Canadian Journal of Cardiology 31 (2015) 873–879

Review

Epidemiology of Sleep Disturbances and Cardiovascular Consequences

Mohammad Badran, MSc,[a] Bishr Abu Yassin, MSc,[a] Nurit Fox, MSc,[b] Ismail Laher, PhD,[a] and Najib Ayas, MD, MPH[b]

[a] *Department of Pharmacology and Therapeutics, Faculty of Medicine, University of British Columbia, Vancouver, British Columbia, Canada*

[b] *Divisions of Critical Care and Respiratory Medicine, Department of Medicine, University of British Columbia; Sleep Disorders Program, UBC Hospital; Division of Critical Care Medicine, Providence Health Care, Vancouver, British Columbia, Canada*

ABSTRACT

It is increasingly recognized that disruption of sleep and reduced amounts of sleep can have significant adverse cardiovascular consequences. For example, obstructive sleep apnea (OSA) is a common underdiagnosed disorder characterized by recurrent nocturnal asphyxia resulting from repetitive collapse of the upper airway; this leads to repetitive episodes of nocturnal hypoxemia and arousal from sleep. Risk factors for disease include obesity, increased age, male sex, and family history. In epidemiologic studies, OSA appears to be an independent risk factor for cardiovascular disease (CVD), and treatment is associated with better outcomes. Habitual short sleep duration is common in today's society. In epidemiologic studies, short sleep duration is associated with a number of adverse health effects, including all-cause mortality, weight gain, and incident CVD. Given the links between sleep disorders and adverse health outcomes, obtaining adequate quality and amounts of sleep should be considered a component of a healthy lifestyle, similar to good diet and exercise.

RÉSUMÉ

On reconnaît de plus en plus que les troubles de sommeil et la réduction du nombre d'heures de sommeil peuvent avoir des conséquences indésirables importantes sur la santé cardiovasculaire. Par exemple, l'apnée obstructive du sommeil (AOS), un trouble sous-diagnostiqué fréquent, est caractérisée par la récurrence d'asphyxie nocturne résultant des épisodes répétitifs de collapsus des voies aériennes supérieures et mène à des épisodes répétitifs d'hypoxémie et d'éveil durant le sommeil. Les facteurs de risque de la maladie comprennent l'obésité, l'âge avancé, le sexe masculin et les antécédents familiaux. Dans les études épidémiologiques, l'AOS semble être un facteur de risque indépendant de la maladie cardiovasculaire (MCV), et son traitement est associé à de meilleurs résultats cliniques. Dans la société actuelle, la durée de sommeil habituelle est souvent courte. Dans les études épidémiologiques, une courte durée de sommeil est associée à plusieurs effets néfastes sur la santé, y compris la mortalité toutes causes confondues, la prise de poids et l'incidence des MCV. Étant donné les liens entre les troubles du sommeil et les effets néfastes sur la santé, une qualité et un nombre d'heures de sommeil adéquats devraient être considérés comme une composante d'un mode de vie sain, au même titre qu'un bon régime alimentaire et l'exercice.

Sleep is an integral part of life, with humans spending approximately 30% of their lives asleep. Poor sleep quality and reduced amounts of sleep can clearly result in daytime sleepiness, decreased alertness, and reduced mental functioning. However, it is increasingly recognized that pathologic disruption of sleep and reduced amounts of sleep may also have substantial adverse cardiovascular outcomes. In this review, we describe the epidemiology and risk factors of the most common respiratory sleep disorder, obstructive sleep apnea (OSA), and its links with cardiovascular disease (CVD). Of note, this article focuses predominantly on robust cardiovascular outcomes. The impact of OSA on physiological and biochemical markers such as systemic inflammation, endothelial dysfunction, and early signs of atherosclerosis (eg, carotid intima media thickness) is discussed in another article in this issue of the *Canadian Journal of Cardiology*. We also summarize the associations between short and long sleep duration and CVD.

Received for publication November 16, 2014. Accepted March 8, 2015.

Corresponding author: Dr Najib Ayas, Respiratory Division, Faculty of Medicine, University of British Columbia, Vancouver, British Columbia V6T 2B5, Canada. Tel.: +1-604-875-4122.

E-mail: nayas@providencehealth.bc.ca

See page 877 for disclosure information.

Obstructive Sleep Apnea

By far the most common respiratory sleep disorder is OSA; in patients with OSA, breathing is interrupted because of recurrent collapse of the upper airway during sleep caused by sleep-induced losses in upper airway tone superimposed on an

http://dx.doi.org/10.1016/j.cjca.2015.03.011

anatomically susceptible upper airway.[1] The severity of OSA is defined according to the apnea hypopnea index (AHI), which is the number of times the airway narrows (hypopnea) or collapses (apnea) per hour of sleep; by consensus, the AHI categorizes patients with sleep apnea into 3 groups: mild (5-15 events/h), moderate (15-30 events/h), and severe (> 30 events/h).[2] Characteristic symptoms of OSA include loud snoring and witnessed apneic episodes.

