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COMMENTARY

OSA/COPD Overlap: Convergence on a Theme?

Commentary on Donovan et al. Poor outcomes among patients with chronic obstructive pulmonary disease with higher risk for undiagnosed obstructive sleep apnea in the LOTT cohort. *J Clin Sleep Med*. 2019;15(1):71–77.

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Obstructive sleep apnea (OSA) is a highly prevalent condition, impacting 14% of adult men and 5% of adult women aged 30–70 years in the United States,[1] characterized by recurrent cessation of airflow, increased respiratory effort, hypoxemia and sympathetic arousal.[2] Untreated OSA has been linked to severe adverse health outcomes including cardiovascular complications,[3–5] pulmonary hypertension,[6] neurocognitive impairment,[7] and metabolic effects,[8] as well as increased economic costs.[9] A small but significant portion of patients with OSA have so-called "overlap syndrome," characterized by comorbid chronic obstructive pulmonary disease (COPD).[10] Although prevalence of the OSA/COPD overlap syndrome remains unknown, evidence suggests that a majority of patients with COPD have comorbid OSA. For example, Soler and colleagues[11] reported an OSA prevalence of 65.9% among patients with moderate to severe COPD referred from a pulmonary rehabilitation facility. Due to the additive respiratory pathophysiology of OSA and COPD, patients with overlap syndrome experience worsened nocturnal hypoxemia and poorer outcomes, relative to patients with either OSA or COPD alone.[10,12,13]

In this issue of the *Journal of Clinical Sleep Medicine*, Donovan and colleagues[14] provide additional insight into the prevalence of OSA/COPD overlap syndrome and its effects on morbidity and mortality. Using survey data from the Long Term Oxygen Treatment Trial (LOTT),[15] a modified STOP-BANG score was calculated, excluding neck circumference as these data were not collected. Participants were subsequently classified as intermediate to high (modified STOP-BANG $\geq$ 3) or low (modified STOP-BANG $<$ 3) risk for OSA, resulting in 74% of patients evaluated being classified as having an intermediate to high risk for OSA. Relative to individuals at low risk, those at intermediate to high risk for OSA met the composite primary endpoint of death or first hospitalization more frequently (adjusted hazard ratio = 1.61, 95% confidence interval [CI], 1.01–2.58, P = .044). Although no differences were observed between groups for separate outcomes of risk of death or first hospitalization, patients at intermediate to high risk for OSA demonstrated poorer outcomes in the secondary endpoint domains of greater frequency of outpatient COPD exacerbations (incidence rate ratio 1.80, 95% CI 1.07–3.02) as well as poorer St. George's Respiratory Questionnaire (SGRQ) and Quality of Well Being (QWB) scores at baseline and at 12 months (P = .046 and P = .009, respectively). Notably, between-group differences in SGRQ and QWB scores were no longer significantly different at 36-month follow-up. The authors postulate that this finding might be due to attrition of individuals completing questionnaires, thus resulting in a lack of statistical power to detect differences between groups past 12 months. Additionally, patients at low risk of OSA might develop OSA in the years following enrollment, resulting in confounding.

In addition to providing valuable insight into the OSA/COPD overlap syndrome, this study demonstrates multiple strengths including robust COPD assessment, creative adaptation of the STOP-BANG questionnaire, and 3-year follow-up. All patients included in the LOTT trial had documented, stable COPD with moderate exercise-induced desaturation, thus avoiding the healthy user effect.[15] By only enrolling patients with sleep surveys completed by bed-partners, there was likely a more reliable history regarding witnessed apneas and presence or absence of snoring, and thus a higher validity to the calculated modified STOP-BANG score. Last, because the authors followed patients for 36 months post enrollment, this study was able to detect longitudinal differences between respiratory symptoms (ie, SGRQ) and quality of life (ie, QWB).

In addition to these strengths, there were several missed opportunities. First, applying the STOP-BANG among patients with COPD is potentially problematic, as the psychometric properties in this patient population are unknown. Second, the study was missing important data including neck circumference, and the modification in the STOP-BANG score likely contributed to its decreased sensitivity. Further, the LOTT trial excluded patients with excessive daytime sleepiness (Epworth score > 15), which likely eliminated many patients with moderate to severe OSA. Nonetheless, despite the STOP-BANG modification and exclusion of sleepy patients, results indicate statistically significant differences in composite primary endpoints of death or first hospitalization, as well as in secondary endpoints of outpatient COPD exacerbations and SGRQ and WQB scores at baseline and 12 months. In aggregate, these results suggest that observed differences

in morbidity and mortality outcomes between patients at intermediate to high risk for OSA and low risk for OSA are significant and likely underestimated in this retrospective review.

To address these limitations and advance understanding of OSA/COPD overlap syndrome, greater insight is required into pertinent etiology and disease trajectory. For example, optimal OSA screening approaches remain unclear. Home sleep apnea tests are inappropriate for patients with moderate to severe COPD,[16] and future research should continue to examine screening devices as well as psychometric performance of OSA screening questionnaires in multiple comorbid populations. Further, research into optimal timing of diagnostic testing and treatment of OSA post-hospitalization or post OSA-associated disease exacerbation can help to guide treatment decision-making. Last, given the fact that adherence to OSA treatment is variable,[17] research regarding optimal "dose" of OSA treatment for symptom resolution and improved outcomes among patients with OSA/COPD overlap, as well as methods of improving adherence to OSA treatment are of utmost importance.

In summary, the study by Donovan and colleagues[14] adds to the growing body of knowledge regarding prevalence of OSA/COPD overlap syndrome and highlights its adverse consequences, including morbidity and mortality. These results should be seen as a call to action for clinicians to identify and screen individuals at risk for OSA/COPD overlap syndrome, as well as for researchers to characterize additional OSA overlap syndromes and to define their impact on patient outcomes. Timely diagnosis and treatment of such patients is required to achieve a significant and durable impact on OSA-associated morbidity and mortality.

CITATION

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