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Editorial

Asleep at the Switch? Are We Failing to Recognize Obstructive Sleep Apnea in Patients with Atrial Fibrillation and Heart Failure?

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See article by Kadhim et al., pages 1457–1464 of this issue.

The growing recognition of the influence of sleep-disordered breathing (SDB) on cardiovascular disease, especially the effect of obstructive sleep apnea (OSA), is reflected in newer guidelines for management of atrial fibrillation (AF) which recommend screening for SDB.[1,2] Several clinical symptom-based questionnaires have been proposed to help identify patients who should be formally assessed for SDB, but these tools have proven to have disappointing utility.[3] As they report in this issue of the *Canadian Journal of Cardiology*, Kadhim et al.[4] investigated the role of self-reported daytime sleepiness in detection of SDB in patients with AF. They examined the utility of the Epworth Sleepiness Scale (ESS) in predicting which patients might have the diagnosis of SDB by the more objective diagnostic criteria of an apnea-hypopnea index (AHI) $\geq$ 5. In a population of 442 consecutive ambulatory AF patients who underwent polysomnography during assessment for rhythm-control management, 66% were found to have SDB (AHI $\geq$ 5) on polysomnography, despite only 11.9% having a diagnostic ESS $\geq$ 11. A similar 10.7% of patients with no SDB on testing also reported daytime sleepiness. Not only was ESS found to be ineffective in identifying clinically important SDB, it was unable to distinguish between those with severe vs milder forms of SDB.

Thus, notwithstanding a pretest probability of SDB potentially as high as 74%, an ESS survey added no diagnostic value in looking for SDB in a population of patients with AF.[4] More concerning is that failure to diagnose mild SDB increases the chances that it would be left untreated and progress to more severe forms. If identified as having SDB, many patients can improve their arrhythmia outcomes by starting therapy with nocturnal positive airway pressure devices (PAP), most commonly referred to as continuous positive airway pressure (CPAP) in Canada.

One might ask why would cardiologists be interested in a symptom such as self-reported daytime sleepiness? Does it matter whether this could reliably predict the need to investigate for sleep disordered breathing (SDB) in a cardiac patient?[4] After all, SDB is not a cardiology diagnosis. However, taken in the larger perspective, perhaps the underlying question is why shouldn't a cardiologist be concerned with the possibility that their patient's cardiac condition might be caused or aggravated by SDB?

Many physicians have experienced patients in whom one of several cardiac diagnoses have been affected by SDB. As our patient population ages, our awareness of such patients is likely to increase. Certainly, we are witnessing a flood of AF and heart failure, and both diagnoses are associated with SDB. AF increases in prevalence with age.[2] Weight increases over time, with a mere 10% gain in weight increasing the risk of OSA by 6-fold,[5] making it unsurprising that OSA increases in prevalence with age.[5] Hypertension is one of the most important etiologic factors in developing AF.[1] Given that there is a bidirectional association between OSA and systemic hypertension,[6] one might conjecture that the overlap between SDB, hypertension, and AF is important to define for optimal cardiac patient management.[7] Furthermore, accumulating data suggest that the cost implications of not detecting and treating OSA will have an impact on the field of cardiology that is too great to ignore.

Atrial Fibrillation and Sleep Disordered Breathing

Anyone working in an AF clinic sees patients referred from primary care because their AF is sufficiently refractory to frustrate initial attempts at management.[1] A practitioner exposed to a series of these patients is soon impressed by the large proportion that either have the diagnosis of OSA, have a body habitus suggesting a high probability of OSA, or on questioning of their sleep partner, have reported loud snoring or concerning nocturnal apneas. Given the known temporal

