Sleep Medicine: Obstructive sleep apnea and cardiovascular implications.

The salient effects of obstructive sleep apnea (OSA) have been recognized for many years. Disruption of the sleep cycle leading to excessive daytime somnolence, loss of productivity, and increased rates of traffic accidents have been well documented. However, only in the last decade has the cardiovascular morbidity associated with OSA been established.

The majority of sleep is a period of cardiovascular quiescence. Normally metabolic rate, sympathetic nervous sympathetic activity, heart rate, cardiac output, and systemic vascular resistance all fall. OSA disrupts the normal relaxing effects of sleep on the cardiovascular system. Ineffective respiratory efforts against the occluded airway cause wide swings in intrathoracic pressures substantially increasing the transmural gradient across the left ventricle and markedly increasing afterload while decreasing stroke volume[1]. Associated hypoxia, especially in the setting of coronary artery disease, may lead to an imbalance of myocardial oxygen supply and demand adversely effecting myocardial contractility. With arousal from sleep, the critical defense mechanism preventing asphyxiation, there is a surge in sympathetic nervous activity and blood pressure[2]. This combination of wide swings in intrathoracic pressures, recurrent hypoxia, neurohormonal activation, and arousals ultimately lead to the deleterious effects on the cardiovascular system.

The link between hypertension and OSA has been well documented in multiple studies. While sleep apnea is a nocturnal phenomena, the vicious cycle of repeated apneas followed by surges in sympathetic activity are postulated to be the underlying etiology of sustained daytime hypertension[1]. This is supported by the increased levels of urine catecholamines demonstrated in this population[3]. In addition, the loss of nocturnal HR and BP variability, known as dipping, supports this theory[4]. A large prospective population based study has demonstrated a significant risk for the development of hypertension in the setting of underlying OSA with an odds ratio for developing hypertension of 2.89[5]. Interestingly, even breathing event indexes previously considered insignificant resulted in a significantly increased risk for developing hypertension. The data regarding refractory hypertension is even more impressive, with one study demonstrating the presence of OSA in 83% of patients who are uncontrolled on three or more antihypertensive medications[6]. In a related study by the same authors, the treatment of OSA completely abolished previously uncontrolled hypertension[7].

As described above, OSA subjects the failing heart to adverse hemodynamic and adrenergic loads leading to increased myocardial oxygen demand in the setting of recurrent hypoxia, which can directly reduce myocardial contractility[8]. This is of particular concern in patients with underlying congestive heart failure. These repetitive stresses place the patient with heart failure and OSA at greater risk of worsening ventricular function, arrhythmias, and, ultimately, reduced survival. OSA has been reported to occur in up to one third of patients with stable heart failure. In The Sleep Heart Health Study, comprising 6424 men and women, the presence of OSA conferred a 2.38 relative increase in the likelihood of having heart failure, independent of other known risk factors[9]. Even more concerning, the mortality of patients with CHF and untreated OSA is nearly 2 fold greater than those with heart failure alone[10]. The results of treatment of OSA in patients with left ventricular dysfunction have been impressive revealing a relative increase in ejection fraction of 25.0 to 33.8 percent ($p<0.001$)[11]. This improvement exceeds any single pharmacologic intervention available today.

Atrial fibrillation (AF) is the most common sustained arrhythmia in the U.S. and is associated with significant morbidity and mortality. OSA has been found to be an independent predictor of atrial fibrillation in patients less than 65 years of age with a hazard ratio of 2.18 (CI 1.34-3.54)[12]. Additionally, the degree of nocturnal oxygen desaturation in these patients, which is an important

consequence of OSA, independently correlates with the risk of incident AF. Untreated OSA significantly increases the risk of recurrence of atrial fibrillation by almost two fold, emphasizing the importance of identifying and treating OSA in this population[13]. The prevalence of complex nocturnal arrythmias is not surprising that given the increased cardiac wall stress, sympathetic nervous system activation, and recurrent hypoxia that accompanies OSA. Retrospective analysis of the data obtained from The Sleep Heart Health Study revealed a two-fold increase in complex ventricular ectopy and three times the rate of non-sustained ventricular tachycardia[14]. Additionally, persons with OSA have a significantly increased risk of sudden cardiac death from cardiac causes during the sleeping hours, which is in striking contrast to the nadir of sudden death from cardiac causes during this time in persons without OSA and in the general population[15].

With the increasing evidence elucidating the relationship between OSA and cardiovascular morbidity several authorities have advocated the regular screening of cardiovascular patients. The American College of Cardiology 2005 guideline states history should include symptoms of sleep disordered breathing and screening is reasonable in all patients presenting with CHF[16]. The Joint National Committee 7 recommends thorough questioning and a high index of suspicion in any individual with HTN and a BMI greater than twenty-seven[17]. The American Academy of Sleep Medicine 2005 practice parameters calls for all patients with a history of CHF, CAD, significant arrhythmias, and stroke to be appropriately screened for sleep disordered breathing. Despite expert consensus and a preponderance of evidence linking OSA with cardiovascular disease, screening for OSA in the cardiovascular patient remains the unrecognized standard of care in the medical community.

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