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Review Article

REVIEW ON SLEEP-DISORDERED BREATHING AND CARDIAC DISORDERS

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A B S T R A C T

Sleep-disordered breathing, mainly involves obstructive sleep apnea (OSA) and central sleep apnea (CSA). It is a most popularly noticed public health burden. OSA, consist of apneas or hypopneas and is associated with upper airway constriction or collapse. OSA results in daytime sleepiness and also serves as a cause for cardiovascular disorders whereas CSA is associated with Cheyne-Stokes respiration (CSR). Indicators of SDB include sleep apnea, hypopnea, snoring, snorting, daytime sleepiness, undersleeping, and oversleeping. The reasons for the increasing prevalence of sleep disorder indicators, includesinvention of artificial light, the rise of shift work, and 24-hour manufacturing. Risk factors identified includes age, gender, and body mass index (BMI).The potential pathogenetic mechanisms of cardiovascular disease in sleep-disordered breathing may includes endothelial dysfunction, hypoxia, inflammation, obesity, metabolic dysregulation, and sympathetic activation.

INTRODUCTION

Sleep, diet and exercise are the core components of health and wellbeing. When sleep is disrupted, particularly over a long period of time, a chain of negative health effects takes place, including cardiovascular compromise. Sleep disorders and cardiovascular disorders can both occur by chance alone, but each may impact the other. Sleep apnea is the most common sleep disorder associated with cardiovascular disease. Sleep apnoea is defined as repetitive episodes of decreased or total cessation of respiratory air flow during sleep , leading to a fall in oxygen saturation of >/= 4% and sleep fragmentation. Repeated disruptions in breathing during sleep are the hallmark of sleep apnea, and these events are associated with drop in oxygen saturation and swings in blood pressure.

Sleep-disordered breathing (SDB), expressed most frequently as obstructive sleep apnea (OSA), is a common syndrome, and becomes progressively more prevalent with increasing age[1]. For the past several decades, a number of cross-sectional studies, performed primarily in relatively small clinical cohorts or using surrogates such as snoring as markers of SDB, have reported linkages between SDB and cardiovascular disease. For example, a high prevalence of OSA has been observed in patients with hypertension[2]. Conversely, hypertension is found in a large percentage of OSA patients. With respect to cardiac disease, early studies linked OSA to ischemic heart disease[3,4]. In addition, it has been shown that OSA is associated with deterioration in left-ventricular functions[5] and that treatment of OSA with continuous positive airway pressure (CPAP) improves cardiac function. If SDB plays a causal role in the pathogenesis of cardiovascular disease, higher mortality would be expected among individuals with OSA. This hypothesis was supported in some[6,7] but not all[8] retrospective studies. Whether SDB is an independent risk factor for cardiovascular disease is an important public health question. According to the 1999–2000 National Health and Nutrition Examination Survey, the prevalence of hypertension in the United States in those over age 55 years is 48%[9]. According to the year 2000 census, there are approximately 59 million Americans age 55 or older. If 25–50% of these individuals also have OSA, then 14–29 million of those people are at increased risk for cardiovascular disease or excess mortality related to OSA.

In the past several years, a persuasive body of data now indicates a causal association, independent of obesity, between SDB and cardiovascular disorders such as hypertension, coronary artery disease (CAD), arrhythmias, congestive heart failure (CHF), and stroke. The association is strongest and most consistent between obstructive sleep apnea and hypertension. This review will summarize the most important studies demonstrating the linkages between SDB and cardiovascular disease, and outline potential responsible mechanisms.

Sleep disordered breathing is characterised by frequent pauses in breathing during sleep, sleep apnea, often resulting in sleep fragmentation and intermittent oxyhemoglobin desaturation[10]. Epidemiologic studies in random samples of subjects have estimated the prevalence of sleep apnea with functional

impairment, the sleep apnea syndrome, in the general adult population to be 1 to 4%[11,12]. A high prevalence of sleep apnea has been reported in patients with hypertension[13], and sleep apnea may increase cardiovascular morbidity and mortality[14-16]. Hemodynamic changes that may occur during apnea include increased pulmonary and systemic arterial pressures and heart rate changes[17,18]. There is a strong evidence suggesting activation of the sympathetic nervous system during apnea[19,20]. Nocturnal hypoxemia with sympathetic activation and hemodynamic changes may seriously affect patients with coronary artery disease, but few studies have focused on this group of patients.

