# Comparison of Platelet Indices in Patients with Obstructive Sleep Apnea and Obstructive Lung Diseases + Obstructive Sleep Apnea Syndrome

🛛 Mustafa Çolak, 🕼 Hikmet Çoban, 🕲 Nurhan Sarıoğlu, 🕲 Gülden Deniz Aksu, 🕲 Fuat Erel

Balıkesir University Faculty of Medicine, Department of Chest Diseases, Balıkesir, Türkiye

# ABSTRACT

**Introduction:** We aimed to observe the changes in platelet activities in patients with obstructive sleep apnea (OSA) and obstructive lung diseases + obstructive sleep apnea (OLDOSA) syndrome.

**Methods:** Adult patients who were followed up with the diagnosis of OSA and OLDOSA syndrome between 06.2018-06.2020 in our clinic were evaluated retrospectively. Changes in platelet indices were investigated.

**Results:** Of the 354 cases included in the study, 240 were male (67.7%) and 114 were female (32.3%). The control group (simple snoring) included 53 patients, the OSA group included 230 patients, and the OLDOSA group included 71 patients. The groups showed similarities in relation to gender (p=0.407). When the mean platelet volume (MPV) and platelet distribution width (PDW) values were evaluated, a significant discrepancy was noted among the different groups (p=0.01, p=0.02, respectively), enhancing coherence. A notable disparity was observed among the groups with regard to cardiovascular diseases (p=0.00).

**Conclusion:** In our study, we found that MPV and PDW values increased in patients with OSA and OLDOSA syndrome compared to the control group in patients with OSA and OLDOSA syndrome. MPV was found to be significantly higher in the OLDOSA group compared to the OSA group. We think that these parameters may be indicators of increased cardiovascular risk in patients with OSA and OLDOSA syndrome.

Keywords: Obstructive sleep apnea, OLDOSA syndrome, platelet indices

# Introduction

Overlap syndrome describes the association of obstructive sleep apnea (OSA) and other pulmonary diseases [asthma, chronic obstructive pulmonary disease (COPD), interstitial lung disease, and cystic fibrosis]. The association of obstructive lung diseases, namely COPD and asthma, with OSA has been defined as obstructive lung diseases + OSA (OLDOSA) syndrome (1).

The co-existence of COPD + OSA is common, and it has been suggested that the reason is the similarity of the risk factors identified for both diseases. Therefore, investigating the presence of COPD in OSA patients and investigating OSA symptoms and findings in COPD patients will enable the diagnosis of cases with overlap syndrome (2). The co-existence of OSA and COPD has a clinically more severe course compared to when each disease is observed alone (3). Considering the high prevalence of both COPD and OSA, overlap syndrome is expected in 29% of OSA patients (4).

Another obstructive lung disease associated with OSA is asthma. In the association between OSA and asthma, sleep apnea may provoke asthma

attacks. In asthmatic patients, nocturnal bronchospasm can lead to sleep disturbances and hypoxemia. Therefore, the number of arousals is higher and nocturnal hypoxemia is observed more severely in patients with OSA + asthma association (5). A large meta-analysis in 2017 reported that 49.5% of asthma patients had OSA and that asthma patients were 2.64 times more likely to have OSA than controls (6). In patients with asthma and COPD, complications with OSA, as well as airway obstruction, become more pronounced.

Platelets play an important role in atherosclerotic plaque formation, progression of atherosclerosis, and thrombosis. Platelets express and secrete substances involved in the process of inflammation, coagulation, thrombosis, and atherosclerosis (7). In addition, platelet activation has been associated with cardiovascular morbidity (8).

