

## The Cardiac Consequences of the Obstructive Sleep Apnea-Hypopnea Syndrome

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### Abstract

The obstructive sleep apnea-hypopnea syndrome (OSAHS) is a common disorder, estimated to occur in 4% of males and 2% of females in the workforce. This incidence increases with age. Obstructive sleep apnea-hypopnea is responsible for acute and chronic heart disease, but is a readily treatable disorder that is both underdiagnosed and underappreciated in health care. Because the cardiac consequences of untreated sleep apnea are so profound and the treatment relatively simple, the disorder needs to be recognized more frequently.

**Key Words:** Sleep apnea, obstructive sleep apnea, hypertension, heart, cardiac, arrhythmia, vascular.

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### What Is Obstructive Sleep Apnea-Hypopnea?

THE OBSTRUCTIVE SLEEP APNEA-HYPOPNEA syndrome (OSAHS) is characterized by repetitive partial (hypopnea) or complete (apnea) closure of the upper airway during sleep. A common disorder, it is estimated to occur in 4% of males and 2% of females in the workforce (1). This incidence increases with age (2). Repetitive airway obstruction is associated with arterial oxygen desaturations, surges in sympathetic activity and/or short awakenings called “electrocortical arousals.” But there is another feature of OSAHS that requires close attention by health professionals.

The association between OSAHS and cardiovascular disease was first observed in 1985 (3). Since then, studies have demonstrated a clear relationship between OSAHS and arterial hypertension (HTN), cardiac arrhythmias and pulmonary hypertension. Currently we are learning more about the immunological and vascular effects of OSAHS on the cardiovascular system.

Physicians should suspect OSAHS in patients with snoring and daytime somnolence and in those with unexplained hypertension or arrhythmias. Al-

though OSAHS was first identified in obese men, one does not need to be obese or male to have the syndrome.

The diagnosis of OSAHS is made with a sleep study, formally called “nocturnal polysomnography” (NPSG). The patient is observed in a sleep laboratory overnight, where physiological parameters such as those recorded in an electroencephalogram (EEG), eye movements, respiration, heart rate, chest and abdominal movement, oxygen saturation and muscle activity are monitored. The most common and effective therapy is continuous positive airway pressure (CPAP), a form of noninvasive assisted ventilation that delivers air under pressure, which acts as a pneumatic “splint” to keep the airway open.

### OSAHS and Hypertension

The prevalence of OSAHS in hypertension is 22–48%. The Sleep Heart Health Study indicated that the risk of HTN increases with escalating degrees of apnea or hypopnea (4). Nieto found that after adjusting for demographics and anthropometric variables, the odds ratio for hypertension for those with a high number of apneas ( $\geq 30$ /hour) was 1.37 relative to those without apneas. This and other studies have confirmed that OSAHS is an independent risk factor for HTN.

OSAHS appears to cause both nocturnal and daytime hypertension. In 1993, Somers described surges in sympathetic discharge in the sural nerve

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after a Mueller maneuver, which is effectively an instance of apnea (5). In 1995, he described persistent sympathetic nerve activity increase during the day in patients with OSAHS, with further increases in blood pressure and sympathetic nerve activity during sleep (6). Hypertension in OSAHS is probably mediated by this enhanced sympathetic nerve activity. The mechanism is thought to involve stimulation of the peripheral chemoreceptors. These chemoreceptors, which are under neural control, are “reset” so that daytime hypertension persists.

Pepperell illustrated that treatment of OSAHS with CPAP produces an immediate or “first night” drop in blood pressure (7). He further demonstrated that blood pressure normalizes during the daytime after one month of therapy with CPAP. It is common to observe that patients with HTN and OSAHS who receive CPAP therapy often need less antihypertensive medication and are sometimes cured of their hypertension.

### **OSAHS and Arrhythmias**

Even healthy humans are vulnerable to arrhythmias during sleep. Gulleminault noted 42 episodes of sinus arrest (lasting 2–9 seconds) in healthy adults during sleep (8). These cardiac events were not associated with OSAHS or significant oxygen desaturation. Individuals with ischemic heart disease are particularly vulnerable to arrhythmias, ST segment depression and T wave inversion.

Atrial arrhythmias and first- and second-degree atrioventricular block have been described in normal subjects during sleep (9). Brodsky monitored 24-hour continuous EKGs in 50 young, healthy males and observed pauses of up to 2.0 seconds in 30% of them (10). Tachyarrhythmias and bradyarrhythmias have been implicated as likely causes of cardiovascular morbidity in patients with OSAHS. The risk of arrhythmia with OSAHS appears to be related to sleep apnea severity. Analysis of electrocardiographic recordings of 458 patients with sleep apnea showed a 58% prevalence of arrhythmias in these patients (11).

### **CPAP as Therapy**

CPAP reduces ventricular irritability in those with OSAHS and central sleep apnea (CSA). CSA is the condition in which absence of respiratory effort leads to cessation of breathing. Javaheri studied 29 patients with sleep apnea and left ventricular ejection fractions of less than 45% (12). Eight patients had OSAHS and 21 had CSA. All patients had stable compensated heart failure without changes in medical therapy for 4 weeks and at least 15 respiratory events per hour during sleep. In 55% of patients with

heart failure and sleep apnea, the first night of CPAP eliminated sleep-disordered breathing and reduced ventricular irritability. Oxygen desaturations and the number of electrocortical arousals (short awakenings) were also reduced. It is known that both desaturations and arousals are associated with increased sympathetic nerve activity. Reduction of sympathetic nerve activity probably diminishes ventricular irritability. In addition, improved saturation may improve myocardial oxygen delivery.

### **Atrial Pacing as Therapy**

Recently Garrigue reported 15 patients with heart failure and arrhythmia (9 patients with sinus node disease and 6 patients with brady-tachy syndrome), who had permanent atrial-synchronous ventricular pacemakers and underwent three consecutive sleep studies (13). The first night was a diagnostic night. Seven patients had OSAHS and eight patients had CSA. The patients were randomly assigned to undergo one of two sets of procedures on the second night and the other set on the third night. During one of the two nights, the basic ventricular rate of the pacemaker was programmed at 40 beats per minute, allowing the inherent atrial rhythm to be evident. During the other night, atrial overdrive stimulation was provided at the mean heart rate from the first night + 15 bpm. Interestingly, when patients had atrial overdrive pacing, there was a reduction of more than 50% in the number of apneas and hypopneas. Although this is a small study, it is intriguing to consider that atrial pacing may be beneficial for those with OSAHS.

### **Immunological and Vascular Effects of OSAHS**

OSAHS affects platelet activation and augments adhesion molecules. These effects may have cardiovascular consequences. Spontaneous nocturnal platelet activation and platelet aggregation are both increased in patients with OSAHS (14). When CPAP therapy is initiated there is an immediate decrease in platelet activation and aggregation, suggesting that CPAP may diminish cardiac risk.

Circulating levels of adhesion molecules—intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and E-selectin—are significantly increased in patients with moderate-to-severe OSAHS, compared with matched controls (15). These molecules mediate cellular interactions and transmigration of circulating leukocytes to the endothelial cells, one of the initial steps in the pathogenesis of atherosclerosis. It has not been determined if CPAP treatment diminishes the levels of these adhesion molecules.

### Summary

OSAHS causes and exacerbates cardiovascular disease. This is probably because hypertension, arrhythmias and adverse vascular effects are increased in patients with untreated OSAHS. In patients with cardiovascular disease or essential hypertension, the diagnosis of OSAHS should be entertained. CPAP therapy is relatively noninvasive and reduces cardiovascular risk.

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