Perspective

Beyond continuous positive airway pressure for cardiovascular risk reduction in patients with obstructive sleep apnea

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Abstract

An accumulating body of evidence suggests a bidirectional relationship between sleep and cardiovascular (CV) health. A high level of evidence has linked obstructive sleep apnea (OSA) with cardiovascular disease (CVD). Accordingly, clinical sleep medicine emphasizes the diagnosis and treatment of OSA in the context of promoting CV health. While continuous positive airway pressure (CPAP), the mainstay treatment for OSA, is effective in improving several sleep-related quality-of-life outcomes and leads to modest reductions in blood pressure, there is currently insufficient evidence to justify using CPAP alone for improving CVD outcomes in OSA. Sleep physicians are uniquely positioned to expand their focus beyond the evaluation of OSA and administering CPAP, in efforts to enhance the CV health of sleep patients. Herein, we suggest the role of sleep physicians as CV preventionists. Key focus areas for managing CV risk beyond CPAP therapy in OSA include identifying comorbid disorders that are vital for optimizing CV health. This involves risk-stratifying patients and providing appropriate counseling, referrals, and treatment as appropriate for comorbid sleep conditions such as insomnia and insufficient sleep, comorbid CV risk factors including hypertension, dyslipidemia, metabolic dysfunction-associated steatohepatitis, as well as counseling for weight management programs, smoking, and alcohol cessation. We urge sleep clinicians to play an active and integral role in optimizing the CV health of patients with sleep disorders.

Key words: OSA; cardiovascular medicine; obesity

Statement of Significance

The field of sleep medicine has emphasized the impact of impaired sleep, particularly obstructive sleep apnea (OSA), on adverse cardiovascular (CV) health. However, there is insufficient evidence that continuous positive airway pressure alone improves CV outcomes. Herein, we share our perspective that sleep physicians should consider their role as CV preventionists by providing appropriate counseling, referrals, and treatment as appropriate for comorbid sleep conditions and CV risk factors. This includes behavioral counseling for insomnia, weight management and pharmacologic treatment of obesity, management of hypertension and hyperlipidemia, treatment of metabolic dysfunction-associated steatohepatitis, as well as smoking cessation. Reimagination of the sleep physician's role to be more inclusive of other preventative health strategies will benefit the overall CV health of OSA patients.

Background

The field of sleep medicine has emphasized the impact of impaired sleep, particularly through obstructive sleep apnea (OSA), on adverse cardiovascular (CV) health. Observational studies have suggested that both insufficient sleep duration and OSA are independently associated with increased cardiometabolic and CV diseases (CVD) [1, 2]. Continuous positive airway pressure (CPAP) has been the mainstay therapy in OSA management. Addressing adherence to CPAP, including troubleshooting mask interface and pressure adjustment, has been a major role of sleep clinicians in managing OSA. While clinical medicine emphasizes improving CV health through improving CPAP adherence, there is insufficient evidence to justify CPAP alone for improving CV health outcomes in OSA. Furthermore, insomnia is also an independent CV risk factor [3]. It is our experience that clinical sleep practices primarily focus on the diagnosis and treatment of OSA as a means of CV risk reduction.

While CPAP is effective in improving several sleep-related quality-of-life outcomes, and leads to modest reductions in blood pressure (BP), studies have failed to demonstrate a CV benefit in the prevention of composite CV outcomes [4]. We advocate for an expanded role of sleep providers in addressing CV health beyond the narrow focus of merely ordering sleep testing followed by CPAP prescriptions for patients with OSA.

An encounter with a sleep physician provides a unique opportunity to not only evaluate sleep but also address CV health associated with OSA and sleep disruption. The objective of this perspective is to address these gaps and share practical suggestions to empower sleep clinicians to go beyond focusing on CPAP in efforts to improve the CV health of sleep patients.