Mean platelet volume (MPV) and platelet distribution width (PDW) are biomarkers of platelet activation (9,10). Increased MPV is a harbinger of cardiovascular disease (CVD), including cerebrovascular and coronary artery disease. It has also been associated with the presence of obesity,



Address for Correspondence: Mustafa Çolak MD, Balıkesir University Faculty of Medicine, Department of Chest Diseases, Balıkesir, Türkiye

E-mail: drmclk@yahoo.com ORCID ID: orcid.org/0000-0002-8458-3535

Received: 28.06.2024 Accepted: 14.04.2025 Publication Date: 21.05.2025

**Cite this article as:** Çolak M, Çoban H, Sarıoğlu N, Aksu GD, Erel F. Comparison of platelet indices in patients with obstructive sleep apnea and obstructive lung diseases + obstructive sleep apnea syndrome. İstanbul Med J. 2025; 26(2): 146-51

<sup>©</sup>Copyright 2025 by the University of Health Sciences Türkiye, İstanbul Training and Research Hospital/İstanbul Medical Journal published by Galenos Publishing House. Licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 (CC BY-NC-ND) International License diabetes mellitus (DM), and metabolic syndrome (11,12). During an inflammatory response, there is an increase in platelet count and platelet swelling, both of which can affect PDW. PDW is increased by changes in platelet morphology and size that occur in inflammatory states (13). In patients with OSA, increased systemic inflammation has been identified, while chronic inflammation has also been described in patients with COPD and asthma (14,15).

Our study was planned to compare platelet activities in patients with OSA and OLDOSA syndrome.

# Methods

The study was conducted between 01.06.2018-08.06.2020 in patients who underwent polysomnography (PSG) as a result of evaluations for sleep apnea in the chest diseases outpatient clinic. The demographic data, smoking history, comorbidities, body mass index (BMI), complete blood parameters taken at first admission, lipid profiles and diagnostic PSG results of three groups [OSA, OLDOSA syndrome and control group (apnea-hypopnea index (AHI) <5] were analyzed. Informed consent was obtained from the patients participating in the study. Patients with a history of hematologic disorder or malignancy or anomalous hematocrit, abnormal white blood cell count and/or abnormal platelet count were excluded. After the present evaluations, we aimed to examine platelet indices in patients with OSA, and OLDOSA syndrome. Ethical approval for this study was obtained from the Balıkesir University Clinical Research Ethics Committee (approval number: 2022/107, date: 28.09.2022).

### **Statistical Analysis**

All analyses were performed using SPSS version 23.0. Numerical variables with normal distribution were defined as mean  $\pm$  standard deviation, and those with non-normal distribution were defined as median (minimum-maximum) Categorical variables were expressed as numbers (percentage). Normality analysis between the groups was performed with the Kolmogorov-Smirnov test. The chi-square test was used to evaluate categorical data. In comparing more than two independent groups, the Kruskal-Wallis test was used for variables that were not normally distributed; the One-Way ANOVA test was used for normally distributed variables; and multiple comparison tests (post-hoc) were used to identify differences between significant groups. According to the Levene's test result, the variances of the groups were considered to be homogeneous, and the Scheffé's test was applied. A critical  $\alpha$  value of 0.05 was considered significant.

# Results

Of the 354 cases admitted to the study, 240 were male (67.7%) and 114 were female (32.3%). The control group (simple snoring) comprised 53 patients, the OSA group comprised 230 patients, and the OLDOSA group comprised 71 patients (27 with COPD, 44 with asthma). When the groups were evaluated according to gender, a similarity was detected between the groups (p=0.74) (Table 1). When the age of the groups was evaluated, a significant difference was found between them (p=0.00) (Table 1).

While the prevalence of smoking history was highest among individuals in the OLDOSA group (60.6%), no statistically significant variance was observed among the groups (p=0.34) (Table 1). The prevalence of

Table 1. General characteristics of patient groups								
	Controls, (n=53)	OSA, (n=230)	OLDOSA, (n=71)	р				
Age	48.53±10.39	51.74±11.57	56.94±11.52	0.00				
Gender, (%)								
Male	34 (64.2)	159 (69.1)	47 (66.2)	0.74				
Female	19 (35.8)	71 (30.9)	24 (33.8)					
Smoking, (%)								
Yes	24 (45.3)	99 (43)	43 (60.6)	0.34				
No	29 (54.7)	131 (57)	28 (39.4)					
Comorbidity, (%)								
Yes	24 (45.3)	162 (70.4)	62 (87.3)	0.00				
No	29 (54.7)	68 (29.6)	9 (12.7)					
Diabetes mellitus (%)								
Yes	9 (17)	84 (36.5)	32 (45.1)	0.00				
No	44 (83)	146 (63.5)	39 (54.9)					
Hypertension, (%)								
Yes	17 (32.1)	125 (54.3)	41 (57.7)	0.00				
No	36 (67.9)	105 (45.7)	30 (42.3)					
CVD, (%)								
Yes	6 (11.3)	58 (25.2)	29 (40.8)	0.00				
No	47 (88.7)	172 (74.8)	42 (59.2)					

