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ORIGINAL ARTICLE

# Sleep quality in COPD patients: correlation with disease severity and health status

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## ABSTRACT

**Objective:** To evaluate clinical predictors of poor sleep quality in COPD patients with and without obstructive sleep apnea (OSA). **Methods:** Consecutive stable patients with COPD were evaluated for OSA by means of overnight polysomnography; for sleep quality by means of the Pittsburgh Sleep Quality Index (PSQI); and for disease impact by means of the COPD Assessment Test. COPD severity was graded in accordance with the 2020 GOLD guidelines. Predictors of poor sleep quality were evaluated by multivariate logistic regression analysis. **Results:** We studied 51 patients with COPD alone and 51 patients with COPD and OSA. Both groups had similar age (66.2 ± 9.2 years vs. 69.6 ± 10.7, p = 0.09) and airflow limitation (p = 0.37). Poor sleep quality was present in 74.8% of the study participants, with no significant difference between COPD patients with and without OSA regarding PSQI scores (p = 0.73). Polysomnography showed increased stage 1 non-rapid eye movement sleep and arousal index, as well as reduced sleep efficiency and stage 3 non-rapid eye movement sleep, in the group of patients with COPD and OSA (p < 0.05). Independent predictors of poor sleep quality were GOLD grade C/D COPD (OR = 6.4; 95% CI, 1.79-23.3; p < 0.01), a COPD Assessment Test score ≥ 10 (OR = 12.3; 95% CI, 4.1-36.5; p < 0.01), and lowest $SaO_2$ < 80% (p < 0.0001). **Conclusions:** Poor sleep quality is quite common in patients with COPD and is associated with severe COPD and poor health status, having a negative impact on overall quality of life. Despite changes in polysomnography, OSA appears to have no impact on subjective sleep quality in COPD patients.

**Keywords:** Pulmonary disease, chronic obstructive; Sleep Quality; Sleep apnea, obstructive; Health status.

## INTRODUCTION

COPD is a common respiratory illness that is characterized by chronic airway obstruction and is associated with abnormal inflammatory responses in the lungs.[1] It has been associated with high morbidity, mortality, and health care costs. Changes in lung mechanics lead to the main clinical manifestations of dyspnea, cough, and chronic expectoration.[2,3]

COPD increases susceptibility to sleep disturbance. Patients may be predisposed to poor sleep quality due to upper and lower airway abnormalities. Patients with COPD and obstructive sleep apnea (OSA) may experience symptoms such as snoring, witnessed apneas, difficulty falling asleep, and fragmented sleep.[4] Nocturnal alterations in ventilation and respiratory symptoms can result in difficulty maintaining sleep, possibly causing daytime somnolence, cognitive changes, and altered immune function.[5] Severe disease has been associated with reduced sleep quality, including decreased total sleep time, decreased sleep efficiency, and sleep fragmentation.[6,7] Potential causes of disturbed sleep in patients with COPD include impaired lung function and hyperinflation, which are exacerbated during sleep.[8] Moreover, OSA may occur in 10-30% of patients with COPD. The co-occurrence of COPD and OSA has been associated with poor health outcomes.[9] Corticosteroid use and increased upper airway edema caused by rostral fluid shift in the supine position, with a consequent increase in neck circumference, may contribute to this co-occurrence. These effects together may increase the work of breathing, leading to increased arousability and sleep disturbance.[10]

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Sleep quality is a major determinant of overall health status and quality of life. Although the importance of sleep in patients with COPD has been extensively studied, nighttime symptoms and their daytime consequences are often not reported by patients and may go unnoticed by physicians.[7]

We hypothesized that patients with COPD + OSA have poorer sleep quality than do those with COPD alone. Therefore, the objective of this study was to describe sleep quality, as measured by the Pittsburgh Sleep Quality Index (PSQI), in patients with COPD+ OSA and in those with COPD alone from three referral centers, as well as to evaluate clinical predictors of poor sleep quality and its possible associations with disease severity.

## METHODS

For this cross-sectional study we recruited COPD patients from three referral centers. All patients were consecutively evaluated, constituting a convenience sample.

