular problems such as coronary artery disease, and heart failure [6]. In a study, red blood cell distribution width (RDW) was found higher in patients with severe OSA compared with the controls, and also RDW was found higher in patients with OSA with cardiovascular disease than in those without [7].

Inflammation and hypoxia can explain the relationship between RDW and OSA. The knowledge of the association between RDW and severity of OSA is limited and controversial. Therefore in the present study, we evaluated the association of OSA and RDW value, and the association of RDW value in OSA patients with hypertension (HT) and without HT.

METHODS

This retrospective study was conducted during January 2017 and September 2018 in a tertiary care center Istanbul. A complete record of 418 patients who were presented to our sleep center and underwent polysomnography (PSG) was performed. After getting the ethical committee approval from the institute we included 112 patients who were diagnosed as having mild OSA with PSG, 111 patients with moderate OSA, and 149 patients with severe OSA. Also, 40 people with an apnea hypopnea index (AHI) <5 on PSG were included as the control group. Six patients who were diagnosed as having hematologic disease, chronic liver/kidney disease, a history of malignancy, and blood transfusion, were excluded. One hundred twelve patients were included, and the RDW-CV results of participants were noted from the routinely conducted blood sample examination.

Polysomnographic recordings of the patients were taken all through the night. Sleep and physiologic changes were monitored using the PSG device (Grass Technologies Comet PSG). Electroencephalography (EEG), 10-channel submental electromyography (EMG), right and left eye electrooculography, electrocardiography (ECG), oronasal airflow (thermal sensor and nasal pressure transducer), body position, calculation of the thoracic and abdominal movement (inductance plethysmograph), monitoring of the arterial blood oxygen saturation from the finger using pulse oximetry, and left and right leg movement sensors (EMG) were used. Apnea was described as a decrease of air flow signal of at least 10 seconds in calculation with the thermal sensor with a $\geq 90\%$ decrease and providing an amplitude criterion of $\geq 90\%$. Apnea-Hypopnea Index (AHI) of 5-14.9 was described as mild OSA, AHI between 15 and 29.9 was described as moderate OSA, and AHI >30 as severe OSA.

The Statistical Package for the Social Sciences (SPSS) Ver. 20.0 was used in the statistical evaluation of the data. The Kolmogorov-Smirnov test was used in the evaluation of the compliance of continuous variables to normal

distribution. The independent samples t-test was used in the comparison of the means of two groups of continuous variables with normal distribution, and the one-way analysis of variance (ANOVA) test was used in the comparison of the means of more than two groups. Dunnett and Tukey multiple comparison tests were used to detect the difference in the event of a significant ANOVA result (the Dunnett test was used in paired comparisons in accordance with the control group, and the Tukey test was used in the paired comparison of the other groups with one another). The Kruskal-Wallis test was used in the comparison of more than two groups that had non-normal distribution paired comparisons were conducted using the Mann-Whitney U test in the detection of significant results. The association between two continuous variables was evaluated using Pearson's Chi-square test. Percentage and frequency are given for the descriptive statistics of categorical variables, and mean and standard deviation are given for the descriptive statistics of continuous variables. P values below 0.05 were regarded as statistically significant.

RESULTS

Total 372 patients diagnosed as having OSA and 40 controls, were included in the study. The demographic and clinical characteristics of the participants are shown in Table 1. There was no significant difference between the OSA and control group regarding the mean RDW value ($p > 0.05$). No statistically significant association was detected between RDW value and AHI in the evaluation of the OSA group. A statistically significant difference was detected in the mean RDW value of patients aged younger than 40 years, and above 40 years in all patients with OSA ($p = 0.03$). Accordingly, the mean RDW was found relatively higher in the group aged above 40 years (Figure 1). There was a weak positive correlation between RDW value and body mass index (BMI) in the OSA group ($p = 0.022$, $r = 0.119$) (Figure 2).

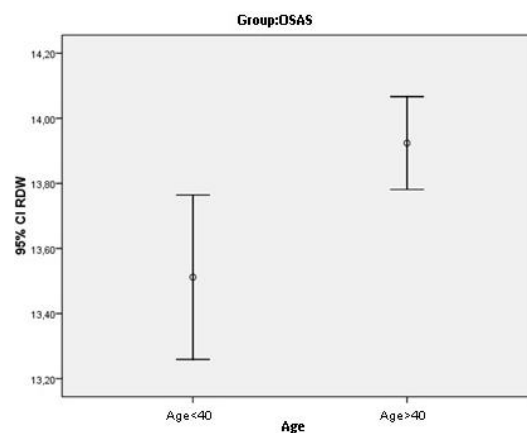


Figure 1: The association between RDW and age (>40 years and <40 years).