CVD: Cardiovascular disease, OSA: Obstructive sleep apnea, OLDOSA: Obstructive lung diseases + obstructive sleep apnea

smoking history was notably greater in the OLDOSA group than in the simple snoring and OSA groups (p=0.01).

When assessed based on the existence of comorbidities, a notable distinction was observed among the groups (p=0.00). Comorbidities were mostly observed in the OLDOSA group (87.3%).

The disparity in prevalence rates of DM and hypertension (HT) showed statistical significance across all groups (p=0.00 and p=0.00, respectively) (Table 1). In subgroup analysis, a significant difference in DM and HT was found in the OSA and OLDOSA groups compared to the control group (p=0.03 and p=0.03, respectively). In addition, although DM and HT were more common in the OLDOSA group than in the OSA group, no significant difference was found between the groups (p=0.21 and p=0.68, respectively).

The prevalence of CVD was 11.3% in the control group, 25.2% in the OSA group, and 40.8% in the OLDOSA group. During the assessment of CVD, a noteworthy difference was detected among all groups (p=0.00) (Table 1). A statistically significant difference was observed in the OSA and OLDOSA groups compared to the control group (p=0.00). Additionally, the OLDOSA group displayed a markedly elevated occurrence of CVD when contrasted with the OSA group (p=0.01).

Among all patients, 66 patients (18.6%) had hyperlipidemia, 11 patients (3.1%) had endocrine system disease (other than DM), 18 patients (5%) had psychiatric disease, 15 patients (4.2%) had urologic disease, 8 patients (2.2%) had rheumatologic disease and 9 patients (2.5%) had neurologic disease.

When BMI was divided into categories of 30 and above, and below 30, a statistically significant difference was found among the groups (p<0.01) (Table 2). A significant difference was detected between the patient group and the control group (p<0.01). Although there were more obese

patients in the OLDOSA group, compared to the OSA group, no significant difference was found between them (p=0.21).

A notable disparity was observed in the hemoglobin and hematocrit values among the groups (p=0.02, p=0.04, respectively) (Table 2). Platelet counts showed no significant variation among the groups (p=0.91).

The mean value of MPV was determined as  $8.60\pm1.20$  in the control group,  $8.72\pm1.13$  in the OSA group and  $9.15\pm1.39$  in the OLDOSA group, and a notable discrepancy was observed among the groups (F=4.23, p=0.01) (Table 2). In the post-hoc analysis, it was identified that the mean MPV level in the OLDOSA group showed a significant increase compared to both the simple snoring group (X=0.54) and the OSA group (X=0.43).

When the effectiveness of MPV for CVD was evaluated, the AUC value was found to be 0.522 in the receiver operating characteristic analysis and not statistically significant (p=0.53).

A remarkable difference was detected among the groups in relation to the PDW median value (p=0.02) (Table 2). When conducting pairwise comparisons among the groups, it was observed that the PDW value exhibited a statistically significant increase in the OSA and OLDOSA groups compared to the group with simple snoring (p=0.02, p=0.01). There was no discernible discrepancy between the OSA and OLDOSA groups (p=0.307).

When comparing the different groups with regard to red cell distribution width and plateletcrit, no statistically significant variance was detected (p=0.32, p=0.77).

