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COMMENTARY

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Obstructive sleep apnea, hypertension, and obesity: A dangerous triad

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Obstructive sleep apnea (OSA) is the most common type of sleep-disordered breathing. It is characterized by recurrent partial or complete obstruction of the upper airways during sleep, which leads to repetitive episodes of reduction (hypopnea) or absence of airflow (apnea) and intermittent hypoxia and arousal.[1]

The major risk factors for OSA are obesity, male sex, and advanced age.[2] The prevalence of OSA is continuously increasing in developed countries in conjunction with the epidemic obesity.[3,4] The present "gold" standard for evaluation of sleep and sleep-related breathing is the polysomnography (PSG) with up to 12 recording channels including nasal and oral airflow, respiratory effort transducers, electroencephalography (EEG), electromyography (EMG), and oximetry.[5]

The severity of obstructive sleep apnea is classified based on the apnea-hypopnea index (AHI)—number of apneic/hypopneic episodes per hour: 5-15, mild; 15-30, moderate; 30 or more, severe.[4]

The Wisconsin Sleep Cohort study recently reported that the prevalence of moderate to severe OSA (ie, AHI ≥ 15 events per hour) was 10% (95% confidence interval (CI): 7-12) among 30- to 49-year-old men; 17% (95% CI: 15-21) among 50- to 70-year-old men; 3% (95% CI: 2-4) among 30- to 49-year-old women; and 9% (95% CI: 7-11) among 50- to 70-year-old women.[6] These estimated prevalence rates represent a substantial increase over the last 2 decades (relative increase of 14%-55%, depending on the subgroup).

There is overwhelming epidemiologic evidence supporting the causal, bidirectional relationship between OSA and hypertension (HTN). Not only that OSA predisposes patients to HTN development, but also increases an incidence of OSA in hypertensive patients.[4,7,8]

Numerous studies have shown the strong association between OSA and cardiovascular morbidity and mortality, including ischemic heart disease, heart failure, arrhythmias, large vessel disease, and cerebrovascular disease.[4,9,10] The main acute changes in OSA are intermittent hypoxia, intrapleural pressure changes, and sleep fragmentation, which together induce endothelial dysfunction, sympathetic nervous system and renin-angiotensin-aldosterone system activation, and increased oxidative stress.[4,11] Another mechanism, that potentially could contribute to the development of HTN in OSA, is increased activity of the renin-angiotensin-aldosterone system (RAAS).[12]

Obesity, especially central adiposity, has been recognized as one of the strongest risk factors for OSA for a long time. Due to current pandemic of obesity in the Western countries, the prevalence of OSA is likely to increase.[13] In the Sleep Heart Health Study, weight gain of 10 kilograms over a 5-year period conferred a 5.2- and 2.5-fold increase in the likelihood of increasing the AHI by 15 events per hour in men and women, respectively.[14] Obesity and OSA tend to coexist and they are associated with inflammation, insulin resistance, dyslipidemia, and high blood pressure (BP), but the causal relation is still not clear.[15]

While continuous positive airway pressure (CPAP) remains the main therapy for OSA, its effect on blood pressure (BP) reduction has not been established yet due to the multifactorial nature of HTN.[4] Moreover, the impact of CPAP treatment on BP is inconsistent: In minimally symptomatic patients, CPAP has a neutral effect on BP,[16] whereas in subjects with resistant hypertension, CPAP can decrease the systolic BP by 5-7 mm Hg.[17]

Although obesity is a risk factor for OSA and an independent risk factor for HTN, the influence of obesity on BP response to CPAP treatment in adults with OSA is unknown. Moreover, data regarding influence of obesity on BP response to CPAP treatment in adults with OSA are still scarce.

In this issue of the Journal, Kuna et al assessed the BP response to CPAP treatment in obese and non-obese adults with

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OSA.[18] This consecutive multicenter study included 188 OSA patients with AHI ≥ 15, which were divided into two groups: obese and non-obese subjects. Additionally, they underwent 24-hour BP monitoring and 24-hour urinary norepinephrine collection at baseline. Obesity was assessed by waist circumference, body mass index (BMI), and abdominal visceral fat volume (captured with magnetic resonance imaging [MRI]). Participants adherent to CPAP treatment were reassessed after 4 months. Primary outcomes were 24-hour mean arterial pressure (MAP) and 24-hour urinary norepinephrine level.

The results indicate that obesity was not the factor that influenced BP response to treatment of adults with OSA and that BP response to CPAP treatment was not related to baseline 24-hour urinary norepinephrine or change in 24-hour urinary norepinephrine after treatment. Several previous studies reported that change in sympathetic nervous activity, measured by plasma or urinary catecholamine levels, did not correlate with the BP response to CPAP treatment.[19-21] Although measurement of urinary catecholamine levels did not detect the effect of sympathetic overactivity on BP in adults with OSA, the authors postulate that it might be possible that measuring muscle sympathetic nerve activity could reveal a significant relationship because sympathetic overactivity has an important role in OSA-related cardiovascular remodeling[22] and contributes to a cardiovascular morbidity in these patients[23]

While the authors found that the participants with OSA had a significant reduction in 24-hour mean arterial pressure following CPAP treatment, there were no significant correlations between the three obesity measures (waist circumference, BMI, and abdominal visceral fat) and change in BP measures. In addition, investigators did not find differences in BP responses comparing obese and non-obese participants. The authors explained negative results by the limited number of subjects in both groups—obese and non-obese patients and suggested that larger studies are necessary.

Although the results appear negative, this current study definitely has several important strengths. First, the objective to determine the BP response after CPAP treatment in obese patients was novel. Second, the authors used several parameters for obesity assessment such as waist circumference, body mass index, and abdominal fat volume and not only body mass index, as it is the case with previous studies.

Continuous positive airway pressure is recognized as an effective therapy for OSA, but adherence is still suboptimal despite numerous developments in machine dynamics including quieter pumps, softer masks, and improved portability.[24] Adherence to CPAP remains relatively low (30%-60%), which continues to be the largest problem with this kind of therapy.[25]

The main limitation of the present study, which was also claimed by the authors, was a limited sample size that significantly decreased statistical power to less than 80%. The study did not include individuals who were non-adherent to CPAP in order to compare them with those who used CPAP. Additionally, the current investigation involved also normotensive individuals. However, previous studies revealed that patients with higher baseline BP and untreated or resistant HTN had the largest benefit from CPAP therapy.[17,26]

It is well known that obesity represents a major risk factor for OSA.[2] Surprisingly, there is still a lack of clinical data on the response (eg, BP reduction) to existing therapies such as CPAP in obese and non-obese patients with OSA. The detailed phenotyping and physiological characteristics of obese and non-obese OSA patients and their response to prescribed therapy remain to be clarified in larger, prospective, and randomized studies in the future.

CONFLICT OF INTEREST

None.

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