Current Evidence Regarding Treatment of OSA With CPAP and CV Outcomes

Observational, non-randomized data have suggested that in patients with severe OSA, the use of CPAP treatment may reduce the risk of nonfatal and fatal CV events [5]. Mechanistically, the use of CPAP has also been shown to improve C-reactive protein, catecholamines, and 24-hour BP in those with severe OSA [6]. Among patients with OSA and comorbid hypertension, CPAP results in approximately 2–4 mm Hg of systolic BP reduction [7]. Although early studies suggested that CPAP may be promising for CV risk reduction in OSA, randomized-control trials in the last decade have not demonstrated a meaningful CV benefit with the use of CPAP [8–10]. One limitation to these findings may be related to challenges with adherence to CPAP therapy, where average CPAP adherence was limited to 3–4 hours per night. Further investigations have suggested that investigating specific endophenotypes in OSA subpopulations may be helpful in identifying those for whom CPAP may lower CV risk. For example, those with OSA and excessive daytime sleepiness may be at a higher risk for CVD events and potentially derive benefit from CPAP, though others have challenged this notion [7, 11, 12]. Additionally, patients with OSA and varying physiological responses may manifest CV risk differently. For example, patients with more pronounced pulse arrival time shortening (the time between the R wave and pulse arrival on photoplethysmography) may have increased CV risk [13]. Patients who exhibit an elevated heart rate response to respiratory events (ΔHR) may be at an increased risk of CV morbidity, and derive a greater benefit from CPAP [14, 15].

Emerging Role of the Sleep Specialist as a CV Preventionist

Sleep medicine providers must prioritize preventive and therapeutic interventions alongside CPAP to effectively reduce CV risk. Sleep specialists are well suited to address CV health because patients presenting with sleep symptoms commonly exhibit a high burden of CV risk. Beyond OSA, patients with other sleep symptoms or disorders such as insufficient sleep (short sleep), insomnia, and primary hypersomnia also have increased CV risk [16–18]. A recent systematic review confirms that there is little in the OSA literature focused on the prevention of OSA and other sleep-related and CV-modifiable risk factors. Thus, by concurrently addressing other comorbid risks associated with sleep disorders, sleep specialists can meaningfully contribute to improving CV health (Figure 1). In this context, we emphasize CV risks that sleep specialists can effectively manage as part of their routine patient care.

Weight Management in OSA
Diet, exercise, and bariatric surgery

Weight-loss interventions in OSA are associated with improvements in OSA severity, cardiometabolic comorbidities, and quality of life [19]. The American Thoracic Society recommends tailored weight management strategies in the routine treatment of adults with OSA who are overweight or obese. In particular, comprehensive lifestyle intervention, which includes a program to support a reduced-calorie diet, increased physical activity, and behavioral counseling has been associated with weight loss, reductions in OSA severity, and improvement in daytime sleepiness in patients with OSA who are overweight or obese [20–22]. There is emerging evidence that virtual/web-based behavioral weight-loss programs from physician referral can also provide significant weight loss to over half of the patients studied [23]. Behavioral weight interventions for adults with obesity have also yielded improvements in obesity in a primary care setting and broader integration into specialty care may enhance these benefits [24]. Referral to virtual/web-based weight-loss programs is not time intensive and may be accomplished with the potential for lasting results [24].

Pharmacologic management of obesity and the role of incretins

Weight loss and aerobic exercise are essential components of OSA treatment and CV risk reduction. Excess body weight is estimated to be responsible for over half of moderate-to-severe OSA [25, 26]. In the Wisconsin-Sleep cohort, a 10% reduction in weight decreased the AHI (apnea–hypopnea index) by 32% [26]. While CPAP has not demonstrated a reduction in CVD risk, a 10% or more weight loss from baseline can result in a 21% or more reduction in CVD [27].