A notable distinction was observed among the groups with regard to minimum oxygen saturation, mean oxygen saturation, and the oxygen

Table 2. Age, body-mass index and platelet index of the patient groups								
		Controls, (n=53)	OSA, (n=230)	OLDOSA, (n=71)	р			
Body mass index	<30	29 (54.7%)	63 (27.4%)	14 (19.7%)	0.00			
	≥30	24 (45.3%)	167 (72.6%)	57 (80.3%)				
Hemoglobin, g/dL		14.3±1.68	14.3±1.62	13.6±1.72	0.02			
Hematocrit, (%)		42.8±4.53	42.8±4.47	41.2±5.03	0.04			
Platelet, (%)		260.91±63.53	265.15±67.18	266.14±80.87	0.91			
MPV, (%)		8.60±1.20	8.72±1.13	9.15±1.39	0.01			
PDW (minmax.)		16.40 (9.8-19.9)	16.50 (8.6-20)	16.70 (7.9-19.2)	0.02			
Pct (minmax.)		0.22 (0.09-0.35)	0.22 (0.10-0.48)	0.23 (0.10-0.38)	0.77			
RDW (minmax.)		13.60 (11-30.2)	13.61 (10.5-28.1)	13.96 (11.9-25.9)	0.32			
Total colesterol		192.32±36.93	200.70±42.34	190.41±34.93	0.23			
HDL		46.57±8.24	45.11±9.35	44.37±8.99	0.54			
LDL		117.53±35.86	117.38±33.90	117.27±31.20	0.99			
AHI score (minmax.)		2.80 (0.10-4.9)	29.45 (5.2-105)	23 (5.4-89.5)	0.00			
Min. O <sub>2</sub> sat (minmax.)		94.55 (91.70-98)	92.94 (77-86)	93 (86-96.05)	0.00			
Average O <sub>2</sub> sat (minmax.)		89.75 (74-96)	82.12 (50-94)	82.91 (53-91)	0.00			
ODI (minmax.)		2.75 (0.0-52.2)	26.65 (0.5-111.20)	19 (2-84.2)	0.00			

OSA: Obstructive sleep apnea, OLDOSA: Obstructive lung diseases + obstructive sleep apnea, MPV: Mean platelet volume, PDW: Platelet distribution width, Pct: Plateletcrit, RDW: Red cell distribution width, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, AHI: Apnea-hypopnea index, ODI: Oxygen desaturation index, min.: Minimum, max.: Maximum

desaturation index (p=0.00, p=0.00 and p=0.00, respectively) (Table 2). In addition, a significant rise was seen in the patient cohorts in contrast to the control group (p=0.00, p=0.00, and p=0.00, respectively). No significant relationship was detected between these parameters and MPV, and PDW.

No significant disparity was detected among all patients regarding total cholesterol, high-density lipoprotein, and low-density lipoprotein levels in the 226 patients for whom data were accessible (p=0.23, p=0.54, p=0.99, respectively) (Table 2).

Upon analysis of the groups in accordance with the AHI, a significant disparity was identified among the groups (p=0.00).

#### Discussion

OSA is a disease characterized by recurrent episodes of full (apnea) or partial (hypopnea) upper respiratory tract obstruction during sleep (14). Its prevalence was reported to be 17% in women and 34% in men between the ages of 30-70 (16). Asthma and COPD are common chronic respiratory disorders and are important causes of impaired quality of life, disability and death worldwide (17,18). The presence of COPD and asthma with OSA separately or together has been defined as OLDOSA syndrome (1). These associations may aggravate the course of OSA by leading to chronic hypoxemia, sympathetic activation, subclinical inflammation, pulmonary HT, and cor pulmonale (19).

Asthma, COPD, and OSA share common risk and aggravating factors such as old age, obesity, smoking, and gastroesophageal reflux. It has been reported that the prevalence of OSA increases in the 40-65 age group and decreases after the age of 65 (20,21). In our study, the mean age was 51.7 years in the OSA group; 55.8 years in the OLDOSA group, and was found to be compatible with the literature. Smoking, a prevalent risk factor for the aforementioned conditions, did not show a statistically significant discrepancy across the groups. However, individuals within the OLDOSA cohort demonstrated a significantly greater smoking history compared to the other two groups. The rise seen within the OLDOSA cohort might be understood through the connection between smoking and the development of obstructive respiratory conditions.

