



Analysis of the Long-Term Correlation Between Obstructive Sleep Apnea and Chronic Obstructive Pulmonary Disease: A 10-Year Retrospective Study

Obstrüktif Uyku Apnesi ile Kronik Obstrüktif Akciğer Hastalığı Arasındaki Uzun Dönem İlişkinin Analizi: 10 Yıllık Retrospektif Bir Çalışma

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ABSTRACT

Aim: The primary objective of this study is to evaluate the prevalence of overlap syndrome (OS) in patients with Chronic Obstructive Pulmonary Disease (COPD) who exhibit symptoms of Obstructive Sleep Apnea (OSA) and are undergoing polysomnography. The study also aims to explore the influence of hypoventilation and long-term oxygen therapy (LTOT) on the severity of OSA.

Materials and Methods: A retrospective analysis was conducted on COPD patients presenting symptoms of OSA who underwent polysomnography between August 2012 and September 2022. Data on the patients' body mass index (BMI), apnea-hypopnea index (AHI), oxygen desaturation index (ODI), minimum and mean oxygen saturation levels (minSpO₂ and meanSpO₂), sleep efficiency, percentage of REM period (REM%), LTOT usage, hematocrit levels, and awake arterial carbon dioxide (PaCO₂) levels were collected.

Results: The study involved 81 COPD patients. Among them, 76 individuals (93.9%) had an AHI>5, with 9 classified as having mild OSA, 24 as moderate OSA, and 43 as severe OSA. The average sleep efficiency was 78.3%, and the mean REM% value was 7.3. Sixteen patients (19.7%) were using LTOT, and a statistically significant higher sleep efficiency was observed in this group ($p=0.048$). Patients with elevated PaCO₂ levels exhibited significantly higher AHI and ODI values compared to those with normal PaCO₂ levels ($p=0.048$, $p=0.008$, respectively). Additionally, the mean minSpO₂ and meanSpO₂ values were lower in the high PaCO₂ group ($p=0.013$, $p=0.008$, respectively).

Conclusion: In individuals with OS, reduced sleep efficiency is noted, and elevated PaCO₂ levels are associated with decreased minSpO₂ and meanSpO₂ levels, higher ODI and AHI values. The utilization of LTOT is linked to improved sleep efficiency.

Keywords: Apnea, hypoventilation, obesity, polysomnography

ÖZET

Amaç: Bu çalışmanın amacı, Kronik obstrüktif akciğer hastalığı (KOAH) olup obstrüktif uyku apnesi (OUA) belirtileri nedeniyle polisomnografi yapılanlarda, overlap sendromu (OS) prevalansını belirlemektir. Ayrıca, hypoventilasyon ve uzun süreli oksijen tedavisinin (USOT) OUA şiddetine etkisini inceledik.

Gereç ve Yöntemler: Ağustos 2012'den Eylül 2022'ye kadar OUA semptomları olup polisomnografi yapılan KOAH hastalarını retrospektif olarak inceledik. Hastaların vücut kitle indeksleri (VKİ), apne-hipopne indeksleri (AHI), oksijen desatürasyon indeksleri (ODI), minimum ve ortalama oksijen satürasyon değerleri (minSpO₂ ve ortalamaSpO₂), uyku aktiviteleri, REM periyodu yüzdeleri (%REM), USOT kullanıp kullanmadıkları, kan hematokrit düzeyleri ve uyanık arteriyel karbondioksit parsiyel basıncı (PaCO₂) seviyeleri kaydedildi.

