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**Research Article**

# Obstructive sleep apnea is associated with nocturnal hypertension and increase stroke risk during sleep: A review analysis

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## ABSTRACT

Sleep apnoea and/or habitual snoring began to be recognised as independent risk factors for arterial hypertension (HTN), cardiac arrhythmias, coronary artery disease, myocardial infarction and ischaemic stroke only during late 20th century.Obstructive sleep apnea (OSA) is characterized by recurrent periods of complete or partial collapse of the upper airway during sleep (apneas and hypopneas), causing sleep fragmentation and frequent awakenings which often result in excessive daytime sleepiness.The basic objective of the study is to analyse the obstructive sleep apnea and its association with nocturnal hypertension and increase stroke risk during sleep.In healthy individuals, sleep is associated with a 10%–15% reduction in systolic and diastolic BP compared to wakefulness. In addition to its effect on the cardiovascular system, an arterial blood flow steal phenomenon has been described in patients with acute stroke.It is concluded that sleep apnoea causes pathological increase in sympathetic activity, contributing to autonomic dysregulation. This dysautonomia probably contributes to worsening of the cardiovascular risk profile in patients with sleep apnoea, and may be responsive to treatment with positive airway pressure ventilation and other sleep apnoea therapies.

**Key words:** Sleep, Apnea, Obstructive, Hypertension, CVD

## INTRODUCTION

The first description of obstructive sleep apnoea (OSA) was provided not by a physician or scientist, but by Charles Dickens in a series of papers titled ‘The posthumous papers of the Pickwick club’ in 1836, in which he described an obese boy who had excessive daytime somnolence, loud snoring and probably right heart failure[1]. In 1889, Hill observed that upper airway obstruction contributed to ‘stupidity’ in children. In 1965, Gastaut *et al* in France performed nocturnal polygraphy of respiratory pauses in patients with obesity, and 10 years later, Lugaresi in Italy associated nocturnal apnoeas with loud snoring[2]. The term OSAS was first defined after the 1972 Rimini conference. Around the same time, the first sleep disorders centre was established in Stanford University, California. Upper airway surgery was used for treatment of snoring in 1964 and was later used for treatment of OSA in 1981 in Japan. During the same period, nasal positive airway pressure was introduced by Sullivan for its treatment in 1981 and soon became the treatment of choice[3].

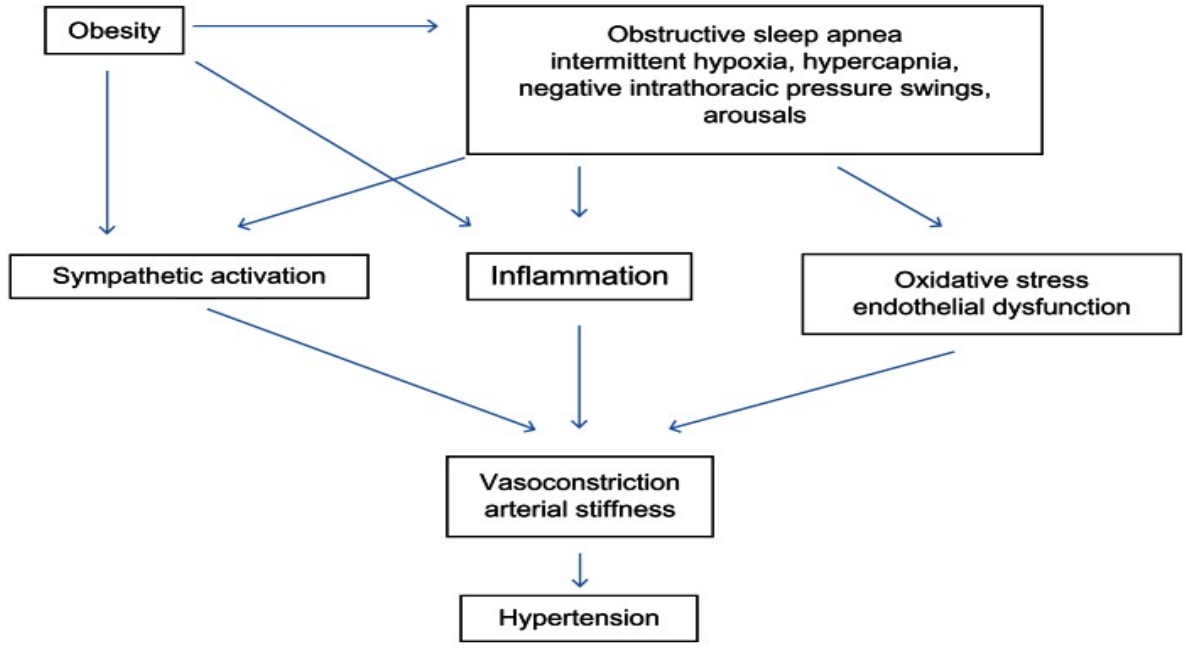
Sleep apnoea and/or habitual snoring began to be recognised as independent risk factors for arterial hypertension (HTN), cardiac arrhythmias, coronary artery disease,