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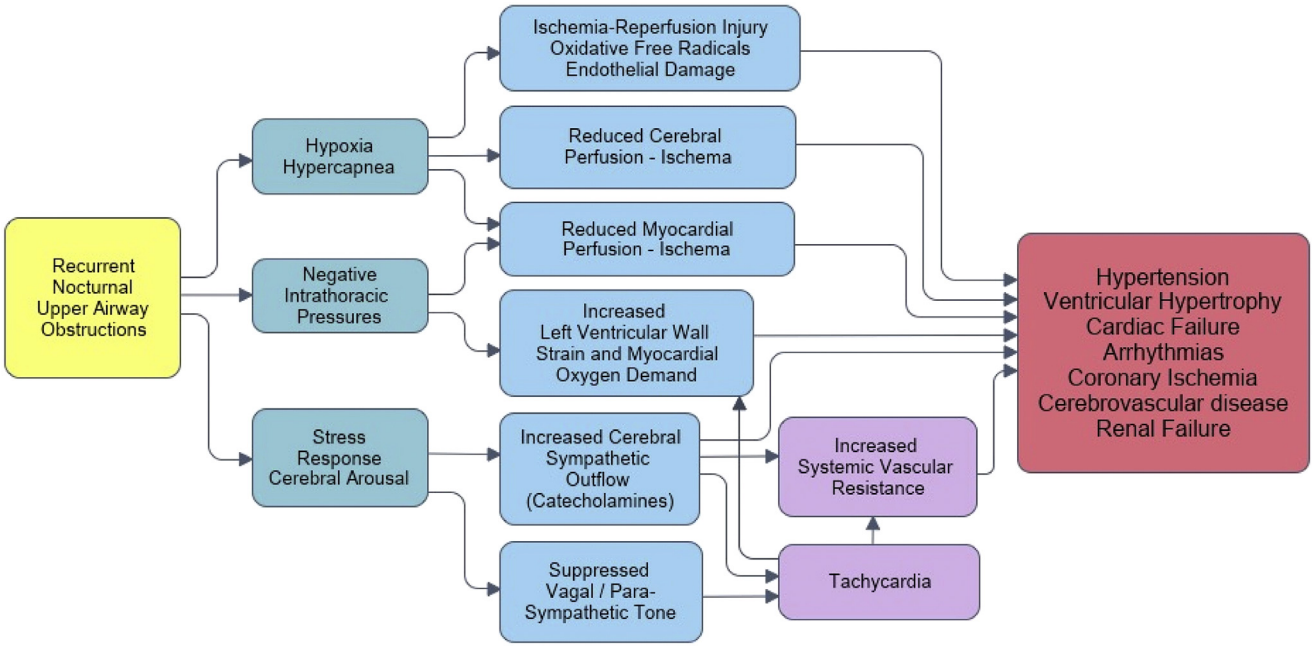

Figure 1. Schematic diagram of relationship between sleep apnea and cardiovascular outcomes.

links between hypertension, AF, and OSA, it is easy to construe a pathophysiologic mechanism by which OSA is involved in the development of AF.[7] Catecholamines are released in response to the acute stress of hypoxia at night.[8] Repeated exposure to the high sympathetic outflow (catecholamines) associated with nocturnal apneas increases vascular tone, eventually promoting hypertension through an irreversible increase in systemic vascular resistance (Fig. 1).

The negative cardiovascular consequences of high catecholamine exposure and associated changes in physiology need to be taken seriously by cardiologists.[9] A core therapeutic tenet of cardiology is that treatment with medications that limit the adverse effects of long-term adrenergic overstimulation improves cardiovascular disease. Reducing adrenergic tone is accomplished mainly through use of β-adrenergic blocking agents, somewhat indirectly with the use of angiotensin-converting enzyme inhibitors, and to a limited extent with the use of alpha-adrenergic blocking agents. Clearly, because these are competitive agents, large flows of sympathetic output from the brain diminish their effectiveness. If nothing else, treating SDB/OSA reduces adrenergic stress and improves outcomes.[10]

Neurocirculatory Consequences of Hypoxia

The consequences of undiagnosed SDB reach beyond refractory cardiac conditions. Cumulative toxicity from repeated nocturnal brainstem hypoxia and hypertension reduces precise control of breathing during the night. This further contributes to gradual degeneration of brain tissue and autonomic control of cardiopulmonary function, worsening SDB and creating a deleterious feedback loop.[11]

The impacts of the changes in physiology associated with OSA on cardiovascular health were comprehensively summarized in a review by Bradley and Floras.[8] OSA has been linked with AF, other arrhythmias, heart failure, and myocardial and cerebral ischemic events. More recent evidence even suggests that OSA adversely affects kidney function.[12] Not only do nocturnal apneas increase blood pressure risk, they facilitate a proarrhythmic environment through repeated exposure to hypoxemia, hypercarbia, intrathoracic pressure changes, and increased circulating inflammatory markers. Apneas also drop heart rates, providing periods of longer R-R duration favourable to ectopic beat initiation. Apnea-associated catecholamine surges further distort the electrophysiologic environment in the heart and strain normal cardiovascular function through tachycardia and blood pressure surges.[8] Treatment of OSA ameliorates many of these proarrhythmic influences and reduces the risk of AF recurrence after catheter ablation[13]