Sleep-disordered breathing, broadly characterized by obstructive sleep apnea (OSA) and central sleep apnea (CSA), is an increasingly recognized public health burden. OSA, consisting of apneas or hypopneas associated with respiratory efforts in the face of upper airway narrowing or collapse, is a common disorder that can be effectively treated with continuous positive airway pressure (CPAP)[21]. OSA not only results in daytime sleepiness and impaired executive function, but also has been implicated as a possible cause of systemic disease, particularly of the cardiovascular system. CSA, which may coexist with OSA, has gained attention because of the association of Cheyne-Stokes respiration with an ever increasing prevalence of heart failure in an aging population.

Snoring is one of the most common aspects of SDB and has been described throughout history. Snoring began to be viewed as an important clinical symptom and is usually the main reason for a patient visit to the hospital. The presence of symptoms is the major factor favouring evaluation of the patient for obstructive sleep apnoea (OSA), central sleep apnoea (CSA) or hypoventilation. However, some patients may have sleep disordered breathing without symptoms but with suggestive physiologic parameters, e.g.; sever restriction on pulmonary function test or unexplained cor- pulmonale. Such a patient should be evaluated with an arterial blood gas and a sleep study.

There are many associations between cardiovascular diseases and sleep disordered breathing (SDB). In particular, the obstructive form of SDB (obstructive sleep apnoea, OSA) has been identified as an important risk factor for a variety of cardiovascular diseases such as arterial hypertension, coronary artery disease and atrial fibrillation. On the other hand, central sleep apnoea (CSA) has mainly been associated with chronic congestive heart failure (CHF) and carries a significantly adverse prognosis. Studies have shown that treatment of the associated cardiac condition can improve the underlying sleep disorder, and vice versa. However, preliminary data from the recent SERVE-HF trial showed an increase in cardiovascular mortality in patients with heart failure with reduced ejection fraction and predominant CSA that were treated by adaptive servo-ventilation.

Obstructive sleep apnoea and cardiovascular disease have common risk factors including age, gender, race/ethnicity, and obesity which could confound the observed association. They are also linked to hypertension, there is a growing body of evidence suggesting that obstructive sleep apnoea is involved in the pathogenesis of altered glucose metabolism. It has long been recognised that obesity plays a pivotal role in the development of obstructive sleep apnoea.

Sleep apnea is hypothesized to increase the risk of developing cardiovascular disease (CVD) and hypertension. Initial support for this hypothesis came from several population studies of snoring and CVD outcomes, suggesting that those who snore are more likely to develop hypertension, myocardial infarction, and stroke[22-23]. Studies of CVD risk factors in patient populations with obstructive sleep apnea syndrome suggest that these persons have a higher than expected prevalence and incidence of CVD[24] but that the strength of these associations is decreased after accounting for confounding by higher weight and age in those with sleep apnea. None of these studies, however, has had detailed information regarding the presence of other CVD risk factors in those with sleep apnea. Patients with CVD have a higher prevalence of sleep disordered breathing by polysomnography[25], but it is unclear whether sleep-disordered breathing preceded CVD or was its consequence. The prevalence of sleep-disordered breathing has been documented in population-based studies to be quite substantial: 24 percent in men and 9 percent in women[26]. These persons, most of whom are asymptomatic with respect to daytime sleepiness, clearly have a higher BMI and blood pressure than do those without sleep-disordered breathing. However, most of these samples have not been characterized in detail regarding other CVD risk factors and future outcomes. Thus, neither studies of obstructive sleep apnea patients nor population studies of sleep-disordered breathing have adequately evaluated the intrinsic host factors that increase the risk of CVD in relation to sleep-disordered breathing or fully assessed its interactions with intrinsic CVD risk factors. The hypothesized pathway between sleep disordered breathing and CVD events is complex and may be bidirectional. For example, some factors, such as obesity, may worsen breathing during sleep. Other factors, such as hypertension, are potentially worsened by sleep-disordered breathing, yet hypertension has also been postulated to influence the severity of sleep-disordered breathing. A detailed analysis of these relations is needed to refine hypotheses of the possible causal mechanisms underlying the potential relation between sleep-disordered breathing and CVD.

More than half of patients with heart failure have sleep abnormalities, which generally fall in to 2 categories. About one third of heart failure patients with left ventricular dysfunction have obstructive sleep apnea, and one third experience chyne- stokes respirations, a form central sleep apnea characterized by deeper, faster breathing. The remaining third will have miscellaneous CVD conditions that disturb sleep.