Bulgular: Çalışmaya toplam 81 KOAH'lı birey dahil edildi. AHI>5 ve OS olan birey sayısı 76 (%93,9) idi. Çalışmaya dahil edilenlerin 9'u hafif, 24'ü orta ve 43'ü şiddetli OSA olarak bulundu. Ortalama uyku etkinliği 78,3 (±16,2) ve %REM değeri 7.3 idi. Hastaların 16'sı (%19.7) USOT alıyordu. Uyku etkinliği USOT kullanan grupta istatistiksel olarak daha yüksekti ($p=0,048$). PaCO₂'si yüksek olan grupta AHI ve ODI değerleri olmayan gruba göre istatistiksel olarak yüksek bulundu (sırasıyla; $p=0,048$, $p=0,008$). Ayrıca minSpO₂ ve meanSpO₂ değerleri PaCO₂'si yüksek olan grupta daha düşük bulundu (sırasıyla $p=0,013$, $p=0,008$).

Sonuç: KOAH-OSA overlap hastalarda uyku etkinliği düşüktür ve nokturnal hypoventilasyon daha düşük minSpO₂ ve meanSpO₂, daha yüksek ODI ve AHI ile ilişkilidir. USOT kullanımı OS'li hastalarda uyku etkinliğini artırmaktadır.

Anahtar Kelimeler: Apne, hypoventilasyon, obezite, polisomnografi

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INTRODUCTION

Obstructive sleep apnea (OSA) is a common sleep disorder with increasing incidence, usually accompanied by desaturation and arousal secondary to the collapse of the upper airways. The sum of the number of apneas and hypopneas per hour (apnea-hypopnea index-AHI) is an essential clinical parameter used to reflect the severity of the disease (1). The most associated risk factors for OSA in adults are increased body mass index, age, and wider neck circumference (>43 cm in males, >38 cm in females) (2). However, OSA can occur in people who do not have any of these risk factors. Additionally, OSA is usually linked to lung conditions such as interstitial lung disorders, chronic obstructive pulmonary disease (COPD), and asthma (3,4). Among these diseases, COPD is the group most frequently associated with OSA. The coexistence of OSA and COPD in the same patient is known as overlap syndrome (OS)/OLDOSA syndrome. The American Thoracic Society recommends a “screening” strategy to detect OS with chronic stable hypercapnia, but studies in this area are limited (5). Patients with OLDOSA syndrome have lower quality of life, more severe respiratory symptoms, and a greater relative risk of hospitalization and mortality than those with either disease condition (6,7). CPAP use in individuals with overlap syndrome has been shown to reduce all-cause hospitalizations and severe COPD acute exacerbations, contributing to better outcomes (8). Given the high frequency of COPD and OSA, a sizable patient population is likely affected by both conditions. Unfortunately, prevalence data for OLDOSA syndrome are insufficient.

In this manuscript, we investigated the frequency of OSA in patients who were diagnosed with COPD in our clinic and underwent polysomnography to evaluate their symptoms.

MATERIALS and METHODS

This retrospective observational study was conducted in accordance with the Helsinki Declaration and received approval from the Ethics Committee of Erciyes University Faculty of Medicine Hospital (Ethics Committee Decision No: 2023/379). We analyzed the medical records of patients diagnosed with COPD and symptomatic for OSA between August 2012 and September 2022 at a tertiary adult pulmonology clinic. Polysomnography recordings obtained through all-night monitoring were analyzed using the following methods: sleep monitoring with six-channel electroencephalography, two-channel electrooculography, and one-channel electromyography; respiratory monitoring with a thermistor and nasal pressure sensor, piezo crystal effort belts for thoraco-abdominal movement detection, and a pulse oximeter; single-lead electrocardiogram; and bilateral tibial electromyography and a body position detector.

The diagnosis of OSA was made according to the diagnostic criteria for OSA in the International Classification of Sleep Disorders Third Edition (7-9). The following parameters were recorded from the polysomnography reports: BMI, AHI, ODI, minSpO₂, and meanSpO₂ values, sleep efficiency, REM%, whether the patients used LTOT, and blood hematocrit levels and awake PaCO₂ levels in the system. Patients with PaCO₂ levels \geq 45 mm Hg were considered to have high PaCO₂ levels.

Data were analyzed using descriptive statistics to determine the frequency of OSA in patients with COPD. The awake PaCO₂ level, an indicator of hypoventilation, was examined, along with exploring the relationship between LTOT use and sleep parameters as well as OSA severity.