OSA is known to play a role in the etiology of DM (22). According to Karakoç et al. (23), the frequency of DM was found to be 3.8% in patients with simple snoring and 12% in patients with severe OSA. A study conducted in Italy reported that DM was more common in patients with COPD than in the general population. The prevalence was 10.5% in the general population and 18.7% in patients with COPD, compared with people without COPD (24). A recent review observed that asthma and DM are two common chronic conditions that frequently coexist (25). In our investigation, a significant discrepancy in the prevalence of DM was noted among the different groups. A significant difference in the measured variable was detected in patient groups compared to the control group. DM was observed at the highest rate in the OLDOSA and OSA groups for other variables. We believe that this elevation can be explained by the co-existence of diseases.

A history of sleep apnea is present in 35-40% of hypertensive patients and HT in approximately 50% of those with sleep apnea (26). In their

meta-analysis, Xu et al. (27) provided evidence that the frequency of HT was increased in individuals with overlap syndrome in comparison to those with either COPD or OSA separately (28). In a study conducted in middle-aged asthmatic subjects, it was shown that the risk of HT increased as FEV<sub>1</sub> decreased (29). In our investigation, the occurrence of HT exhibited notable disparities among the groups. A significant difference was observed in patient groups compared to the control group. Due to the co-existence of diseases, the highest incidence rate was in the OLDOSA group, consistent with the literature. However, no significant difference was found between OLDOSA and the OSA group.

Diseases such as heart failure, cerebrovascular disease, atrial fibrillation, coronary artery disease and HT are strongly associated with OSA (30). The main events involved in this relationship are increased sympathetic activation, oxidative stress, vascular inflammation, endothelial dysfunction, arterial stiffening, and hypercoagulation, which can be triggered by sleep fragmentation and intermittent hypoxia. With effective treatment of OSA, the increased risk burden for CVD can be eliminated (27). The variation in CVD prevalence was noticeable across all groups. Additionally, a significantly higher prevalence was noted in the OLDOSA group compared to the OSA group. We anticipate that both the presence of OSA in the etiology and the frequent occurrence of cardiovascular comorbidities in airway diseases explain this situation.

Obesity plays a role as a predisposing factor for various diseases such as OSA, obesity hypoventilation syndrome, asthma, pulmonary HT, pneumonia, and acute respiratory distress syndrome. There is also evidence of a strong relationship between COPD and obesity (31,32). In a study, the prevalence of obesity in COPD patients was reported to be 18% (33). Obesity is observed in 70% of patients with OSA (34). It has been shown that 36% of adult asthmatics are obese and have a later-onset asthma phenotype (35). In our study, obesity was found to be significantly higher in the OSA and OLDOSA groups compared to the control group. This phenomenon may be explained by the prevalence of obesity as a shared risk factor in the pathogenesis of these conditions. Although obesity was observed at a higher rate in the OLDOSA group compared to the OSA group, no significant difference was found between them.

Several investigations have demonstrated heightened platelet activation and aggregation among individuals diagnosed with OSA (36-38). Hypoxia along with chronic inflammation can trigger platelet activation (39,40). There are different studies reporting a relationship between MPV, which is one of the activation markers, and sleep apnea (41,42). Archontogeorgis et al. (43) demonstrated an increase in MPV among individuals diagnosed with overlap syndrome (COPD + OSA) in comparison to the control group. Furthermore, it was observed that MPV was higher in patients with overlap syndrome compared to the OSA group (43). In another study evaluating the relationship between OSA and MPV, Sarioglu et al. (44) found no significant relationship. In our study, MPV values exhibited notable variations across all the groupings. Furthermore, there was a marked elevation in the OLDOSA group in relation to the OSA group. We hypothesize that these results explain the highest level of platelet activation in the OLDOSA group, due to the co-existence of the diseases. Minimum oxygen saturation and average oxygen saturation, which are indicators of hypoxia, were found to be

significantly lower in the patient groups than in the control group. These results support the finding that platelet activation is high in the OSA and OLDOSA groups.

