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Cardiovascular Sequelae of Sleep Apnea

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Abstract

Obstructive sleep apnea (OSA) is characterized by recurrent complete and partial upper airway obstructive events, resulting in intermittent hypoxemia, autonomic fluctuation, and sleep fragmentation. In individuals with hypertension, heart failure, coronary artery disease, pulmonary hyper tension, atrial fibrillation, and stroke, OSA prevalence can range from 40% to 80%. OSA is frequently under diagnosed and under treated in cardiovascular practise, despite its significant incidence in patients with heart disease and the susceptibility of cardiac patients to stresses and unfavourable cardio vascular outcomes. In patients with pulmonary hypertension, resistant/poorly managed hypertension, and recurrent atrial fibrillation following cardioversion or ablation, screening for OSA is advised.

Keywords: OSA, SDB, Apnea.

Introduction

A known risk factor for the emergence of hypertension and other cardiovascular illnesses is sleep disordered breathing (SDB). The burden of cardiovascular disease caused by SDB is predicted to increase in the coming years due to the links between SDB and obesity and ageing. Fortunately, a large body of treatment research indicates that SDB should be included in the category of "modifiable" risk factors. Although treating sleep Apnea would seem like the easiest method to lower cardiovascular risk, many patients reject or use just a small portion of the laborious, cutting-edge therapies, and many go undetected Progress in this field of study will provide a logical strategy for the treatment and prevention of SDB's cardio vascular consequences.

Acute Effects of Sleep Apnea on the Cardiovascular System 1. Central hemodynamic effects

Hypercapnia, intrathoracic pressure oscillations, arterial oxygen desaturation, and, in most instances, disturbed sleep are all symptoms of OSA episodes. Transient reductions in left ventricular stroke volume are caused by the extremely low intrathoracic pressures created by difficult breathing[1]. Additionally, minor, momentary drops in systemic arterial pressure are caused by respiratory straining. Due to lower heart rate and decreased stroke volume, which can be significant in certain people, cardiac output decreases during obstructive apnea[2]. Apnea-induced restrictions on stroke volume and heart rate are quickly lifted upon breathing resume, permitting release of the increased cardiac output into a peripheral vascular bed that has been constrained by an increase in sympathetic vasomotor outflow. As a result, the systemic arterial pressure increases noticeably and briefly during the immediate postapnea phase[3].

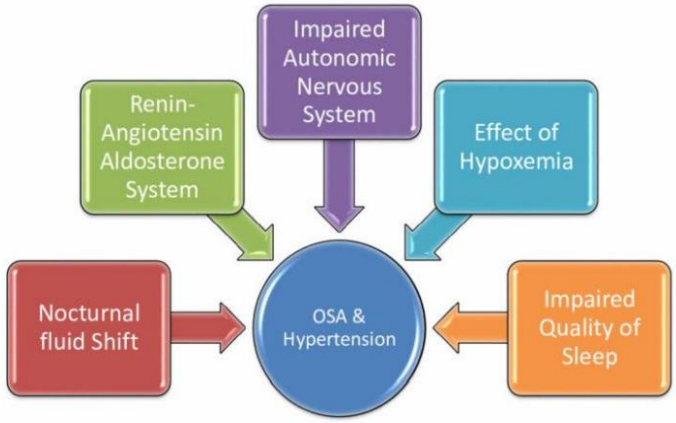
Peripheral circulation: Apnea-induced vasoconstriction has been observed in the forearm and the finger of patients with OSA.[4] Most arterial beds experience vasodilation after being exposed to hypoxia or hypercapnia acutely, and they hypothesise that prolonged asphyxic exposures affect the fundamental neuronal and local processes that regulate vascular resistance[5].

Pulmonary circulation: The pulmonary circulation experiences cyclical patterns of vasoconstrictions and relaxations during episodes of OSA, which result in pronounced changes in pulmonary artery pressure[6].These fluctuations are caused by the local vascular effects of alveolar hypoxia and hypoxemia, because they can be abolished by supplemental oxygen[7].

Cerebral circulation: Because of the cerebral circulation's extreme sensitivity to variations in PaO2 and PaCO2, bouts of OSA have a significant impact on blood flow in this vascular bed. During apneas, cerebral blood flow gradually rises before dropping suddenly during the post-apnea hyperventilation interval[8].

Associations Between Sleep Apnea and Cardio vascular Disease.

Hypertension: The pathophysiology of HTN in OSA is complex and is dependent on various factors, such as an increase in sympathetic tone, peripheral vasoconstriction, increased renin-angiotensin aldosterone activity, and altered baroreceptor reflexes[9]. The factors linking the pathophysiology of HTN and OSA are hypoxemia, nocturnal fluid shift, an increase in sympathetic tone with a decrease in parasympathetic tone, impaired quality of sleep, and renin-angiotensin-aldosterone system.



Factors relating hypertension and obstructive sleep apnea (OSA)

Figure 1:

In individuals with HTN and OSA, the fluid from the lower limbs is redistributed to the neck at night, which worsens blockage, raises blood pressure, and results in bouts of hypopnea or hypoxia. Aldosterone levels that are higher also promote fluid retention, which worsens upper airway obstruction[10]. The hormonal system known as renin-angiotensin-aldosterone controls the body's fluid, electrolyte, and blood pressure levels. Angiotensinogen is transformed to angiotensin I, which

is then converted to angiotensin II by the kidneys' production of renin and enzymes.

Angiotensin II is a potent vasoconstrictor peptide that raises blood pressure by constricting the blood vessels. Regular bouts of upper airway blockage cause hypoxia, which in turn causes renin to become more active. Patients with OSA had greater levels of angiotensin II and aldosterone, especially when they also have co-existing HTN, according to a 2016 meta-analysis of 13 studies[11].

