

Coexistent obstructive sleep apnea in patients with chronic obstructive pulmonary disease: Several unanswered questions need to be addressed

Chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea (OSA) are highly prevalent diseases and thus likely to coexist in the same patient; a disorder otherwise known as overlap syndrome (OS).^[1,2] A growing body of evidence has already tried to explore associations between these two diseases, in terms of epidemiology, overlapping pathophysiology, shared risk factors, presence of other comorbidities, clinical outcomes, and optimal management.^[3]

OSA and COPD share common risk factors and pathophysiological mechanisms and are both accompanied by several comorbidities. Age, obesity, and tobacco exposure are well-recognized risk factors,^[3] while both disorders are associated with systemic inflammation, oxidative stress, excitations in sympathetic activity, and endothelial dysfunction.^[1] Because OSA is characterized by intermittent whereas COPD by sustained hypoxia,^[3] impaired oxygenation during both wakefulness and sleep is observed in OS, and it is more pronounced compared to COPD or OSA alone.^[3]

Synergistically, these factors can increase the risk for the development, or progression of already-established comorbidities in OS. Notably, there is a growing interest on whether OS is associated with a higher burden of comorbidities than OSA or COPD alone.^[4] Cardiovascular disease (CVD) is the most prevalent one,^[5] which can alter patients' outcomes and lead in poor prognosis.^[1] In a landmark study,^[6] nontreated patients with OS carried a higher mortality and hospitalization risk compared to patients with COPD only. Overall and despite the existing evidence on OS, there are still debatable questions when OSA and COPD interact, so as to understand the cumulative impact of OS on the afflicted patients.

a. *Who to screen?* Clearly, there is an increasing demand to identify OSA among the COPD population and to search for characteristics and clinical phenotypes that could predict concurrent OSA in COPD.^[2] Obesity and common OSA symptoms (e.g., snoring, witnessed apneas, and excessive daytime sleepiness [EDS]) should guide clinicians to investigate for coexistent OSA, as well as presence of morning headaches and pulmonary hypertension, which could not only be attributed to COPD severity.^[3] Interestingly, body mass index (BMI) and smoking pack years, but not the

Epworth Sleepiness Scale (ESS)' score, were found to be predictors of coexistent OSA in a group of COPD patients.^[7] Moreover, increased risk for OSA in patients with COPD was related to higher scores in COPD Assessment Test and more prevalent cardiometabolic disease.^[8] In addition, the degree of airflow limitation is another issue to consider, as moderate-to-severe COPD is related to a high prevalence of OSA.^[9] Of note, hyperinflation and emphysema are inversely correlated with the severity of OSA in COPD patients,^[3] reinforcing the fact that the chronic bronchitis phenotype of COPD is strongly associated with OSA.

- b. *How to screen?* Well-accepted screening tools for OSA are not always valid in COPD individuals.^[10] Nevertheless, among them, the STOP-BANG questionnaire (SBQ) was found to be the most accurate.^[11] Interestingly, BMI ≥ 25 kg/m² and the presence of CVD perform better than other screening tools, such as the ESS or the SBQ, in identifying OSA in COPD.^[10]
- c. *How to diagnose?* Whereas COPD can easily be diagnosed by spirometry, OSA diagnosis requires a sleep study, which is more expensive and time-consuming. Sleep physicians should choose between the gold standard polysomnography (PSG) and respiratory polygraphy. This choice depends also on the policy for insurance coverage in different countries. It is worth noting that oximetry ideally combined with capnometry, apart from screening, might improve our understanding concerning the burden of hypoxia during sleep in COPD.
- d. *How to treat OS?* Effective treatment of OS with the appropriate type of positive airway pressure (PAP) device is another matter of debate. Different strategy approaches should be applied to OS patients with severe OSA and mild COPD than to those with mild OSA and severe COPD. Where OSA predominates, continuous PAP (CPAP) is the preferred modality, while bi-level PAP (BPAP) would be more appropriate when COPD prevails in OS. Interestingly, the severity of nocturnal hypoxia and daytime hypercapnia in OS patients precludes the success of treatment with CPAP and shows that BPAP should be the first choice in such patients.^[12]

In accordance with these findings, in this issue of this journal,^[13] the authors provide important evidence to support the screening of OSA in COPD patients with EDS.

In this cross-sectional study, the authors assessed for the presence of EDS (based on ESS score) in 301 stable COPD patients with severe and very severe airflow obstruction. Those with EDS ($n = 47$) underwent an attended PSG. A high prevalence of concurrent OSA in the subgroup of sleepy COPD participants was noted (70.2%), while the overall prevalence of OSA was approximately 10%. Of note, the selective evaluation with PSG of sleepy-only COPD patients, might have underestimated the true prevalence of OSA in this cohort.

Collectively, these findings add significant evidence to the existing literature on predicting the risk of OSA and highlight the need for further research on this topic.^[2] Considering the fact that OSA is fully reversible after treatment, its diagnosis is highly important, as previous data has shown that in patients with OS treatment of OSA can improve COPD related outcomes and increase patients' survival.^[6]

Objective sleep evaluation should be offered to all COPD patients, not only in the presence of well-known risk factors or symptoms of OSA,^[13] but whenever sleep-related issues are mentioned.^[14] Indeed, accumulating evidence shows that OS patients typically complain of fatigue, whereas insomnia is also a salient feature of sleep-reported issues in COPD patients.^[2] In conclusion, future research in this topic is needed so as to shed more light on the puzzling associations between OSA and COPD.

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Conflicts of interest

There are no conflicts of interest.

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