PDW is an index of platelet volume heterogeneity and may increase in the activation of platelets (45). Some authors reported that MPV and PDW increased in OSA and showed a positive correlation after controlling for possible confounding factors (46). Białas et al. (47) demonstrated a correlation between increased PDW and reduced survival rates in patients diagnosed with COPD. Archontogeorgis et al. (43) showed that the PDW value was significantly higher in patients with OSA and overlap syndrome compared to controls. Our research revealed a notable variance in the PDW value across all the groups. A notable disparity was identified, particularly when comparing the groups of patients and the control group. This result was consistent with studies in the literature. We observed that the PDW value was even higher in the OLDOSA group, where two diseases leading to platelet activation coexist.

#### **Study Limitations**

Our research encountered certain constraints. The sample size of patients involved was restricted, potentially impacting the study's ability to identify any existing effects. Furthermore, given the retrospective nature of our observational study, one must acknowledge the possibility of unaccounted confounding variables influencing the outcomes.

# Conclusion

Both OSA and OLDOSA syndrome are correlated with elevated platelet activation leading to an increased risk of thrombosis. Patients with OLDOSA syndrome may face an elevated susceptibility to thrombosis as a result of the correlation between OSA and obstructive pulmonary disease. It is our contention that MPV and PDW, recognized as markers of platelet activation, ought to be regarded as viable assessment tools for CVD within this particular patient cohort. Therefore, we think that by including MPV and PDW in clinical evaluation, possible increased disease risks can be detected earlier and the disease burden can be reduced. This is the first study to evaluate platelet activation in OLDOSA syndrome. There is a need for research with a larger population to evaluate the association of MPV and PDW with increased cardiovascular risk in these patients.

#### Ethics

**Ethics Committee Approval:** Ethical approval for this study was obtained from the Balıkesir University Clinical Research Ethics Committee (approval number: 2022/107, date: 28.09.2022).

**Informed Consent:** Informed consent was obtained from the patients participating in the study.

#### Footnotes

Authorship Contributions: Surgical and Medical Practices - M.Ç., H.Ç., N.S., G.D.A., F.E.; Concept - M.Ç., H.Ç., N.S., F.E.; Design - M.Ç., H.Ç., N.S., F.E.; Data Collection or Processing - M.Ç., H.Ç., G.D.A., F.E.; Analysis or Interpretation - M.Ç., H.Ç., N.S.; Literature Search - M.Ç., G.D.A.; Writing - M.Ç., H.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

