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EDITORIAL

Are we underestimating the lifelong benefits of therapy for obstructive sleep apnea?

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Obstructive sleep apnea (OSA) is a complex disorder involving the cardiovascular (CV), pulmonary, and metabolic systems. Characterized by marked daytime fatigue and reduced quality of life, OSA is independently associated with increased risk of hypertension,[1] cardiovascular disease (CVD),[2] including myocardial infarction (MI)[3] and ischemic stroke,[4] metabolic syndrome,[5] and all-cause mortality.[6] Currently, the most common treatment for OSA is continuous positive airway pressure (CPAP) during sleep, though its efficacy in reducing daytime fatigue and CVD risk factors depends largely on compliance to therapy, which is poor in the general population.[7] Lamberts et al[8] performed a large epidemiological study of OSA, using the Danish National Patient Registry (NPR; ~4.5 million; including 25,389 people diagnosed with OSA), which confirmed associations between OSA and risk of ischemic stroke and MI. Yet, that study failed to show that CPAP reduces the incidence of these adverse CV events.[8] On the other hand, a more recent study, which examined the same Danish NPR across a very similar time period, revealed that in people with OSA, CPAP reduces all-cause mortality.[9] This editorial evaluates these seemingly conflicting results, whereby CPAP appears to reduce mortality but not two of the largest contributors to mortality: stroke and MI.

Of interest, the study by Lamberts et al found that the associations between OSA and risk of MI and ischemic stroke occurred only in young people (aged 18–49 years).[8] However, the prevalence of OSA in this sample was only 0.7%, which is lower than in most other random populations (3%–7%).[10] Thus, many people with undiagnosed OSA likely contributed to the NPR control group, thereby biasing toward the null hypothesis and perhaps explaining the lack of an OSA effect in the older groups. Additionally, these authors were unable to find an effect of CPAP on stroke or MI incidence in any age-group. However, they do suggest that use of CPAP in the younger population with high CV risk warrants further investigation. This seems reasonable, especially considering possible benefits of CPAP on symptoms of daytime sleepiness,[11] plus the known CV benefits of CPAP, including reductions in both nocturnal and daytime blood pressure.[12–14] Thus, starting therapy earlier in life has a greater potential to reduce the long-term effects of OSA on the CV system, including reducing the burden of hypertension.[15] Should CPAP also be recommended for older people with OSA for CV outcomes alone? Lamberts et al[8] claim that OSA may have less of a role in the development of CVD in the elderly because the emergence of other CV risk factors, including hypertension, may attenuate the relative contribution of OSA to MI and stroke. However, given the

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findings by Jennum et al,[9] we believe a reinterpretation is warranted. This newer analysis revealed that CPAP therapy improves survival rate by approximately 30% in middle-aged and elderly men.[9] Furthermore, two main limitations of this study may have resulted in an underestimate of the benefits of CPAP, as partly acknowledged by these authors. First, there was no information on the severity of sleep apnea (eg, the apnea-hypopnea index [AHI]). Since people with more severe symptoms are more likely to be treated, we contend that the group that received CPAP likely had higher OSA burden at the onset of the study. If the disease burden was higher and yet survival improved, then the benefits of CPAP would be underestimated. Second, there was no information on CPAP adherence: if adherence was poor yet survival improved, this would also underestimate the potential benefit of consistently used CPAP.

Additionally, Jennum et al failed to find an effect of CPAP in the younger cohort (aged 20–39 years) and in women of any age. But, given the protective CV effect female sex has prior to menopause,[16] and the relatively low inherent risk of dying in the young, we would not expect CPAP therapy to affect mortality rates in populations with such low vulnerability (given the short duration of the study relative to life expectancy).

Taken together, we feel these studies provide strong evidence for the benefits of CPAP therapy across the life spans of people with OSA. In the young, CPAP reduces hypertension and may reduce the risk of an early-life adverse CV event.[8] In middle-aged and elderly people with OSA, CPAP improves overall survival possibly via similar effects on the CV system.[9] Such beneficial effects of CPAP could presumably be extrapolated to any other therapy that reduces the AHI. There are numerous other emerging therapies for OSA[17] and great effort to improve adherence to CPAP therapy.[18] Thus, future clinical trials of therapies for OSA ideally should employ large population approaches, and include randomized comparative-effectiveness trials, or placebo-controlled trials (eg, The Apnea Positive Pressure Long-term Efficacy Study).[19] Additionally, incorporation of information on adherence to therapy, plus important health status indicators such as blood pressure, AHI, and body mass index will aid investigation of the associations between OSA disease burden, CV risk, and the effect of therapy on survival.

Disclosure

The authors report no conflicts of interest in this work.

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