Glucagon-like peptide 1 (GLP-1) based therapies have emerged as a powerful pharmacologic tool in weight loss. GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) are gastrointestinal peptides also known as incretin hormones. Liraglutide was the first GLP-1 receptor agonist (GLP-1RA) approved for obesity. In a trial of patients without diabetes, weight loss was significantly greater in the 3 mg liraglutide group (–8.0 vs. –2.6 kg in the placebo group) [28]. Semaglutide is also a once-weekly GLP-1RA. Studies have demonstrated weight loss in individuals with and without type 2 diabetes [29]. There is also evidence of CVD benefits with both liraglutide and semaglutide for secondary
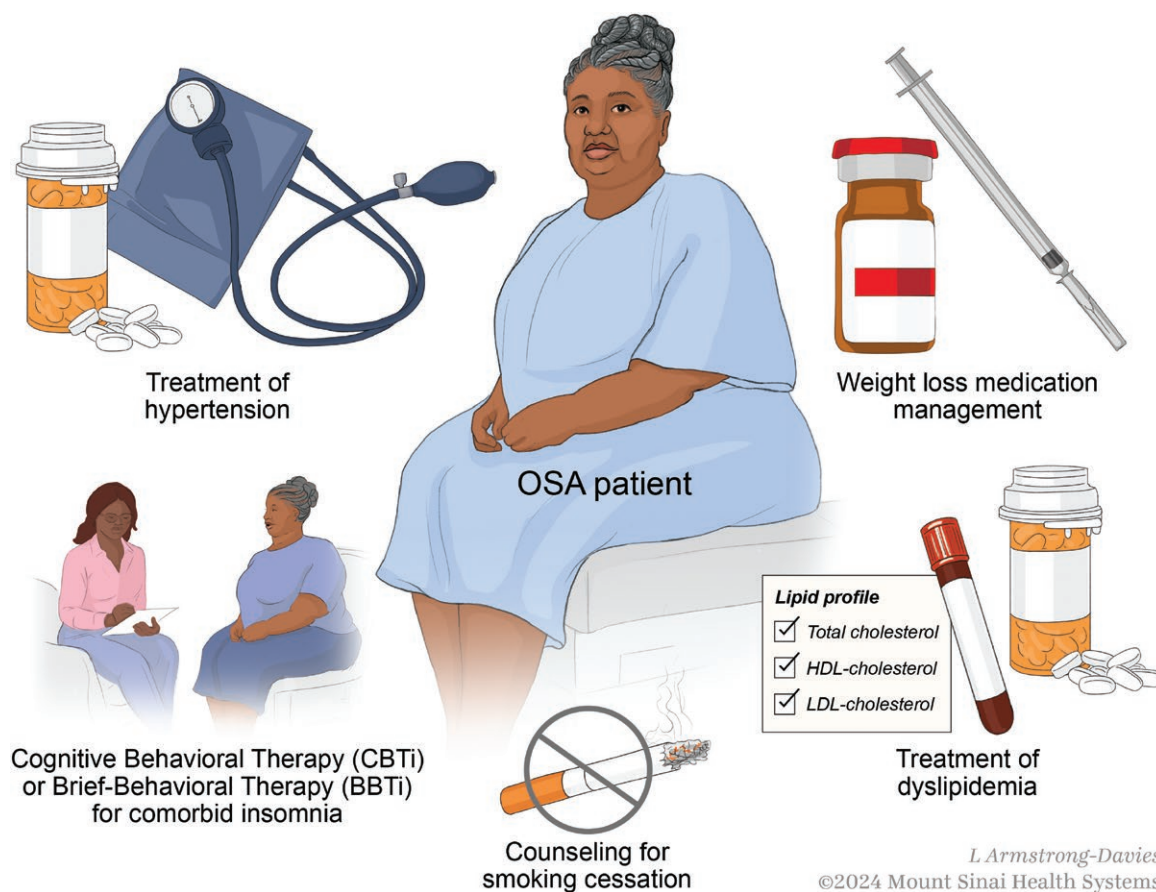
Figure 1. Holistic/integrated approach to patient with sleep apnea and cardiometabolic disease (L. Armstrong-Davies, ©2024 Mount Sinai Health Systems).

CVD prevention. In the Semaglutide Effects on Cardiovascular Outcomes in People with Overweight or Obesity (SELECT) trial, CV events occurred less frequently in the semaglutide group (6.5% vs. 8% in placebo, HR 0.80, $p < 0.001$). Tirzepatide, the most recently approved GLP-1, is a dual GIP and GLP-1RA with significant efficacy for weight reduction. A meta-analysis of six tirzepatide trials found that tirzepatide 15 mg resulted in a mean −20.9% change in body weight compared with −3.9% in the placebo group [30, 31].