Table 1: Demographic & Clinical Characteristics of the Participants

| Parameters | Total (n=372) | Mild (n=112) | Moderate (n=111) | Severe (n=149) | Control (n=40) | P value |
|--------------------|---------------|--------------|------------------|----------------|----------------|---------|
| BMI | 31.1 ± 5.4 | 30.7 ± 5.0 | 31.5 ± 5.9 | 32.0 ± 4.7 | 29.9 ± 4.9 | 0.269 |
| Age | 48.5 ± 12.0 | 46.3 ± 11.8 | 49.6 ± 12.0 | 49.5 ± 11.9 | 49.2 ± 11 | 0.219 |
| Sleep Efficiency | 79.5 ± 17.8 | 80.7 ± 14.6 | 80.4 ± 24.2 | 78.6 ± 13.2 | 77 ± 19.2 | 0.579 |
| AHI | 29.4 ± 25.8 | 10.0 ± 2.7 | 21.4 ± 4.4 | 57.3 ± 22.9 | 2.3 ± 1.4 | <0.001 |
| Minimum Saturation | 82.3 ± 8.3 | 85.1 ± 6.5 | 83.3 ± 5.6 | 77.34 ± 6.9 | 90.4±2.2 | <0.001 |
| Average Saturation | 92.9 ± 4.0 | 93.8 ± 3.7 | 93.9 ± 1.8 | 90.9 ± 5.0 | 95 ± 1.7 | <0.001 |
| RDW | 13.8 ± 1.2 | 13.7 ± 1.2 | 13.8 ± 1.3 | 13.9 ± 1.1 | 13.8 ± 1.2 | 0.685 |
| HTC | 41.2 ± 4.6 | 41.1 ± 4.6 | 40.8 ± 4.5 | 41.8 ± 4.8 | 40.5±4.5 | 0.227 |

BMI: Body Mass Index; AHI: Apnea hypopnea index; AI: Apnea Index; RDW: Red Cell Distribution width; HTC: Hematocrit

A statistically significant difference was detected regarding the mean RDW value between the group with normal weight and the obese OSA group (p=0.011). There was a significant negative correlation between RDW value and minimum oxygen saturation and the mean value of oxygen saturation during sleep in OSA group (p=0.002, r=-0.159; p=0.004, r=-0.148) (Figure3, Figure 4).

statistically significant difference was detected in the mean RDW value in the control group according to the presence of HT (p>0.05). However, no difference was detected between the RDW values of patients with and without HT in the mild and moderate OSA groups; the mean RDW value was found to be statistically significantly higher in the group with HT in the comparison with group without HT in severe OSA group (p=0.044).

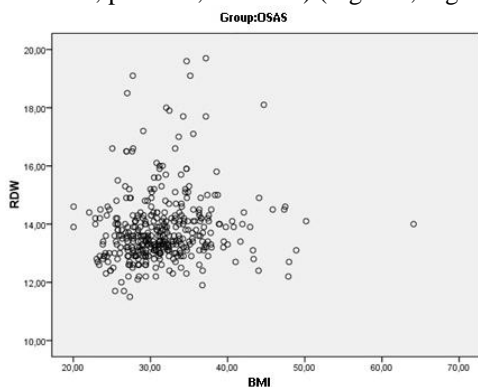


Figure 2: The association between RDW and BMI

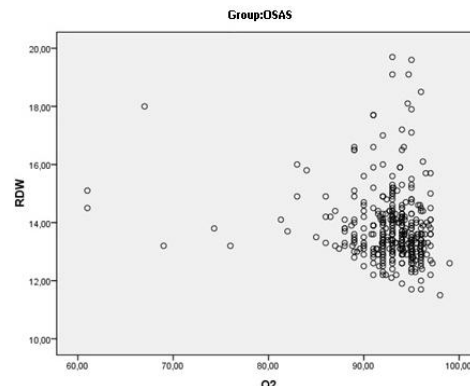


Figure 4: The association between RDW and mean oxygen saturation

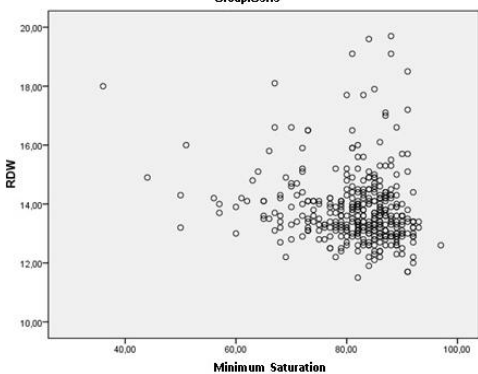


Figure 3: The association between RDW and minimum oxygen saturation

A statistically significant difference was found in the mean RDW in the presence of HT in all OSA groups (p=0.031). The mean RDW of the group with HT was higher than that of the group without HT (Figure5). No