The study was approved by the local research ethics committee (Protocol no. 68781017.3.0000.5192) and was performed in accordance with the Declaration of Helsinki. All participants gave written informed consent.

We included patients in the 44- to 91-year age bracket with a confirmed diagnosis of COPD and without hospitalization in the past three months. COPD was defined on the basis of pulmonary function testing as an $FEV_1/FVC$ ratio of < 0.70 and an $FEV_1$ of < 80% of the predicted value.[11] We excluded patients with respiratory diseases other than COPD, patients with previously diagnosed OSA, obese patients (i.e., those with a BMI > 40 kg/m$^2$), patients with neurological diseases, patients using home oxygen therapy, and patients who could not visit the sleep laboratory.

All patients underwent overnight polysomnography in a sleep laboratory with standard equipment (Alice 6; Philips Respironics, Murrysville, PA, USA), undergoing the following: electroencephalography, electrooculography, submental electromyography, electromyography of the left and right anterior tibial muscles, electrocardiography, inductance plethysmography with two thoracoabdominal bands, oronasal airflow measurement with a thermistor and a nasal pressure cannula, pulse oximetry, and body position monitoring. Sleep and sleep stages were determined by an experienced observer, in accordance with the recommendations of the American Academy of Sleep Medicine. Apnea was defined as an airflow reduction > 90% for more than 10 s, and hypopnea was defined as an airflow reduction > 30% associated with oxygen desaturation > 3% or arousal from sleep.[12] COPD + OSA was defined as an apnea-hypopnea index (AHI) ≥ 15 events/h.

COPD severity was graded as A, B, C, or D, in accordance with the 2020 GOLD guidelines.[2,13]

Sleep quality was evaluated with the PSQI[14] and the Epworth Sleepiness Scale.[15] The PSQI provides a sensitive and specific measure of sleep quality. A global PSQI ≥ 5 was adopted for identification of "poor" sleepers. COPD severity was graded on the basis of the COPD Assessment Test (CAT) score, the modified Medical Research Council dyspnea scale score, and the frequency of exacerbations in the past year, which is associated with disease severity in COPD patients.[16,17]

### *Statistical analysis*

Normal distribution was evaluated with the Kolmogorov-Smirnov test, and the results were expressed as mean ± SD, median (IQR), or percentage, as appropriate. The two-tailed unpaired t-test or Mann-Whitney U test was used for independent variables, and the chi-square test was used for between-group comparisons. Univariate and multivariate logistic regression models were used to evaluate the presence of poor sleep quality and its predictors, which included age > 65 years, sex, GOLD grades C and D COPD, a CAT score ≥ 10, presence of hypertension and diabetes, a BMI > 25 kg/m$^2$, an AHI ≥ 15 events/h, and an Epworth Sleepiness Scale score > 10. A two-sided p-value of < 0.05 was considered significant. Data management and statistical analyses were performed with the IBM SPSS Statistics software package, version 22.0 (IBM Corporation, Armonk, NY, USA).

## RESULTS

As can be seen in Figure 1, of the 115 COPD patients enrolled in the study, 13 were excluded from analysis, a total of 102 COPD patients therefore being included. The sample included 51 patients with COPD alone and 51 patients with COPD + OSA (mean age, 66.2 ± 9.2 years vs. 69.6 ± 10.7 years, p > 0.05). Their baseline clinical characteristics, spirometric classification, GOLD classification, sleep efficiency, and oxygen data as assessed by polysomnography are presented in Table 1. Polysomnography data showed increased stage 1 non-rapid eye movement sleep and arousal index, as well as reduced sleep efficiency and stage 3 non-rapid eye movement sleep, in the COPD + OSA group (p < 0.05).

There were more males in the COPD + OSA group than in the COPD group (72.5% vs. 47.1%, p < 0.01). All patients were using long-acting beta-adrenergic agonists and long-acting anticholinergic bronchodilators, and adherence to the inhaled medications was checked. Those with GOLD grade D COPD (with a history of two or more exacerbations) were also using inhaled corticosteroids. There was a significant difference between the COPD and COPD + OSA groups regarding the lowest $SaO_2$ as assessed by polysomnography (p = 0.0153).

