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## Editorial

# Obstructive Sleep Apnea Effects on the Right Ventricle and Beyond

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*See article by Vitarelli et al., pages 823-831 of this issue.*

Obstructive sleep apnea (OSA) is a common condition that is being increasingly appreciated as an important cardiovascular risk factor.<sup>1</sup> OSA is thought to affect roughly 10% of the North American population,<sup>2</sup> with increasing prevalence reported over time related to the obesity pandemic and improvements in diagnostic technology. Historically, the importance of OSA was debated because many individuals felt that the associations attributed to disease were in fact related to confounding variables such as obesity and diabetes.<sup>3</sup> However, definitive data from well-conducted animal studies, large-scale epidemiologic studies, and human interventional trials have shown that OSA in and of itself is problematic and not simply a marker of confounding variables.<sup>4,5</sup>

Despite the fact that OSA is an established risk factor for cardiometabolic dysfunction, cardiologists in general have not embraced OSA as an important cardiac risk factor. Several factors are likely important<sup>3</sup>:

- Lack of awareness. Because sleep medicine is a young field and rarely taught in medical school, residency, or cardiovascular fellowship, its importance is often overlooked. With increasing data and improved education over time, the knowledge of OSA management and its importance should gain gradual acceptance. Similarly, many patients are not aware that they might have a treatable condition and thus will not volunteer symptoms of sleepiness or fatigue unless prompted.
- Concern about the cumbersome nature of diagnostic tests needed to diagnose OSA. In-laboratory polysomnography is perceived as a burden on the patient, and thus many patients and clinicians are reluctant to use the test. However, more invasive procedures such as cardiac catheterization or electrophysiological testing are rarely refused, emphasizing the need to understand the

major effects of OSA on overall health before denying diagnostic testing. Moreover, home sleep testing is now available, through which an acceptable management approach can be obtained in the home with minimal burden to the patient.<sup>6</sup>

- Concern about continuous positive airway pressure (CPAP) therapy. CPAP is the treatment of choice for OSA based on randomized controlled trials; however, it is not universally accepted by patients. Reasons for CPAP nonadherence include patient discomfort with the CPAP mask or machine, the perception that other therapies such as dental appliances are sufficient, or the lack of acceptance by the patient that sleep apnea poses a significant health risk.<sup>7</sup> Thus, adherence to therapy can be an issue. However, adherence to CPAP is comparable to that of standard treatment approaches for other chronic medical therapies, such as inhalers in asthma and anticonvulsants in epilepsy, suggesting that a nihilistic approach to CPAP is not justified. Efforts to develop new treatments for sleep disorders are ongoing, and patient acceptance of therapy can be excellent with adequate education and support.<sup>1</sup>
- Concern about lack of randomized controlled trials. As stated, the sleep field is quite young and thus definitive multicentre randomized trials showing hard end-point (such as mortality) benefits from CPAP are still evolving. Logistic and ethical concerns have made such rigorous definitive trials challenging to accomplish. By randomizing patients to a control arm, symptomatic patients may be left untreated for prolonged periods, increasing their risk of serious complications, including motor vehicle accidents and reduced quality of life.<sup>8</sup> Conversely, asymptomatic patients may have poor adherence to therapy, making them less than ideal candidates for randomized trials. Thus, surrogate outcome measures that could allow shorter-term studies are desirable.

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See page 822 for disclosure information.

In this issue of the *Canadian Journal of Cardiology*, Vitarelli et al.<sup>9</sup> report findings that address some of these concerns. Using 3-dimensional (3D) echocardiography and speckle tracking echocardiography, they assessed right ventricular

(RV) function in patients with OSA, who were free of cardiac or pulmonary comorbidities, before and after CPAP therapy. At baseline, 3D RV ejection fraction (RVEF) and global RV strain, both measures of RV systolic function, were lower in patients with moderate and severe OSA compared with controls. There was also evidence of RV dyssynchrony seen in parallel with the other RV findings. Both depressed RV function and RV dyssynchrony were independent of the presence of pulmonary hypertension and independently related to sleep apnea severity based on the apnea hypopnea index (AHI). This index represents the number of apneic and hypopneic events per hour during sleep; the higher the AHI, the more severe the sleep apnea. Interestingly, after a 4-month period of CPAP therapy in a subgroup of 15 patients with severe OSA (mean pretreatment AHI of  $57.9 \pm 9.1$  events/h), there was a significant lowering of pulmonary artery pressure, improvement in RV dyssynchrony parameters, and an increase in 3D RVEF. These data provide a rationale for using echocardiographic techniques to assess the cardiovascular health of patients with OSA and their response to therapy.

Although this study was nonrandomized, had a relatively small number of participants, and used an echocardiographic technique that has not been extensively validated for evaluation of RV function, the findings are consistent with other studies that have assessed the effects of OSA on cardiac structure and function. Shivalkar et al.<sup>10</sup> evaluated 43 patients with severe OSA. Compared with age-matched controls, patients with OSA were hypertensive. There was RV dilatation, hypertrophy of the interventricular septum, reduced tissue Doppler-determined systolic and diastolic velocities of the left and right ventricles, and normal pulmonary artery pressures. Six months after treatment with CPAP, significant improvements were observed in the symptoms and hemodynamic status as well as left ventricular and RV morphologic characteristics and function. Colish et al.<sup>11</sup> have also shown that CPAP treatment is associated with reduction in right atrial and RV size as demonstrated by both serial transthoracic echocardiography and cardiac magnetic resonance imaging (CMRI) studies at 3, 6, and 12 months.<sup>11</sup>

These studies suggest that sophisticated clinical trials could be designed using RV structure and function as a surrogate outcome measure for OSA interventions over a relatively short duration of follow-up. However, previous work has demonstrated that obesity is associated with RV dysfunction independent of the presence of OSA and therefore would require specific consideration in future trials.<sup>12</sup> Even within the small sample size of the trial by Vitarelli et al.,<sup>9</sup> and despite excluding morbidly obese patients, there was a trend toward more severe sleep apnea with increasing BMI. Other considerations include determining which modality to use to assess RV function. CMRI is a reference standard for assessing cardiac volumes and function; it supports strain analysis and has an advantage over echocardiography in its ability to characterize myocardium (eg, assess for fibrosis). The sophisticated echocardiographic approaches used by Vitarelli et al. require expertise. However, echocardiographic techniques have some advantages over CMRI, including lower cost, wide availability, less discomfort from claustrophobia, and the ability to study individuals with contraindications to CMRI, eg, patients with pacemakers or defibrillators.

Questions remain for the clinician as well as the scientist. First, should all patients with cardiovascular disease be assessed for sleep disorders and if so, what is the financial and clinical impact of this approach? Second, what alternative therapies are available or should be considered for patients who are intolerant of CPAP? We suggest the use of a clinical approach in which home sleep monitors are provided to patients in clinic and the recordings are interpreted by a board-certified sleep specialist. This simple strategy enables physicians to diagnose patients with suspected OSA easily and hopefully with treatment to improve patient symptoms and outcomes.

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### Disclosures

The authors have no conflicts of interest to disclose.

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