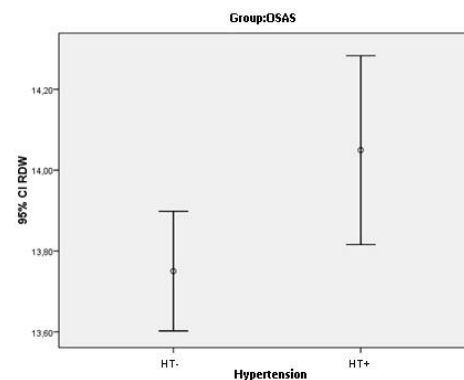


Figure 5: The association between RDW and patients with and without hypertension

DISCUSSION

Controversial results were found in previous studies investigating the AHI and sleep parameters with RDW in OSA groups. The exact mechanism of RDW values in patients with OSA and its association with AHI has not yet been clarified. However, researchers suggested that it could be associated with inflammation in OSA and oxidative stress, which has an important role in the pathogenesis of OSA [9-11]. We found no association with RDW and severity of OSA. Kurt et al. evaluated the association of these severity of OSA and RDW values in a study with 98 patients. Similar to our study, no association was found between RDW and disease severity [8]. Moreover, 360 patients with OSA were evaluated and no association was found between disease severity and RDW values [12]. Contrary to our study, researchers showed that RDW was higher in OSA. In addition, hematocrit and RDW showed a positive correlation with the AHI. These findings showed the importance of complete blood counts and indexes in patients with OSA and suggest that hematocrit and RDW might be an indicator associated with the severity of OSA [13].

Yosef et al. investigated the association of sleep parameters and RDW in addition to AHI levels and reported a significant correlation with RDW and the oxygen desaturation index, Epworth sleepiness scale (EES), and minimum oxygen saturation in their study [8]. Similarly, we also found a significant negative association between RDW and minimum saturation and mean saturation levels in the OSA group. Ozsu et al. reported a significant difference between the OSA and control group regarding RDW levels in their study. However, no association with disease severity was detected. A significant association was found between RDW, AHI, mean oxygen saturation, and systolic pulmonary arterial pressure. RDW was evaluated as an independent marker for cardiovascular diseases [14]. Similarly, researchers in another study reported a positive correlation between RDW and the AHI, and a negative correlation between RDW and minimum saturation [15].

RDW was found significantly higher in a severe OSA group compared with a control group in another study. In addition, a negative correlation was detected between RDW and minimum oxygen saturation [16]. However, we found no association between RDW and disease severity, and a similar negative correlation was found between RDW and minimum oxygen saturation and mean oxygen saturation, which might be explained as the effect of hypoxemia on RDW. OSA is a condition that develops with repetitive obstructions of the upper airway during sleep and has an important role in cardiovascular diseases. Intermittent hypoxia/reoxygenation is detected in OSA and this is a significant risk factor for cardiovascular and

metabolic changes. The presence of inflammation has a role in the development of these complications [17].

Many previous researchers found no association between RDW and the severity of disease. RDW was found higher in the OSA group with cardiovascular diseases compared with the OSA group with no cardiovascular disease [18]. RDW is a numeric calculation of the dimensional variability of the erythrocytes in the circulation and is calculated as one component of the complete blood count in the differential diagnosis of anemia [19]. Though the systemic HT was found to have the strongest association between OSA and cardiovascular diseases, various studies showed increased risk of various cardiovascular diseases such as heart failure, arrhythmias, and coronary artery disease [20]. Our study confirmed these results and we detected HT in 29.8% of the patients in our study and the RDW value in the OSA group with HT, was found higher than in the group with no HT. Researchers investigating the association between RDW level with sex and age found no association between RDW and sex [21]. Similarly, we found no association between RDW and sex. In line with our study, researchers detected no association between RDW, age, and sex in another study [15].

Recent studies investigated RDW values in an OSA group after continuous positive air pressure (CPAP) treatment. In the study, 138 patients with OSA and 34 healthy controls were evaluated. Although the results were controversial in view of recent studies, RDW was found to be associated with OSA severity and RDW values were not changed after CPAP treatment [22]. The exact mechanism between RDW and OSA is not clear but it can be related to oxidative stress, hypoxia and chronic inflammation. Oxidative stress has been shown to be associated with RDW. The inflammation may influence erythropoiesis, erythrocyte deformability, promoting anisocytosis [23]. The limitations of our study are that it was a retrospective study and lack of evaluation of patients for other cardiac comorbidities.

CONCLUSION

In conclusion, in the light of these data, RDW must be taken into consideration during follow-up in severe OSA, and especially in the presence of hypertension. More comprehensive studies based on inflammatory biomarkers and hematologic parameters are required for evaluation of OSA and cardiovascular diseases.

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