Table 2 presents the associations between PSQI component and global scores for both groups. PSQI component scores showed no significant differences

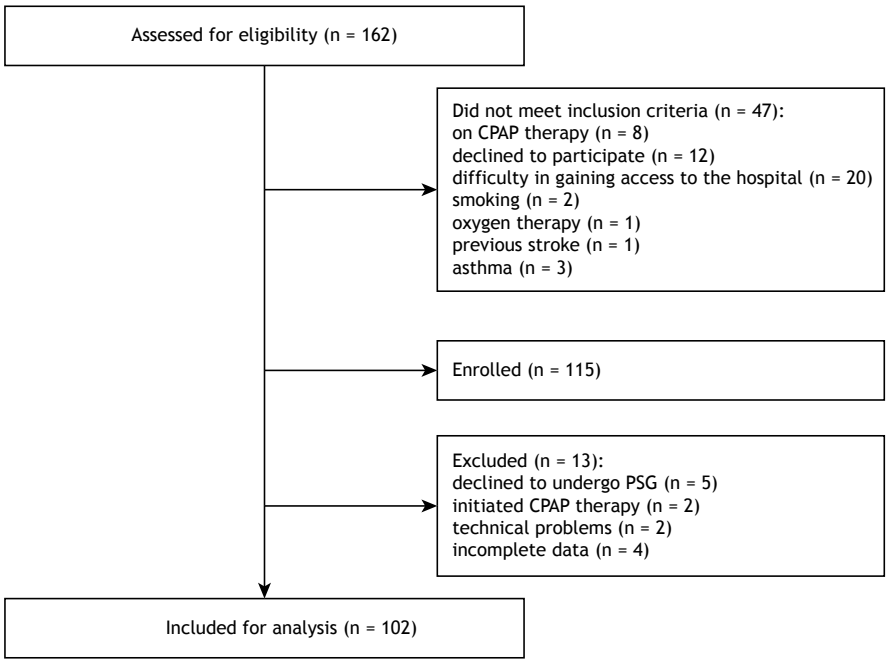


**Figure 1.** Flow chart of the study design. PSG: polysomnography.

between the groups. However, high PSQI global scores were observed in both groups.

Table 3 presents the results of the univariate and multivariate logistic regression analyses. GOLD grade C/D COPD and a CAT score ≥ 10 were independently associated with poor sleep quality (a PSQI ≥ 5), as was lowest $SaO_2$ < 80% ($p < 0.0001$). Sleep quality was not significantly associated with OSA, comorbidities, or BMI.

## DISCUSSION

In the present study we demonstrated the negative impact of COPD on sleep quality in a large sample of patients from three referral centers. We found that 1) poor sleep quality was very common in patients with COPD, even if they did not have comorbid OSA; 2) OSA had no impact on poor sleep complaints in COPD patients; and 3) frequent exacerbations (GOLD grade C/D COPD) and severe COPD (a CAT score ≥ 10) were associated with poor sleep quality.

Sleep has major effects on breathing and gas exchange in patients with COPD. The efficiency of diaphragmatic contraction may diminish during sleep, leading to increased reliance on accessory muscles to maintain ventilation.[18,19] Additionally, nocturnal hypoxemia can occur in patients with COPD despite adequate oxygenation during wakefulness; it frequently occurs during rapid eye movement sleep, leading to ventilation-perfusion mismatch.[20] Moreover, the supine position contributes to worsening airflow obstruction, which exacerbates hyperinflation and hypoventilation.[21] These factors increase susceptibility to sleep disturbance. However, sufficient attention has not been given to the effects of COPD-related impairments on sleep quality.[10]

We also examined the impact of comorbid OSA on sleep quality in patients with COPD. Poor sleep quality, as measured by the PSQI, was noted, regardless of comorbidity with OSA. This is in accordance with data showing that individuals with COPD sleep poorly.[4,6] OSA was present in half of the sample, even though none of the participants had received a previous diagnosis of OSA, thereby suggesting a low awareness of OSA in this population. We found that COPD + OSA patients had more pronounced oxygen desaturation during sleep. Thus, treating OSA would prevent an increase in oxyhemoglobin desaturation and interference with sleep quality in patients with COPD. Silva Junior et al.[20] showed that 60% of patients with COPD without daytime hypoxemia had some sleep disorder; in addition, they found that an $SaO_2$ of 90-94% during wakefulness predicted sleep disorders.