Statistical Analysis

Statistical analyses were conducted using SPSS software (Statistical Package for the Social Sciences, version 15.0; IBM Corp., Armonk, NY, USA) and Turcosa. Shapiro-Wilk's test statistics, a histogram, and a Q-Q plot were employed to assess the distribution of the study's data. The results were then presented as mean, standard deviation, or median. For categorical data, frequency and group percentages were reported. Unpaired t-test, Mann-Whitney U test, and Kruskal-Wallis test were utilized to compare data distributed by PaCO₂ levels and LTOT using the status of patients with OS. Pearson correlation was employed for the correlation analysis, with values ranging between -1 and 1. p-values were considered statistically significant if they were less than 0.05.

RESULTS

A total of 81 individuals with COPD were included in the study. Five individuals with AHI <5 were excluded from the study. Most of the patients were male (65.4%). The mean age of the patients was 64.4 ± 9.73 , which was higher in women than in men (67.5 and 63.6, respectively; $p = 0.236$). The mean sleep efficiency was found to be 78.3% (± 16.2). The mean value of REM% was 7.3. Sixteen of the patients (19.7%) were receiving LTOT. The number of individuals with AHI > 5 and OS was 76 (93.9%). Of those included in the study, nine had mild OSA, 24 had moderate OSA, and 43 had severe OSA (Table).

No statistically significant correlation exists between BMI and AHI variables ($r = 0.2162$, $p = 0.053$). The mean minSpO₂ value of the participants was 67.2 ± 17.0 , and the meanSpO₂ value was 84.0 ± 7.7 . There is no statistically significant difference between the OSA severity categories regarding BMI averages ($p = 0.378$). A negative, weak, statistically significant correlation was observed between BMI and minSpO₂ variables ($r = -0.3746$, $p < 0.001$). No

Table. Demographic, polysomnographic values and hematocrit and PaCO₂ levels of the patients

	Men (n=52)	Women (n=29)	Total (n=81)
Age			
Mean (SD)	63.6 (10.4)	67.5 (8.47)	64.4 (9.73)
BMI			
Mean (SD)	33.6 (10.2)	39.7 (7.69)	35.8 (9.77)
PaCo2			
Normal	43 (82.7%)	23 (79.3%)	66 (81.5%)
High	9 (17.3%)	6 (20.7%)	15 (18.5%)
AHI			
Mean (SD)	38.7 (27.6)	43.6 (37.1)	40.4 (31.2)
ODI			
Mean (SD)	61.8 (37.9)	73.1 (51.9)	65.6 (42.6)
Sleep Duration			
Mean (SD)	306 (58.9)	304 (65.9)	306 (61.1)
Sleep Efficiency			
Mean (SD)	79.3 (13.8)	76.7 (19.9)	78.4 (16.2)
Hematocrit			
Mean (SD)	45.4 (7.37)	44.1 (6.08)	45.0 (6.93)
Median			45.8 [23.0, 61.1]
[Min, Max]	46.4 [23.0, 61.1]	44.6 [30.0, 55.4]	
REM%			
Mean (SD)	8.06 (6.43)	5.79 (7.77)	7.25 (6.98)
OSA Severity			
Mild	4 (7.7%)	5 (17.2%)	9 (11.1%)
Moderate	16 (30.8%)	8 (27.6%)	24 (29.6%)
Severe	29 (55.8%)	14 (48.3%)	43 (53.1%)
Non-OSA	3 (5.8%)	2 (6.9%)	5 (6.2%)
minSpO2			
Mean (SD)	69.8 (16.8)	65.5 (12.1)	68.2 (15.3)
meanSpO2			
Median			86.5 [61.0, 94.0]
[Min, Max]	88.0 [67.0, 94.0]	82.0 [61.0, 94.0]	
Using LTOT			
No	46 (88.5%)	19 (65.5%)	65 (80.2%)
Yes	6 (11.5%)	10 (34.5%)	16 (19.8%)

BMI: body mass index, **PaCO₂:** partial arterial pressure of carbon dioxide, **AHI:** apnea-hypopnea index, **ODI:** oxygen desaturation index, **minSpO₂:** minimum oxygen saturation, **meanSpO₂:** mean oxygen saturation, **REM%:** REM period percentages, **LTOT:** long-term oxygen use

statistical correlation was found between BMI and sleep efficiency, hematocrit levels, and REM%.