A High Clinical Risk Demands a High Clinical Index of Suspicion

Although the treatment of SDB may fall within the bailiwick of respirology, the negative consequences of abnormal pulmonary and systemic circulatory pressures, hypoxemia, and altered brainstem function favour development of cardiovascular disease. Therefore, cardiology has real "skin in the game," making the following considerations worthwhile: 1) AF may often be an unrecognized end-organ consequence of SDB/OSA; 2) much as stroke should trigger screening for the possibility of AF, AF should trigger screening for presence of OSA/SDB; and 3) given that severe AF patients may exhibit refractoriness to therapy if they have unrecognized and untreated OSA/SDB, it is in the best interests of cardiology to participate in the diagnosis of this risk factor and refer affected patients for treatment to improve cardiac outcomes.[10]

Detecting Which Patients Have Sleep-Disordered Breathing

In an ideal world there would be a list of clinical signs and symptoms that reliably indicated an increased pretest

probability of SDB. Such a risk assessment tool could be used to guide which patients needed definitive testing.[14] Unfortunately, the available questionnaires only predict modest changes in probability.[15] For a population of patients with a low *a priori* probability of SDB, shifting the estimated risk from a pretest probability of 10% by 20% to reach a posttest probability of 30% makes a clinically important change when evaluating the need for further assessment. However, in a population with a pretest probability of $>$ 60% (most severe AF patients are likely in this range), moving to $>$ 80% probability does not shift the preexisting level of urgency to do more formal screening.

Can clinical judgment identify which patients in an AF clinic population have SDB better than SNOOZE-AF[4] can? Maybe the better question is whether cardiologists can use patients' histories to identify which of their population of AF patients do not have SDB? Likely not. So what would be the best strategy for screening such a high-risk population? Given that these patients have a moderate or high probability of OSA, screening all AF and heart failure patients with home sleep apnea testing might prove to have the highest utility. Compared with formal polysomnography, home sleep apnea testing is a relatively inexpensive, yet still sensitive and specific, screening test in a high-risk patient group.[16] Therapy with the use of CPAP has a relatively high front-end cost, on the order of $2500 Canadian, but these costs may pale compared with the annual costs of many modern pharmaceutical agents and repeated hospitalizations. If CPAP can prevent progression of cardiovascular disease, it may prove to be more cost-effective than pharmaceutical management of the resultant cardiovascular diseases after the fact.

How to Improve the Cardiology-Respirology Arrhythmia Management Interface

Rather than divide the arrhythmia/SDB field, cardiologists and respirologists need to work together to serve this patient population better. Given the impact of this condition on many cardiac conditions, cardiology needs to better appreciate the link between SDB/OSA and AF and heart failure and actively participate in the screening and diagnosis of SDB in cardiac patients. Currently in Canada, access to diagnosis and treatment of OSA varies by province, with most having limited funding for diagnostic testing or CPAP treatment,[17] or insufficient numbers of specialists treating sleep apnea.[18] Out of self-interest, cardiologists should be joining the call for provinces to support easier access to home sleep apnea testing. This might overcome the barriers imposed by requiring screening to be done by sleep-laboratory polysomnography alone. Working with provincial funding authorities to overcome limitations to access and billing restrictions placed on out-of-hospital screening methods would certainly be a first step.

Screening Conclusions

The study by Kadhim et al. highlights that one should not be reassured by an absence of symptoms of sleepiness and that more AF patients should be referred for diagnostic sleep testing.[4] Given the proliferation of expensive interventions and pharmaceuticals for the therapy of AF, the role of OSA management should be more vigorously assessed within this clinical population. A large-scale trial, powered sufficiently to identify cost-effectiveness and possible benefits from therapy of SDB on clinical outcomes, is required to validate: 1) the use of OSA screening with home sleep apnea testing; 2) the benefit of CPAP therapy in patients with difficult-to-control AF who have SDB. Inconsistent application of tools, such as clinical questionnaires that have low discretionary power, will not solve the challenge arising from the increasing prevalence of SDB-associated cardiac disease.

Disclosures

M.P. receives sleep test interpretation fees from Maple Respiratory. P.T.P. has no conflicts of interest to disclose.

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