In the present study, patients with GOLD grade C/D COPD and most of the symptomatic patients (i.e., those with a CAT score ≥ 10) had higher PSQI scores. This is in agreement with previous reports stating that poor sleep quality in patients with COPD is related to poorer health status, disease that is more severe, and impaired ability to perform activities of daily living.[8,22-24]

The results of a study involving 480 COPD patients showed that higher PSQI scores were associated with an increased risk of exacerbations during the study's 18-month follow-up period.[25] The patients with high PSQI scores had a shorter time to symptom-based exacerbation and a higher risk of hospitalization. Moreover, chronic sleep deprivation and poor sleep

**Table 1.** Clinical characteristics of the study participants.[a]

| Variable | Total | Group | | p |
|---|---|---|---|---|
| | | COPD | COPD + OSA | |
| | (N = 102) | (n = 51) | (n = 51) | |
| Age, years | | 66.2 ± 9.1 | 69.6 ± 10.7 | 0.1546* |
| Males | 59 (57.8) | 24 (47.1) | 35 (68.6) | 0.0359† |
| Hypertension | 40 (39.2) | 23 (45.1) | 17 (33.3) | 0.3106† |
| Diabetes mellitus | 80 (78.4) | 43 (84.3) | 37 (72.5) | 0.2287† |
| Spirometric data | | | | |
| $FEV_1$, L | | 1.1 ± 0.2 | 1.3 ± 0.4 | 0.0717‡ |
| $FEV_1$, % predicted | | 44.6 ± 0.2 | 46.6 ± 0.2 | 0.2872‡ |
| FVC, L | | 2.0 ± 0.6 | 2.2 ± 0.8 | 0.0943‡ |
| FVC, % predicted | | 35.5 ± 15.4 | 61.5 ± 0.2 | 0.0902‡ |
| $FEV_1$/FVC, % predicted | | 55.3 ± 15.6 | 57.2 ± 14.4 | 0.2639‡ |
| Spirometric classification | | | | |
| Mild | 26 (25.5) | 12 (23.5) | 14 (27.5) | |
| Moderate | 36 (35.3) | 14 (27.5) | 22 (43.1) | 0.1091† |
| Severe | 40 (39.2) | 25 (49.0) | 15 (29.4) | |
| mMRC score | | | | |
| < 2 | 61 (59.8) | 31 (60.8) | 30 (58.8) | 1.000† |
| ≥ 2 | 41 (40.2) | 20 (39.2) | 21 (41.2) | |
| CAT score | | | | |
| < 10 | 22 (21.6) | 11 (21.6) | 11 (21.6) | 0.8098† |
| ≥ 10 | 80 (78.4) | 40 (78.4) | 40 (78.4) | |
| GOLD A/B COPD | 65 (63.7) | 35 (68.6) | 30 (58.8) | |
| GOLD C/D COPD | 37 (36.3) | 16 (31.4) | 21 (41.2) | 0.4101† |
| $FEV_1$, % predicted | | | | |
| < 40 | 43 (42.2) | 25 (49.0) | 18 (35.3) | 0.3734* |
| 41-59 | 34 (33.3) | 15 (29.4) | 19 (37.2) | |
| > 60 | 25 (24.5) | 11 (21.6) | 14 (27.5) | |
| PSG data | | | | |
| Sleep efficiency, % | | | | |
| < 85 | 79 (77.4) | 39 (76.5) | 40 (78.4) | 1.0000† |
| > 85 | 23 (22.6) | 12 (23.5) | 11 (21.6) | |
| Median $SaO_2$, % | | | | |
| ≥ 90 | 93 (91.2) | 48 (47.1) | 45 (44.1) | 0.4851† |
| < 90 | 9 (8.8) | 3 (2.9) | 6 (5.9) | |
| Lowest $SaO_2$, % | | | | |
| ≥ 90 | 17 (16.7) | 10 (9.8) | 7 (6.9) | |
| 80-89 | 63 (61.8) | 36 (35.3) | 27 (26.5) | 0.0153* |
| < 80 | 22 (21.5) | 05 (4.9) | 17 (16.6) | |
| Stage 1 sleep, % | | 9.8 ± 6.0 | 20.7 ± 14.6 | < 0.0001‡ |
| Stage 2 sleep, % | | 52.7 ± 12.9 | 49.1 ± 12.9 | 0.0619 ‡ |
| Stage 3 sleep, % | | 20.3 ± 9.5 | 15.7 ± 9.5 | 0.0127‡ |
| REM sleep, % | | 15.2 ± 8.57 | 14.4 ± 7.6 | 0.3219‡ |
| Arousal index, events/h | | 19.5 ± 12.2 | 37.6 ± 21.2 | < 0.0001‡ |
| Sleep efficiency, % | | 73.0 ± 16.2 | 68.0 ± 17.0 | < 0.0001‡ |
| AHI, events/h | | 6.8 ± 4.3 | 34.1 ± 20.2 | < 0.0001‡ |
| ODI, events/h | | 5.1 ± 7.4 | 23.4 ± 21.6 | < 0.0001‡ |