A study found that presence of sleep apnea was associated with 1.2 fold increased odds of presence of cardiovascular disease and persons with an AHI ≥ 30 events/hr had 1.37-fold increased odds of hypertension in compared to those without OSA.Also, SDB in the form of both OSA and CSA are frequently observed in patients with heart failure and substantial evidence links SDB as an etiologic factor in the pathogenesis of various arrhythmias, particularly atrial fibrillation. Treatment of SDB with CPAP appears to reduce this risk.The study concluded that there is compelling evidence suggesting an association, probably causal, between sleep disordered breathing, especially, obstructive sleep apnea, and diverse cardiovascular disorders as well as

increased mortality.[32]Another study says that sleep apnea was observed at the same frequency in the ACS group and the CHF group including higher sympathetic nerve activity, and there was no significant difference in frequency of desaturation. This study suggested that sleep disorder breathing is frequently and similarly associated with both CHF and ACS.[33] Another study shows that men with angina pectoris have a high occurrence of sleep-disordered breathing compared with controls without known heart disease. Moreover, it was found that sleep-disordered breathing measured as ODI or AHI was an independent predictor of CAD.[3]

Another study shows that OSA is increasingly associated with cardiovascular risk factors and disease, there are mounting data suggesting a potentially important causative role of OSA in cardiovascular disease, particularly systemic hypertension.[35]Another study says that because of the acute and profound effects of sleep disordered breathing on vascular tone, hypertension is thought to be a major mechanism by which sleep-disordered breathing might influence future CVD risk.[37] Another study says that causal relationship between sleep-disordered breathing and hypertension has been supported by both animal experimental and epidemiological studies. An animal experiment using acanine model demonstrated that daytime blood pressure increased after experimentally induced intermittent airway occlusion during nocturnal sleep and fell after a nighttime sleep with quiet breathing.[38] A A recent study strongly suggest that atrial fibrillation is independently associated with severe CSA in addition to age and left atrial size in HF patients.[39] Another study concluded that SDB, with a preponderance of CSA, was found to be highly prevalent in patients with highgrade aortic stenosis scheduled for TAVI and SDB prevalence was independent of left ventricular function.[40]Another study shows there is a relationship between sleep disordered breathing and they explained that defining the risk of CHD attributable to SDB is difficult because those with the latter have been recognized to have co-morbidities such as obesity, hypertension, and hyperlipidaemia that place many at higher risk for cardiovascular disease. There was a step wise increase in CVD risk factor levels with greater severity of SDB. Experimental and clinical studies demonstrate that sympathetic overactivity, an important mechanism in the pathogenesis of hypertension, occurs with SDB. Repetitive occlusion with hypoxia, hypercapnia, and the dramatic changes in the intrathoracic pressure result in diverse autonomic, humoral, neurohumoral, and haemodynamic responses. These may affect the cardiovascular function during the day even when the breathing is normal[41]. Urinary catecholamines are elevated in untreated OSA subjects and return to control levels after effective treatment of apnoea[42] shows that the metabolic syndrome represents a mediating factor in the link between OSA and cardiovascular disease remains to be determined. Alternatively, the metabolic syndrome itsself might potentiate the effects of OSA on cardiovascular disease. It may be that associations among those metabolic disorders point to a maladaptive autonomic response of chemoreceptors, reacting to hypoxia, hypercapnia, and acidosis commonly found in sleep apnoea[43]

Activation of the sympathetic nervous system through hypoxia and hypercapnia triggers an inflammatory response cascading in several down stream consequences including hyper tension, diabetes and dyslipidemia[44], all of which represent significant risk factor for cardiovascular morbidity.

Among patients with coronary artery disease CPAP treatment significantly reduces the risk of cardio vascular death, acute coronary syndrome, and hospitalisation for heart failure[45]. Moreover, CPAP therapy has significant effect on lipids levels[46]. CPAP studies show significant improvement in insulin sensitivity and left ventricular function with a corresponding decrease in blood pressure[47].

CONCLUSION

There is a strong association between sleep-disordered breathing (SDB) and cardiovascular disorders. The association is most consistent between obstructive sleep apnea (OSA) and hypertension. Epidemiologic and clinic-based studies provide evidence for an etiological role of OSA in hypertension, independent of obesity. Furthermore, several studies suggest amelioration of hypertension with therapy for sleep apnoea. Emerging data also suggest a role for OSA in causing coronary artery disease. This association is bolstered by evidence suggesting that continuous positive airway pressure (CPAP) therapy improves early signs of atherosclerosis and may impede progression to clinically important cardiovascular disease. SDB (both OSA and central sleep apnea) is frequently observed in patients with heart failure. OSA may be a risk factor for incident heart failure. The current data do not provide consistent evidence for whether treatment of SDB will improve survival or other end points in patients with heart failure, and larger trials are currently underway to better elucidate that relationship. Substantial evidence also links SDB to an increased risk of various arrhythmias. Treatment of SDB with CPAP appears to significantly attenuate that risk.

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