Sleep efficiency was statistically higher in the group using LTOT (85% and 74%, respectively; p=0.048), but no significant correlation was found with REM%. Additionally, BMI and AHI values did not differ significantly in the group that received LTOT compared to the group that did not. The minSpO₂ value was found to be significantly lower in the group without LTOT compared to the group that received LTOT (58.2 vs 70.7, respectively; p=0.003). The mean hematocrit level of the participants was 44.9 ± 6.9. Hematocrit levels did not statistically significantly relate to AHI, ODI, BMI, minSpO₂ factors,

PaCO₂ categories, or LTOT usage status (p > 0.05). A positive, weak, and statistically significant correlation was observed between hematocrit and SpO₂ < 90 duration (r = 0.3125, p = 0.029).

AHI and ODI values were statistically higher in the group with high PaCO₂ than in the group without (p = 0.048 and p = 0.008, respectively) (Figure). Additionally, the mean values of minSpO₂ and meanSpO₂ were lower in the high PaCO₂ group compared to the group without high PaCO₂ (p = 0.013 and p = 0.008, respectively). No significant relationship was observed between PaCO₂ levels and BMI, age, or sleep efficiency.

DISCUSSION

Our study showed that the incidence of OSA increases in patients with COPD, independent of BMI. This condition is called ‘Overlap Syndrome’. It has been demonstrated that high PaCO₂ causes more severe OSA and lower minSpO₂ and meanSpO₂. Also, the use of LTOT increased sleep efficiency and improved nocturnal desaturations. However, correction of nocturnal hypoxemia with LTOT alone is not recommended in these patients. COPD is a lung condition that results in continuous, frequently worsening airflow restriction due to anomalies in the airways and alveoli. In low- and middle-income countries, COPD is one of the three leading causes of death worldwide (9). Hypoventilation is the leading cause of decreased oxygen saturation during

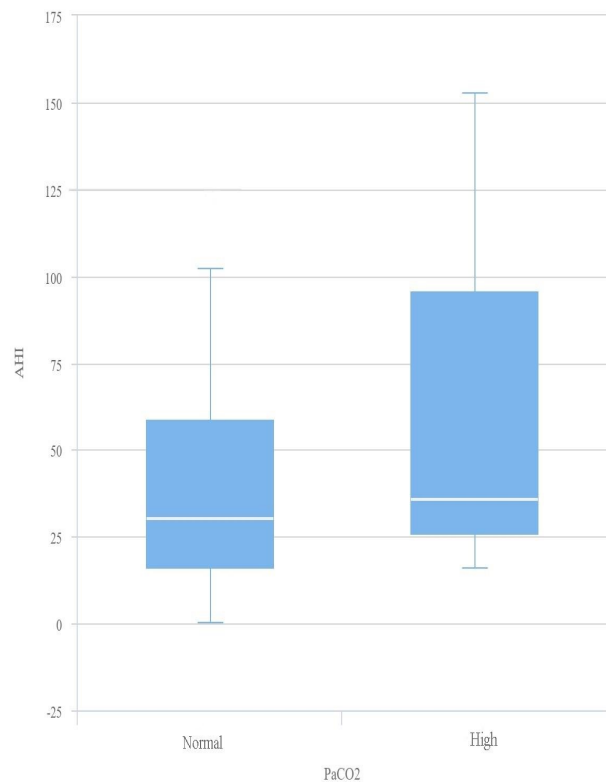


Figure. Box plot graph for PaCO₂ and AHI variables.