OSA: obstructive sleep apnea; mMRC: modified Medical Research Council dyspnea scale; CAT: COPD Assessment Test; PSG: polysomnography; REM: rapid eye movement; AHI: apnea-hypopnea index; and ODI: oxygen desaturation index. [a]Data presented as mean ± SD or n (%). *Chi-square test. **Chi-square test with Yates' correction. ‡t-test.

quality have been reported to impact immune function and increase susceptibility to infections.[26] Furthermore, frequent sputum production has been associated with nocturnal sleep disturbances and poor sleep quality.[27] In our study, patients with GOLD grade C/D COPD represent those with frequent exacerbations and more unstable respiratory symptoms, which negatively impact sleep quality. Consequently, poor sleep quality

**Table 2.** Pittsburgh Sleep Quality Index component and global scores for the group of patients with COPD alone and for that of those with COPD and obstructive sleep apnea.[a]

| PSQI components | Group | | p |
|---|---|---|---|
| | COPD (n = 51) | COPD + OSA (n = 51) | |
| Subjective sleep quality | 1 (1-2) | 1 (1-2) | 0.59 |
| Sleep latency | 1 (0-2) | 1 (0-2) | 0.27 |
| Sleep duration | 1 (1-2) | 1 (1-2) | 0.98 |
| Sleep efficiency | 1 (0-3) | 1 (0-2) | 0.84 |
| Sleep disturbances | 1.5 (1-2) | 1 (1-2) | 0.41 |
| Use of sleep medications | 0 (0-1) | 0 (0-0) | 0.35 |
| Daytime dysfunction | 0 (0-1) | 0 (0-2) | 0.17 |
| Global PSQI score | 7.5 (5.0-11.0) | 7.0 (4.0-11.0) | 0.73 |
| PSQI ≥ 5[b] | 39 (78) | 38 (75) | 0.68 |

PSQI: Pittsburgh Sleep Quality Index; and OSA: obstructive sleep apnea. [a]Data presented as median (IQR), except where otherwise indicated. [b]Data presented as n (%).