The recurrent episodes of apnea and hypopnea lead to arousal, sleep fragmentation, hypoxemia, and hypercapnia. The poor sleep quality leads to reduced vigilance, daytime sleepiness, and an increased risk of motor vehicle accidents.[3] Furthermore, the recurrent arousals and hypoxemia/reoxygenation result in activation of the sympathetic nervous system, oxidative stress, acute increases in blood pressure, and activation of systemic inflammation.[4] These may represent pathogenic mechanisms whereby OSA can lead to an increased risk of CVD (Fig. 1).

The gold standard for the diagnosis of OSA is overnight polysomnography (PSG). This entails an overnight stay during which the patient is continuously monitored in an attended setting, with collection of a variety of physiological signals, including electrical activity using electroencephalography, eye movements, oxygen saturation, heart rate, respiratory excursion, and airflow.[2] Portable unattended monitoring is being used increasingly, especially in the context of patients with a high pretest probability of disease. These studies often have more limited channels (eg, lack of electroencephalographic signals) and lack the sensitivity and specificity of full PSG; however, they are less costly and may be more convenient for patients.[5]

Prevalence of OSA

Although estimates of the prevalence of OSA vary (largely because of differences in the methods and definitions used), it is clear that OSA is common and underdiagnosed. From a community-based study of middle-aged (30-60 years) men and women performed in 1988 in Wisconsin, it is estimated that approximately 24% of men and 9% of women have OSA (defined as an AHI > 5 events/h) and that 9% of men and 4% of women have moderate to severe OSA (ie, AHI > 15 events/h).[6] Recently, based on the increased prevalence of obesity over the past 2 decades, these data have been extrapolated, resulting in a current estimated OSA prevalence that is 14%-55% higher.[7] Similar prevalence estimates have been found in other geographic regions, including Europe and Asia.[8,9] The prevalence increases with age; Ancoli-Israel et al.[10] studied elderly individuals aged ≥ 65 years. Using portable sleep studies, the investigators showed that 62% of participants had 10 or more episodes of apnea and hypopnea per hour of sleep.

In 1997, it was estimated that nearly 82% of men and 92% of women with moderate or severe OSA were not diagnosed clinically.[11] Although the percentage of undiagnosed patients may now be less, the undiagnosed population of OSA remains very high in both North America and other countries.[12] Given the high prevalence of disease and associated adverse health and safety outcomes, the societal economic costs of OSA in Canada likely exceed billions of dollars per year.[13]

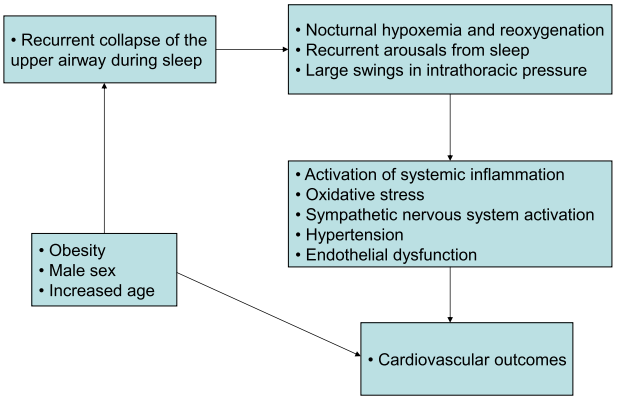

Figure 1. Mechanistic links between obstructive sleep apnea and cardiovascular disease.

Risk Factors for OSA

There are many risk factors for OSA. The strongest modifiable risk factor for OSA is obesity, especially central obesity (eg, neck circumference); nearly 60%-90% of patients with OSA are obese.[3] There are multiple potential mechanisms whereby obesity may lead to OSA, including narrowing of the upper airway because of fat deposition, reduced upper airway function, and reduction in lung volumes leading to a less stable upper airway.[14] Longitudinal studies have shown that a 10% increase in weight was associated with a 6-fold increase in the risk of development of OSA during a 4-year follow-up period, whereas a 10% weight loss was associated with a 26% decrease in AHI (95% confidence interval [CI], 18%-34%).[15] Interventions to promote weight loss improve OSA and should be recommended in obese patients.[16] Although obesity is likely a cause of OSA rather than vice versa, some have argued a potential bidirectional association with OSA, perhaps resulting from metabolic dysregulation or fatigue contributing to a lack of activity with OSA and potentially contributing to weight gain.[17]

Men have approximately twice the prevalence rate of OSA as women. There are a number of factors that could account for the difference in prevalence between the sexes. Some of these may be structural in nature, eg, upper airway fat deposition might be greater in men than in women because men tend to have predominantly upper body fat, whereas women tend to have lower body fat distribution. Female and male hormones may also play roles. Postmenopausal women have a 2- to 3-fold increased risk of OSA compared with premenopausal women, which is not accounted for by body mass index, age, or other risk factors,[18] and women with polycystic ovary disease also have an increased rate of OSA.[19] Male hormones also have an impact on sleep-disordered breathing. In a randomized clinical trial of 67 obese men with OSA, 1000 mg of testosterone undecanoate administered at 0, 6, and 12 weeks worsened OSA severity after 7 weeks in hypogonadal men when compared with placebo. After 18 weeks, AHI was essentially the same in both groups, and although the oxygen desaturation index was slightly greater (by 4.5 events/h), this was no longer statistically significant. This suggests that testosterone at these doses has only a temporary effect on OSA severity.[20,21]