sleep in COPD. Nocturnal hypoxemia measurements of overnight oxygen saturation (nighttime oximetry) and polysomnography are more commonly used. Patients with COPD-OSA overlap have a worse prognosis than either condition alone. During sleep, patients with OS have more frequent nocturnal desaturations than OSA patients without COPD, and hypoxemia and hypercapnia are more frequent (10). Individuals with OS have lower meanSpO₂, more profound oxidative stress, more inflammation, vascular endothelial dysfunction, and accelerated atherosclerosis in patients (10,11). So, these patients should be detected early, and positive pressure ventilation should be applied to reduce exacerbations and mortality. OSA has been reported with a frequency of 84.6% in COPD patients, who are mainly used for the evaluation of excessive daytime sleepiness (12). In our study, this rate was slightly higher (93.7%). This may be due to the higher number of patients.

One study showed a high prevalence of OSA (58%) in COPD patients without OSA symptoms was associated with BMI (13). However, in our study, the frequency of OSA increased independently of BMI in patients with COPD. This may be because our participants were symptomatic patients, and the number of patients was lower. Also, this is a retrospective study, and prevalence could not be assessed because not all COPD patients were screened. Another reason is that low BMI is associated with the severity of COPD. It is known that nocturnal hypoventilation is more common in severe COPD patients and that breathing disorders during sleep are increased.

Hypercapnia seen in patients with OSA is attributed to comorbidities such as obesity, which causes hypoventilation, COPD, and the severity of OSA. In patients with obesity hypoventilation syndrome or COPD concurrent with OSA, hypercapnia may persist during wakefulness. A previous study indicated that individuals who are hypercapnic, even when awake, have lower meanSpO₂ levels than those without hypoventilation. Additionally, awake hypoventilation was more frequently observed in individuals with the overlap syndrome of OLDOSA. The study also found that the group with PaCO₂ levels >45 had a lower AHI than the group without hypercapnia. It has been reported that PaCO₂ levels are higher in patients with more airflow limitation (forced expiratory volume in 1 second - FEV₁ levels) in pulmonary function tests. In our study, patients with daytime hypercapnia had higher mean values of AHI and ODI. Consistent with existing literature, hypoventilated patients exhibited lower meanSpO₂ and minSpO₂ values. Our study also revealed that patients with awake hypoventilation spent less time in rapid eye movement (REM) sleep compared to those without hypoventilation (14). OSA should be considered even in COPD patients with mild airflow limitation. However, patients with COPD, even without OSA, experience difficulties

initiating and maintaining sleep compared to healthy individuals and report excessive daytime sleepiness (ESS) (15). Nocturnal oxygen desaturation affects approximately half of individuals with COPD. Increased airway collapse and impaired ventilation control, particularly during the REM period, lead to hypoventilation and gas exchange abnormalities (16). Studies have shown that 27-70% of patients with COPD who are not hypoxemic while awake may experience significant desaturation, particularly during REM sleep (17). Furthermore, obstructive events were observed to increase with higher PaCO₂ and lower pH when oxygen was administered only at night to individuals with OS (18). Supplemental oxygen therapy has been shown to reduce mortality when used for more than 18 hours a day in patients with nocturnal hypoxemia. Some studies, including ours, have indicated that correcting nocturnal hypoxemia in patients with COPD can improve sleep quality (19,20). However, oxygen therapy alone is not recommended for treating nocturnal hypoxemia. Previous systematic reviews have demonstrated an increased prevalence of cardiovascular diseases such as coronary artery disease, hypertension, heart failure, and peripheral vascular disease in patients with overlapping COPD and OSA (21,22). The most common conditions observed in this group were hypertension and pulmonary hypertension. Our study did not assess the prevalence of cardiovascular diseases due to the unknown severity of COPD and the patients' comorbidities.