**Table 3.** Unadjusted and adjusted ORs for associations between clinical variables and sleep quality in patients with COPD and obstructive sleep apnea and in those with COPD alone.

| Variable | Univariate analysis | | | Coefficient | | Multivariate analysis | | |
|---|---|---|---|---|---|---|---|---|
| | OR (95% CI) | | p | (β) | SE | OR (95% CI) | | p |
| Age > 65 years | 0.52 | (0.20-1.33) | 0.17 | | | | | |
| Female sex | 1.10 | (0.45-2.74) | 0.82 | | | | | |
| GOLD C/D COPD | 6.47 | (1.80-23.40) | < 0.01 | 1.53 | 3.25 | 4.64 | (1.18-18.28) | 0.02 |
| CAT score ≥ 10 | 12.32 | (4.16-36.50) | < 0.01 | 2.30 | 5.70 | 9.92 | (3.22-30.54) | < 0.01 |
| Hypertension | 0.76 | (0.30-1.92) | 0.57 | | | | | |
| Diabetes | 0.54 | (0.20-1.47) | 0.22 | | | | | |
| BMI > 25 kg/m$^2$ | 1.05 | (0.43-2.58) | 0.90 | | | | | |
| Lowest $SaO_2$ < 80% (PSG) | 0.20 | (0.05-0.82) | 0.04 | 1.00 | 0.27 | 4.45 | (3.91-4.96) | < 0.0001 |
| OSA (AHI > 15 events/h) | 0.78 | (0.32-1.94) | 0.60 | | | | | |
| ESS score > 10 | 1.57 | (0.60-1.20) | 0.36 | | | | | |
| Constant | | | | −2.53 | 0.07 | 0.08 | (0.01-0.50) | 0.07 |

CAT: COPD Assessment Test; PSG: polysomnography; OSA: obstructive sleep apnea; AHI: apnea-hypopnea index; and ESS: Epworth Sleepiness Scale.

may be a marker for an exacerbating COPD phenotype and indicate a need for closer follow-up. On the other hand, promoting better sleep quality may reduce the risk of exacerbations and improve survival.

Comorbidities may worsen prognosis in patients with COPD. OSA has a high incidence, and patients with comorbid COPD + OSA may have a poorer prognosis than those with either COPD or OSA alone.[23] Reduced exercise tolerance may lead to obesity and muscle weakness, which may contribute to greater upper airway collapse. These factors may also contribute to the occurrence of both COPD and OSA.[9,28-30] Kapur et al.[12] described the negative impact of OSA on sleep and quality of life. Our study demonstrated that patients with COPD sleep poorly regardless of whether or not they have OSA. Current concepts about OSA endotypes (such as arousal threshold and reduced pharyngeal dilator function) and phenotypes (such as insomnia complaints, tiredness, and daytime sleepiness) play an important role in the different clinical manifestations and the subjective complaints related to sleep.[31] This variability in the clinical expression of OSA may have influenced our findings regarding sleep quality. Therefore, it is essential to identify OSA in order to prevent its negative effects on sleep quality in patients with COPD, as well as to predict disease complications and guide clinical management.[32]

One possible limitation of the present study is that depression, anxiety, or other psychological aspects of COPD were not assessed, and they might have an impact on disease control and sleep quality. Another limitation is the cross-sectional design of our study, which allows us to infer an association, but not causality, between COPD severity and poor sleep quality. The absence of a control group without COPD is yet another limitation of the study. However, the strength of our study lies in the large sample size, use of a strict protocol, performance of complete polysomnography, and detailed characterization of patients with COPD.

In the present study, OSA had no impact on worsening sleep problems (PSQI scores), although there were changes in polysomnography. Nocturnal symptoms related to COPD and frequent awakenings have the potential to impact quality of life.[5] Therefore,

we believe that it is important to shed light on this topic and identify predictors of poor sleep and their relationship to clinical outcomes.

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## AUTHOR CONTRIBUTIONS

DCSC: study conception and design, and analysis and interpretation of data; TCL and MVFP: study conception and design; OLLF: writing and reviewing of the manuscript, study conception, and analysis and interpretation of data; VKR, LAPON, and ADMF: study conception and design, analysis and interpretation of data, and final approval of the version to be submitted; FJPQJ: study conception and design, writing of the manuscript, and final approval of the version to be submitted; MMC: study design, writing of the manuscript, and final approval of the version to be submitted; and RPP: study conception and design, and final approval of the version to be submitted.

## CONFLICT OF INTEREST

None declared.

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