These promising medications have been recently investigated in patients with OSA and obesity. In a small randomized, double-blind trial of nondiabetic patients with obesity and moderate-to-severe OSA, liraglutide as an adjunct to diet/exercise reduced the mean AHI compared with placebo (−12.2 vs. −6.1 events/hour) [32]. SURMOUNT-OSA is a larger randomized, placebo-controlled 52-week phase 3 clinical trial, evaluating the safety and efficacy of tirzepatide for the treatment of patients with obesity and moderate-to-severe OSA [33]. This study showed that in patients with moderate-to-severe OSA and obesity, tirzepatide provided a robust improvement in the AHI, reduction in hypoxic burden, improvement in BP, as well as sleep-related patient-reported outcomes. These results are promising, not only because of the improvement in OSA severity, but also the adjunct promise of CVD risk reduction. Randomized controlled trials over the last decade have not demonstrated a CVD risk reduction with CPAP in moderate-to-severe OSA [10]. The improvement in OSA is most likely attributed to significant weight loss (−18% vs. −1% change in body weight from the baseline), which was one of the secondary outcomes of the study. While weight loss improves OSA in some cases, it may resolve OSA in others [34]. Thus, it is important to recognize that the beneficial effect on OSA by GLP-1 is likely through weight loss.

Behavioral therapies for insufficient sleep and insomnia

The American Academy of Sleep Medicine (AASM) recommends 7–9 hours of sleep per night. Both insomnia and short sleep duration below 6 hours have been linked with adverse CV outcomes [35]. Sleep clinicians should take a thorough approach to investigating the underlying factors contributing to short sleep duration and insomnia. One effective intervention that can be employed for insomnia is cognitive behavioral therapy for insomnia (CBTi), which is regarded as the first-line treatment for the condition [36]. CBTi is an evidence-based behavioral intervention with a focus on changing the physiological factors, behaviors, and thoughts that contribute to insomnia [37]. One challenge that has emerged with CBTi is that healthcare providers may struggle to connect patients with professionals skilled in this discipline. This difficulty is often due to a shortage of certified CBT-I providers and sleep psychologists, along with limited insurance coverage and the financial burden associated with accessing CBT-I services. Telehealth has emerged as an option for patients after the coronavirus disease 2019 (COVID-19) pandemic to in-part bridge this gap and has been demonstrated to be effective in improving sleep duration and sleep efficiency [38]. When a sleep clinician is not able or skilled in the provision or cannot

offer a timely referral for CBTi, there is promising evidence for the benefit of brief behavioral intervention, which can be implemented by any trained sleep clinician, in improving sleep quality and duration [39]. These interventions are also important to consider in patients with OSA, as 30%–40% of patients with OSA are felt to have significant symptoms of insomnia [40]. This new overlap syndrome has been referred to as COMISA, or Comorbid Insomnia and Sleep Apnea [41]. Recognizing this newly identified overlap is crucial, as the combination of these conditions may result in higher morbidity and mortality compared with each disorder alone [42].

Hypertension, chronic kidney disease, metabolic dysfunction-associated steatohepatitis, hyperlipidemia, smoking cessation, and alcohol cessation

Although often the purview of primary care and other specialists, sleep medicine providers can improve CV outcomes by identifying those with comorbid hypertension, hyperlipidemia, chronic kidney disease, and metabolic dysfunction-associated steatohepatitis through basic laboratory analysis, followed by a prompt referral to the appropriate specialist. There is emerging evidence that statins may reduce CV risk after CPAP initiation in those with hyperlipidemia [43].