We acknowledge several limitations of this study. Initially, only patients with symptomatic OSA (ESS score \geq 10) were included. This may explain the prevalence of co-existing OSA in patients with COPD and excessive daytime sleepiness. Previous studies have reported a significant relationship between AHI and ESS. It has been demonstrated that the sensitivity of ESS in detecting OSA can be up to 79% (23-28). However, OSA can also occur in cases without excessive daytime sleepiness. Therefore, we may have missed some OSA patients who are asymptomatic due to the limited sensitivity of ESS. Another limitation is that the severity of airflow limitation, the number of exacerbations, and comorbidities of the patients could not be included in the study due to insufficient records.

Conclusion

The coexistence of COPD and OSA is more prevalent than previously estimated. OSA tends to be more severe in patients with high PaCO₂ levels. While LTOT can enhance sleep efficiency, it may not be adequate for patients with the OLDOSA syndrome. Early identification of the OLDOSA syndrome and treatment with positive airway pressure can significantly decrease mortality, exacerbations, and morbidity.

Ethics Committee Approval: Ethical approval was obtained from the Ethics Committee of Erciyes University, Faculty of Medicine (Approval Date: 31.05.2023, Number: 2023/379).

Informed Consent: Written informed consent was obtained from all participants in this study.

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REFERENCES

- Foster GD, Borradaile KE, Sanders MH, Millman R, Zammit G, Newman AB, et al. A randomized study on the effect of weight loss on obstructive sleep apnea among obese patients with type 2 diabetes: The Sleep AHEAD study. *Archives of Internal Medicine*. 2009;169(17):1619-1626.
- Stelmach-Mardas M, Brajer-Luftmann B, Kuśnierczak M, Batura-Gabryel H, Piorunek T, Mardas M. Body mass index reduction and selected cardiometabolic risk factors in obstructive sleep apnea: meta-analysis. *Journal of Clinical Medicine*. 2021;10(7):1485.
- Alkhalil M, Schulman ES, Getsy J. Obstructive sleep apnea syndrome and asthma: the role of continuous positive airway pressure treatment. *Ann Allergy Asthma Immunol*. 2008;101(4):350-357.
- Inönü Köseoğlu H, Kanbay A, Köktürk O. An important concomitancy: interstitial lung diseases and sleep related breathing disorders. *Tuberkuloz ve Toraks*. 2014;62(3):231-235.
- Malhotra A, Schwartz AR, Schneider H, Owens RL, DeYoung P, Han MK, et al. Research priorities in pathophysiology for sleep-disordered breathing in patients with chronic obstructive pulmonary disease. An official American thoracic society research statement. *American Journal of Respiratory and Critical Care Medicine*. 2018;197(3):289-299.
- Kendzierska T, Leung RS, Aaron SD, Ayas N, Sandoz JS, Gershon AS. Cardiovascular outcomes and all-cause mortality in patients with obstructive sleep apnea and chronic obstructive pulmonary disease (overlap syndrome). *Annals of the American Thoracic Society* 2019;16(1):71-81.
- Ioachimescu OC, Janocko NJ, Ciavatta MM, Howard M, Warnock MV. Obstructive Lung Disease and Obstructive Sleep Apnea (OLDOSA) cohort study: 10-year assessment. *Journal of Clinical Sleep Medicine : JCSM : Official American Academy of Sleep Medicine Publication*. 2020;16(2):267-277.
- Sterling KL, Pépin JL, Linde-Zwirble W, Chen J, Benjafield AV, Cistulli PA, et al. Impact of positive airway pressure therapy adherence on outcomes in patients with obstructive sleep apnea and chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine* 2022;206(2):197-205.
