# Obstructive Sleep Apnea and Cardiovascular Disease

Subjects: Respiratory System

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Among the mechanisms which explain the association between obstructive sleep apnea and myocardial infarction (MI), common risk factors include male sex, age, hypertension, obesity, and smoking. However, other direct effects of obstructive sleep apnea merit consideration. The combination of repetitive apnea–hypopnea, hypoxia, and arousal from sleep increases sympathetic activity, which is maintained during wakefulness, thus increasing myocardial oxygen demand. The mechanistic understanding which connects obstructive sleep apnea and cardiovascular disease is poorly understood due to the diverse and complicated elements of obstructive sleep apnea and the multiple other comorbid conditions (especially obesity) impacting cardiovascular health. When obstructive apnea or hypopnea occurs, the upper airway collapses throughout sleep, affecting a complete or partial interruption of airflow even with sustained respiratory struggle. The sympathetic tone is stimulated, and respiratory work increases as opposed to the closed upper airway, increasing negative intrathoracic pressure. Stimulation of the sympathetic tone across the parasympathetic system affects heart rate and blood pressure. Awakening from sleep terminates the asphyxia event, with re-establishing airflow and re-oxygenation but further increased sympathetic tone. Obstructive sleep apnea seems to be correlated with increased levels of inflammatory cytokines. Furthermore, metabolic dysregulation is observed in obstructive sleep apnea patients (with abnormalities in both fat and glucose metabolism.

Keywords: obstructive sleep apnea ; obesity ; cardiovascular diseases ; weight loss

## 1. Hypertension

Obstructive sleep apnea is common in middle-aged and older people, although hypertension is also prevalent among middle-aged and older people. This increases the chance of significant complications between hypertension and obstructive sleep apnea. The level of the complications of hypertension and obstructive sleep apnea is significantly greater than expected. Hypertension is prevalent in patients with obstructive sleep apnea and contributes to vascular injury and cardiovascular events. Several pathophysiologic mechanisms contribute to the increased risk of hypertension in individuals with obstructive sleep apnea, including upregulation of neurohormonal pathways, endothelial dysfunction, and inflammation [1]. Although patients with obstructive sleep apnea have a higher incidence of hypertension [2], the inverse is also true because patients with hypertension are more likely to experience sleep-disordered breathing, especially those who have failed to respond to traditional treatment. Up to 84% of this subset of patients may have undetected obstructive sleep apnea [3].

Animal experiments have provided direct proof that obstructive sleep apnea causes hypertension. When obstructive sleep apnea is induced, it results in acute transient rises in nighttime blood pressure and ultimately culminates in persistent daytime hypertension [2]. When blood pressure is strictly regulated in rats, it also decreases sleep apneas [4].

In humans, a causal link between obstructive sleep apnea and hypertension has not been established because variables such as age and obesity confound the association. However, epidemiological data suggest that hypertension was found in approximately 50% of patients with obstructive sleep apnea (7).

## 2. Dyslipidemia

Obstructive sleep apnea is commonly associated with elevated plasma triglycerides, low-density lipoprotein cholesterol (LDL-c), and total cholesterol. Moreover, the reduction in high-density lipoprotein (HDL) may, in part, be due to deleterious oxidative processes commonly found in patients with obstructive sleep apnea [5][6][7]. The effect of treating obstructive sleep apnea in children with adenotonsillectomy is variable as regards the impact on lipid profiles [8] because chronic intermittent hypoxia may affect both lipid biosynthesis and lipid peroxidation [9].

## 3. Type 2 Diabetes

Inflammation in patients with type 2 diabetes is characterized by elevated levels of proinflammatory cytokines or a rising number of white blood cells in the blood or tissue. Stimulation of the inflammatory process often indicates abnormalities such as tissue injury and organ dysfunction. Obesity might cause chronic low-grade inflammation and hat is involved in type 2 diabetes. In addition, adipose-specific cytokines (leptin adiponectin, leptin, and interleukin 6 (IL-6)) are secreted by visceral adipocytes and inflammatory cytokines (tumor necrosis factor α (TNF-α)). An elevated amount of fatty tissue draining into the chemokines, portal vein, and IL-6 production can induce liver and systemic insulin resistance [10][11]. Although obesity is a serious risk factor for type 2 diabetes mellitus, coexistent severe obstructive sleep apnea may independently add to the risk. In addition, the relationship between intermittent hypoxia and insulin resistance [12] has been assessed by evaluating the effect of hypoxia–reoxygenation cycles on insulin target tissues. Rodent models suggest that chronic exposure to intermittent hypoxia induces insulin resistance [13].

## 4. Atrial Fibrillation

Obstructive sleep apnea is a common risk factor for atrial fibrillation [14]. Recurrent episodes of obstructive sleep apnea may lead to cardiac structural and electric remodeling. Repetitive episodes of obstructive sleep apnea in an animal model can cause atrial fibrosis and important changes in connexin-43 distribution and expression, thus leading to slow atrial conduction. This increases the vulnerability to arrhythmias, including atrial fibrillation [15]. Furthermore, untreated obstructive sleep apnea doubles the risk of recurrence of atrial fibrillation in patients after electrical cardioversion. And treatment of obstructive sleep apnea with CPAP attenuates the risk of atrial fibrillation [16]. Obstructive sleep apnea shares many common risk factors with atrial fibrillation. The prevalence of both atrial fibrillation and obstructive sleep apnea is rising due to increases in obesity and cardiovascular disease. The close association between obstructive sleep apnea and cardiovascular disease, and atrial fibrillation and cardiovascular disease may obscure a directly causal relationship between atrial fibrillation and obstructive sleep apnea. The interplay of the pathophysiology of these chronic diseases is complex and likely bidirectional. And obstructive sleep apnea may contribute to atrial fibrillation, and, in turn, atrial fibrillation promotes the development of obstructive sleep apnea. Nonetheless, these entities are associated with one another, independently of other cardiovascular diseases [17].

## 5. Heart Failure

Sleep apnea is predictable in patients with heart failure, with a prevalence of between 50% and 70% [18]. Mainly, central sleep apnea accounts for two-thirds of the sleep apnea cases in this population, while obstructive sleep apnea is less frequent. Central sleep apnea is a frequent concomitant finding in patients with severely impaired cardiac function [18]. Another study aimed to assess the prevalence of sleep-disordered breathing and its associated risk factors in French patients with heart failure showed that 30% of syndromes were classified as central and 70% as obstructive [19]. Coexisting sleep apnea in patients with heart failure has been associated with an increased risk of adverse outcomes, including mortality [20]. Several pathophysiological processes resulting from apneic events may explain this association. These involve stimulation of the sympathetic nervous system [21] and increased preload and afterload resulting from perturbation of intrathoracic pressure while struggling to inspire against blocked airways [22]. Moreover, worsening hypertension, increased risk of arrhythmias including sudden cardiac death [23], and myocardial infarctions [24] are other mechanisms by which sleep apnea may worsen outcomes in patients with heart failure [25].

The relationship between obstructive sleep apnea and cardiovascular events remains unclear. A systematic review and meta-analysis conducted by Loke, Yoon K., et al. suggested that obstructive sleep apnea may be an independent risk factor for cardiovascular, stroke, and overall mortality. Due to imprecision and inconsistencies in the data, the strength of potential association between obstructive sleep apnea and ischemic heart disease remains unclear [26]. A cohort study evaluating the relationship between obstructive sleep apnea-related variables and the risk of CV events revealed that several obstructive sleep apnea-related factors other than the apnea–hypopnea index were important predictors of a composite CV outcome [27]. Hence, the need for a randomized controlled trial is crucial.

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