#### References

- Ioachimescu OC, Teodorescu M. Integrating the overlap of obstructive lung disease and obstructive sleep apnoea: OLDOSA syndrome. Respirology. 2013;18:421-31.
- Köktürk O. Kronik obstrüktif akciğer hastalığında uyku sorunları. Kronik Obstrüktif Akciğer Hastalığı Toraks Kitapları; 2000:167-88.
- 3. Mohsenin V, Valor R. Sleep apnea in patients with hemispheric stroke. Arch Phys Med Rehabil. 1995; 76: 71-6.
- López-Acevedo MN, Torres-Palacios A, Elena Ocasio-Tascón M, Campos-Santiago Z, Rodríguez-Cintrón W. Overlap syndrome: an indication for sleep studies? : A pilot study. Sleep Breath. 2009; 13: 409-13.
- Köktürk O, Çiftçi B. Overlap sendromu. Tüberküloz ve Toraks Dergisi. 2003; 51: 333-48.
- 6. Kong DL, Qin Z, Shen H, Jin HY, Wang W, Wang ZF. Association of obstructive sleep apnea with asthma: a meta-analysis. Sci Rep. 2017; 7: 4088.
- Nording HM, Seizer P, Langer HF. Platelets in inflammation and atherogenesis. Front Immunol. 2015; 6: 98.
- Renga B, Scavizzi F. Platelets and cardiovascular risk. Acta Cardiol. 2017; 72: 2-8.
- Park Y, Schoene N, Harris W. Mean platelet volume as an indicator of platelet activation: methodological issues. Platelets. 2002; 13: 301-6.
- Vagdatli E, Gounari E, Lazaridou E, Katsibourlia E, Tsikopoulou F, Labrianou I. Platelet distribution width: a simple, practical and specific marker of activation of coagulation. Hippokratia. 2010; 14: 28-32.
- 11. Vizioli L, Muscari S, Muscari A. The relationship of mean platelet volume with the risk and prognosis of cardiovascular diseases. Int J Clin Pract. 2009; 63: 1509-15.
- 12. Papanas N, Symeonidis G, Maltezos E, Mavridis G, Karavageli E, Vosnakidis T, et al. Mean platelet volume in patients with type 2 diabetes mellitus. Platelets. 2004; 15: 475-8.
- 13. Song YJ, Kwon JH, Kim JY, Kim BY, Cho KI. The platelet-to-lymphocyte ratio reflects the severity of obstructive sleep apnea syndrome and concurrent hypertension. Clin Hypertens. 2016; 22: 1.
- 14. Çoşğun İG, Gürel A. Obstructive sleep apnea and bladder pain syndrome/ interstitial cystitis in women. Sleep Breath. 2024; 28: 999-1003.
- Fu JJ, McDonald VM, Gibson PG, Simpson JL. Systemic inflammation in older adults with asthma-COPD overlap syndrome. Allergy Asthma Immunol Res. 2014; 6: 316-24.
- Heinzer R, Vat S, Marques-Vidal P, Marti-Soler H, Andries D, Tobback N, et al. Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study. Lancet Respir Med. 2015; 3: 310-8.
- Masoli M, Fabian D, Holt S, Beasley R; Global Initiative for Asthma (GINA) Program. The global burden of asthma: executive summary of the GINA Dissemination Committee report. Allergy. 2004; 59: 469-78.
- WHO. World Health Organization: World Health Report. WHO, Geneva. 2011. Available from http://www.who.int/mediacentre/factsheets/fs315/en/index.html
- Banerjee D, Yee BJ, Piper AJ, Zwillich CW, Grunstein RR. Obesity hypoventilation syndrome: hypoxemia during continuous positive airway pressure. Chest. 2007; 131: 1678-84.
- 20. Stradling JR. Sleep-related breathing disorders. 1. Obstructive sleep apnoea: definitions, epidemiology, and natural history. Thorax. 1995; 50: 683-9.

- Phillips BA, Anstead MI, Gottlieb DJ. Monitoring sleep and breathing: methodology. Part I: Monitoring breathing. Clin Chest Med. 1998; 19: 203-12.
- Punjabi NM, Ahmed MM, Polotsky VY, Beamer BA, O'Donnell CP. Sleepdisordered breathing, glucose intolerance, and insulin resistance. Respir Physiol Neurobiol. 2003; 136: 167-78.
- Karakoç Ö, Akçam T, Gerek M, Birkent H. Obstrüktif uyku apnesi ve kronik hastalıklar. KBB-Forum. 2008; 7: 15-20.
- Cazzola M, Bettoncelli G, Sessa E, Cricelli C, Biscione G. Prevalence of comorbidities in patients with chronic obstructive pulmonary disease. Respiration. 2010; 80: 112-9.
- Torres RM, Souza MDS, Coelho ACC, de Mello LM, Souza-Machado C. Association between asthma and type 2 diabetes mellitus: mechanisms and impact on asthma control-a literature review. Can Respir J. 2021; 2021: 8830439.
- Christiansen SC, Zuraw BL. Treatment of hypertension in patients with asthma. N Engl J Med. 2019; 381: 1046-57.
- Xu J, Wei Z, Wang X, Li X, Wang W. The risk of cardiovascular and cerebrovascular disease in overlap syndrome: a meta-analysis. J Clin Sleep Med. 2020; 16: 1199-207.
- 28. Somers VK, White DP, Amin R, Abraham WT, Costa F, Culebras A, Sleep apnea and cardiovascular disease: an American Heart Association/american College of Cardiology Foundation Scientific Statement from the American Heart Association Council for High Blood Pressure Research Professional Education Committee, Council on Clinical Cardiology, Stroke Council, and Council On Cardiovascular Nursing. In collaboration with the National Heart, Lung, and Blood Institute National Center on Sleep Disorders Research (National Institutes of Health). Circulation. 2008; 118: 1080-111. Erratum in: Circulation. 2009; 119: e380.
- 29. Peker Y, Balcan B. Cardiovascular outcomes of continuous positive airway pressure therapy for obstructive sleep apnea. J Thorac Dis. 2018; 10(Suppl 34): 4262-79.
- Sova M, Sovova E, Hobzova M, Zapletalova J, Kamasova M, Kolek V. The effect of continuous positive airway pressure therapy on the prevalence of masked hypertension in obstructive sleep apnea patients. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2015; 159: 277-82.
- Zammit C, Liddicoat H, Moonsie I, Makker H. Obesity and respiratory diseases. Int J Gen Med. 2010; 3: 335-43.
- 32. Franssen FM, O'Donnell DE, Goossens GH, Blaak EE, Schols AM. Obesity and the lung: 5. Obesity and COPD. Thorax. 2008; 63: 1110-7.
- Schokker DF, Visscher TL, Nooyens AC, van Baak MA, Seidell JC. Prevalence of overweight and obesity in the Netherlands. Obes Rev. 2007; 8: 101-8.
- Göçmen H, Karadağ M. Obstructive sleep apnea syndrome epidemiology. Turkiye Klinikleri J Surg Med Sci. 2007; 3: 7-10.