- Meghji J, Mortimer K, Agusti A, Allwood BW, Asher I, Bateman ED, et al. Improving lung health in low-income and middle-income countries: from challenges to solutions. *The Lancet*. 2021;397(10277):928-940.
- Van Zeller M, Basoglu OK, Verbraecken J, Lombardi C, McNicholas WT, Pepin JL, et al. Sleep and cardiometabolic comorbidities in the obstructive sleep apnoea-COPD overlap syndrome: data from the European Sleep Apnoea Database. *ERJ Open Res*. 2023;9(3): 00676-2022.
- Papaioannou AI, Fouka E, Nena E, Bakakos P, Steiropoulos P. Patient-reported outcome measurements in patients with COPD-obstructive sleep apnea overlap syndrome: Time for Action? *Journal of Personalized Medicine*. 2022;12(12):1951.
- Guilleminault C, Cumiskey J, Motta J. Chronic obstructive airflow disease and sleep studies. *The American Review of Respiratory Disease*. 1980;122(3):397-406.
- Owens RL, Malhotra A. Sleep-disordered breathing and COPD: the overlap syndrome. *Respiratory Care*. 2010;55(10):1333-44; discussion 44-46.
- Beaudin AE, Raneri JK, Ayas NT, Skomro RP, Smith EE, Hanly PJ. Contribution of hypercapnia to cognitive impairment in severe sleep-disordered breathing. *J Clin Sleep Med*. 2022;18(1):245-254.
- Sandek K, Andersson T, Bratel T, Hellström G, Lagerstrand L. Sleep quality, carbon dioxide responsiveness and hypoxaemic patterns in nocturnal hypoxaemia due to chronic obstructive pulmonary disease (COPD) without daytime hypoxaemia. *Respiratory Medicine*. 1999;93(2):79-87.
- Grassion L, Gonzalez-Bermejo J, Arnulf I, Patout M. Diagnosing sleep disordered breathing in patients with chronic pulmonary disease: which test for which patient? *Breathe*. 2023;19(1):220199.
- Lewis CA, Fergusson W, Eaton T, Zeng I, Kolbe J. Isolated nocturnal desaturation in COPD: Prevalence and impact on quality of life and sleep. *Thorax*. 2009;64(2):133-138.
- Alford NJ, Fletcher EC, Nickeson D. Acute oxygen in patients with sleep apnea and COPD. *Chest*. 1986;89(1):30-38.
- Calverley PM, Brezinova V, Douglas NJ, Catterall JR, Flenley DC. The effect of oxygenation on sleep quality in chronic bronchitis and emphysema. *The American Review of Respiratory Disease*. 1982;126(2):206-210.
- Owens RL, Derom E, Ambrosino N. Supplemental oxygen and noninvasive ventilation. *European Respiratory Review*. 2023;32(167):220159.
- 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(7):1199-1207.
- Shawon MS, Perret JL, Senaratna CV, Lodge C, Hamilton GS, Dharmage SC. Current evidence on prevalence and clinical outcomes of co-morbid obstructive sleep apnea and chronic obstructive pulmonary disease: A systematic review. *Sleep Med Rev*. 2017;32:58-68.
- Warnken-Miralles MD, López-García F, Zamora-Molina L, Soler-Sempere MJ, Padilla-Navas I, García-Pachón E. Sarcopenia index in hospitalized patients with chronic obstructive pulmonary disease exacerbation. *Medicina*. 2021;81(3):323-328.
- Cavallès A, Brinchault-Rabin G, Dixmier A, Goupil F, Gut-Gobert C, Marchand-Adam S, et al. Comorbidities of COPD. *European Respiratory Review: An Official Journal of the European Respiratory Society*. 2013;22(130):454-475.
- Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: Revised European Consensus on definition and diagnosis. *Age and Ageing*. 2019;48(1):16-31.
- Jaitovich A, Barreiro E. Skeletal muscle dysfunction in chronic obstructive pulmonary disease. What we know and can do for our patients. *American Journal of Respiratory and Critical Care Medicine*. 2018;198(2):175-186.
- Evans RA, Morgan MD. The systemic nature of chronic lung disease. *Clinics in Chest Medicine*. 2014;35(2):283-293.
- Amra B, Rahmati B, Soltaninejad F, Feizi A. Screening questionnaires for obstructive sleep apnea: An updated systematic review. *Oman Medical Journal*. 2018;33(3):184-192.