Alterations in arterial wall structure and biomechanics People with OSA have been found to have thicker carotid intima-media and stiffer arteries. Endothelium-derived regulators of vascular stiffness with opposing activities, NO and ET-1, are present in lower and higher concentrations in the blood, respectively[12]. Mitogenic factors known to participate in remodelling (e.g., vascular endothelial growth factor, basic fibroblast growth factor, platelet - derived growth factor) are upregulated during hypoxia and during inflammation. Inflammation triggers secretion of enzymes that disrupt the balance between matrix metalloproteinases and their inhibitors[13]. It has recently become evident that adventitial fibroblasts contribute to hypoxia-induced vascular remodeling14. The release of ATP from adrenergic nerve terminals during hypoxia-induced sympathetic stimulation causes proliferation and migration of adventitial fibroblasts into the intima and media of pulmonary arteries and may also be a stimulus for remodelling in the systemic circulation.

Development of atherosclerotic lesions

OSA-induced oxidative stress and inflammation, and are likely contributors to the development of atherosclerotic lesion. ROS-activated proinflammatory transcription factors, such as activator protein-1 and nuclear factor-kB, stimulate the production of inflammatory cytokines that cause proliferation of vascular smooth muscle cells in the intimal layer and adhesion of leukocytes to the endothelium[15]. Multiple sources of evidence suggest that OSA promotes thrombosis, because enhanced platelet activation and aggregation, enhanced erythrocyte adhesiveness and aggregation, increased fibrinogen levels, and diminished fibrinolytic activity have all been observed in patients with OSA.

Cerebrovascular disease

An association exists between OSA and atrial fibrillation; therefore, thromboembolism may be an important cause of stroke in OSA patients. Beelke et al. 16 recently demonstrated that apneainduced changes in intrathoracic pressure cause interatrial shunting in patients with patent foramen ovale. In the setting of hyper coagulability, this anomaly could give rise to embolization.

Metabolic Syndrome and Type 2 Diabetes

Independent of adiposity level, OSA has been linked to a higher risk of the metabolic syndrome and type 2 diabetes. Both OSA and the metabolic syndrome have a connection to central obesity and have comparable patho physio logical characteristics (e.g., systemic inflammation, endo the lial dysfunction). In addition, intermittent hypoxia of adipose tissue, sympathetic activation, induction of adipocytokines, and oxidative stress may promote the development of metabolic risk factors.

Genetic aspects of OSA-related cardiovascular disease

The fact that cardiovascular disease is not a universal finding in patients with OSA suggests a role for genetic predisposition. Several investigators have studied the role of angiotensin converting enzyme (ACE) gene poly morphisms. In aggregate, these studies suggest complex, potentially important interactions between ACE gene

insertion/ deletion polymorphisms and SDB as mechanisms for OSA-related hyper tension. The ACE D allele is associated with hyper tension in subjects with mild-moderate OSA, whereas in patients with severe OSA, the ACE D allele may have a protective influence[17].

An association between OSA and a leptin receptor gene polymorphism has recently been reported[18]. In this study, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglyceride levels were higher in OSA patients with the Arg/Arg genotype. OSA is also associated with TNF-a and b2- adrenergic receptor polymorphisms Putative mechanisms by which OSA activates the sympathetic nervous system, initiating a cascade of events that results in cardiovascular disease. CNS, central nervous system; RAAS, renin-angiotensin-aldosterone system.

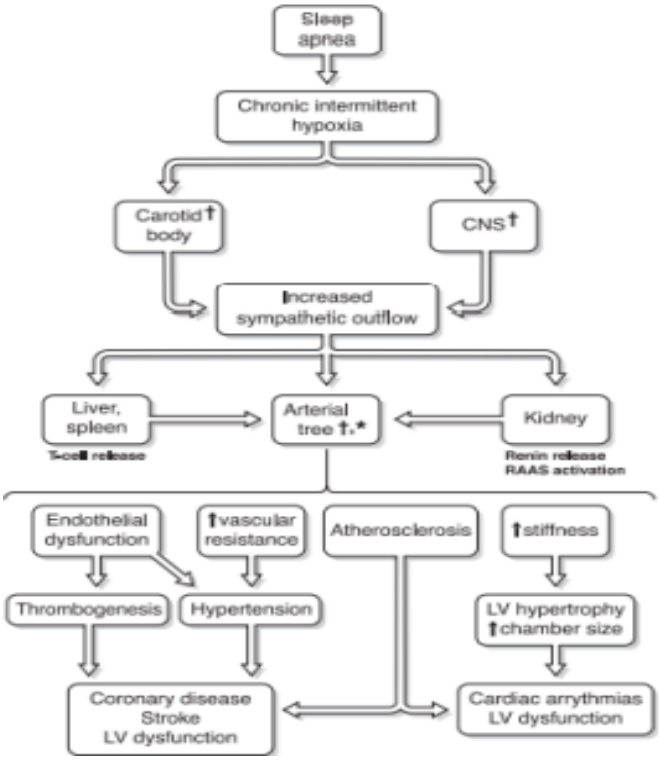


Figure 2:

Conclusion

Although OSA increases the risk of all-cause and cardiovascular mortality, this condition is often underrecognized and undertreated in cardiovascular practice. A strong association is present between OSA and numerous cardiovascular conditions. It is recommended to screen for OSA in patients with resistant/ poorly controlled hyper tension, PH, and recurrent AF after either cardio version or ablation. All patients with OSA should be considered for treatment, including behavioural modifications and weight loss as indicated. CPAP should be offered to patients with severe OSA, whereas oral appliances can be considered for patients with mild to moderate OSA or for CPAP-intolerant patients. Follow-up sleep testing should be performed to assess the effectiveness of treatment.

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