- 35. Erdoğan T, Karakaya G, Kalyoncu AF. Comorbid diseases in aspirin-exacerbated respiratory disease, and asthma. Allergol Immunopathol (Madr). 2015; 43: 442-8.
- Geiser T, Buck F, Meyer BJ, Bassetti C, Haeberli A, Gugger M. In vivo platelet activation is increased during sleep in patients with obstructive sleep apnea syndrome. Respiration. 2002; 69: 229-34.
- Hui DS, Ko FW, Fok JP, Chan MC, Li TS, Tomlinson B, et al. The effects of nasal continuous positive airway pressure on platelet activation in obstructive sleep apnea syndrome. Chest. 2004; 125: 1768-75.
- Minoguchi K, Yokoe T, Tazaki T, Minoguchi H, Oda N, Tanaka A, et al. Silent brain infarction and platelet activation in obstructive sleep apnea. Am J Respir Crit Care Med. 2007; 175: 612-7.
- Onder I, Topcu S, Dökmetas HS, Türkay C, Seyfikli Z. Platelet aggregation size and volume in chronic obstructive pulmonary disease. Mater Med Pol. 1997; 29: 11-3.
- 40. Stokes KY, Granger DN. Platelets: a critical link between inflammation and microvascular dysfunction. J Physiol. 2012; 590: 1023-34.
- 41. 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: 447-54.
- 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: 481-5.
- 43. Archontogeorgis K, Voulgaris A, Papanas N, Nena E, Froudarakis M, Mikhailidis DP, et al. Mean platelet volume and platelet distribution width in patients with obstructive sleep apnea syndrome and concurrent chronic obstructive pulmonary disease. Clin Appl Thromb Hemost. 2018; 24: 1216-22.
- 44. Sarioglu N, Demirpolat G, Erel F, Kose M. Which is the ideal marker for early atherosclerosis in obstructive sleep apnea (OSA) - Carotid intima-media thickness or mean platelet volume? Med Sci Monit. 2017; 23: 1674-81.
- Bae MH, Lee JH, Yang DH, Park HS, Cho Y, Chae SC. White blood cell, hemoglobin and platelet distribution width as short-term prognostic markers in patients with acute myocardial infarction. J Korean Med Sci. 2014; 29: 519-26.
- 46. Yousef A, Alkhiary W. The severity of obstructive sleep apnea syndrome is related to red cell distribution width and hematocrit values. J Sleep Disord Ther. 2015; 4: 192.
- 47. Białas AJ, Pedone C, Piotrowski WJ, Antonelli Incalzi R. Platelet distribution width as a prognostic factor in patients with COPD pilot study. Int J Chron Obstruct Pulmon Dis. 2017; 12: 2261-7.