Cigarette smoking is a major risk factor for CVD. Patients who quit smoking have a lower 5-year CVD risk compared with those who continue to smoke [44]. Smoking may reduce the amount of slow-wave sleep as well as rapid eye movement (REM) sleep and may exacerbate insomnia. Furthermore, the reduced amount of sleep achieved based on the effects of nicotine may also interfere with the ability of patients to abstain from nicotine [45]. Improving sleep quality may even be a method by which to enhance the efforts of patients to abstain from cigarette smoking [46]. The CV risk in the OSA population continues to be above that experienced by never smokers, although remains below the risk of those that continue to smoke [44]. It is postulated that individuals with untreated, undiagnosed OSA may use the stimulating effects of nicotine from cigarettes to partially counteract their sleep disturbances and excessive daytime sleepiness [47].

In addition to cigarette smoking, alcohol usage also has dramatic effects on sleep. Although alcohol reduces sleep latency, it increases sleep fragmentation and decreases overall REM sleep [48]. Alcohol consumption has also been linked to increased CV risk of which the increase in risk occurs immediately after consumption [49]. Screening for alcohol use and cigarette smoking often takes place during the patient's assessment, presenting an additional opportunity for the sleep physician to enhance the CV health of patients with sleep disorders.

Current and future landscape of the sleep specialists' practice as a cardiac preventionist

There is limited data regarding the current landscape of sleep physicians' engagement beyond OSA diagnosis and CPAP therapy in their efforts to address CV health in patients with OSA or other sleep disorders. Our collective observation at the receiving end of consultations has been that diagnosing OSA and managing CPAP therapy represent the primary tasks in a sleep clinician's daily practice.

A recent systematic review confirms that there is little in the OSA literature focused on the prevention of OSA and modifiable risk factors [50]. Out of all the publications, 720 examined risk factors and prevention of OSA, while 23 674 articles focused on OSA therapeutics. We can only infer that the disproportionately limited focus in the published literature on lifestyle modifications and behavioral interventions also influences provider practices when treating OSA [50].

Clinical sleep medicine is evolving from simply focusing on OSA diagnosis and CPAP prescription in patients with OSA, to the identification and management of modifiable sleep-related and traditional CV risk factors. As such, sleep clinicians are uniquely positioned to play a more active role in optimizing CV health in their patients. While the extent of their involvement may be open to debate, we believe that a more holistic approach—incorporating care beyond OSA and engaging in behavioral and lifestyle counseling for CV health—can significantly improve the CV outcomes of patients with sleep disorders. We recommend that rather than the sleep specialist taking on the role of the primary care physician, they should work collaboratively with other healthcare providers to address CV risk factors that intersect with sleep disorders, ultimately benefiting the patient. Referral pathways may also need to be evaluated, as these may vary depending on practice setting, healthcare system, and country. This operational aspect of sleep medicine is rarely discussed in medical literature, yet it could be a crucial focus as the field navigates its next steps.

Conclusion

Sleep clinicians have often prioritized managing OSA through sleep studies and CPAP implementation, placing significant emphasis on these approaches in their practice. While this is certainly important, especially in patients with symptomatic OSA, this focus may inadvertently minimize attention to other comorbid disorders, such as insomnia and circadian rhythm disorders, which can also significantly impact CV disease risk. While addressing and treating symptomatic OSA remains critical, implementing CPAP therapy to merely improve CV risks is controversial based on the current body of evidence. We envision the sleep clinician of the future as a preventionist. This holistic approach to sleep care involves not only comprehensive sleep management but also offering appropriate behavioral and lifestyle counseling. It includes established CV risk reduction strategies and appropriate referrals and consultations for weight management, hypertension, and hyperlipidemia, and supporting smoking cessation efforts.

Disclosure Statement

Author Contributions

William Healy (Conceptualization [equal], Project administration [equal], Supervision [equal], Writing—original draft [equal], Writing—review & editing [equal]), Vaishnavi Kundel (Writing—original draft [equal], Writing—review & editing [equal]), Pam Taub (Writing—original draft [equal], Writing—review & editing [equal]), Yeilim Cho (Writing—original draft [equal], Writing—review & editing [equal]), Sara Healy (Writing—original draft [equal], Writing—review & editing [equal]), and Younghoon Kwon (Conceptualization [equal], Writing—original draft [equal], Writing—review & editing [equal])

Data Availability

No new data were generated or analyzed in support of this article.

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