myocardial infarction and ischaemic stroke only during late 20th century. The same research also recognised that patients with untreated sleep apnoea had higher risk of cardiovascular morbidity compared with patients with treated sleep apnoea[4]. Recently, population studies have suggested that sleep apnoea may be a risk factor for vascular dementia.

Obstructive sleep apnea (OSA) is characterized by recurrent periods of complete or partial collapse of the upper airway during sleep (apneas and hypopneas), causing sleep fragmentation and frequent awakenings which often result in excessive daytime sleepiness[5]. In more severe forms of the disease, periods of obstructed breathing result in profound intermittent hypoxia (IH) with underlying bursts in sympathetic nerve activity (SNA) and dramatic increases in heart rate (HR) and blood pressure (BP)[6]. The severity of OSA is determined by the apnea hypopnea index (AHI) which is a measure of the number of periods of obstructed breathing per hour of sleep[7].

**Objectives**

The basic objective of the study is to analyse the obstructive sleep apnea and its association with nocturnal hypertension and increase stroke risk during sleep.




Pathophysiological mechanism of sleep apnea and hypertension

**Hypertension and cardiovascular risk**

In healthy individuals, sleep is associated with a 10%–15% reduction in systolic and diastolic BP compared to wakefulness. Referred to as "BP dipping", this reduction coincides with the sympathetic withdrawal and subsequent parasympathetic predominance that occurs when going from wake to non-rapid eye movement (NREM) sleep[8]. Indeed all measures of cardiovascular activity show diurnal variations in activity with levels higher during the day and reducing during sleep, due to the interacting effects of the sleep wake and circadian cycles. Compared with wakefulness, NREM sleep is associated with lower BP, HR, cardiac output, and systemic vascular resistance. Rapid eye movement (REM) sleep on the other hand is punctuated by transient surges in SNA, HR, and BP. However, as REM constitutes only approximately 20% of total sleep, the net effect on cardiovascular measures is still a reduction from wake levels[9].

Sleep-related BP dipping is considered important for cardiovascular health, whilst absent or diminished nocturnal dipping of BP has been shown to be a strong independent

predictor of cardiovascular risk. In the Ohasama study of 1464 individuals, it was shown that nighttime, as well as daytime BP measured by 24 hour ambulatory blood pressure monitoring (ABPM), were linearly related with stroke risk[9].

**Sleep apnoea and stroke**

While sleep apnoea has been shown to indirectly increase the risk of stroke by its effect on vascular risk factors as aforementioned, it has also been independently associated with increased risk of stroke.In the landmark study by Yaggi *et al* investigators found an independent increase in risk of stroke and all-cause mortality with a HR of 2.24 in patients with AHI ≥35/hour. This risk remained elevated despite controlling for traditional stroke risk factors such as HTN, AF, smoking status, diabetes and hyperlipidaemia[10]. A study of 394 patients aged 70–100 years old found an AHI≥30 associated with an increased risk of ischaemic stroke in an elderly non-institutionalised male population. In a study of 1189 patients, AHI≥20 was associated with an increase in the risk of having stroke over the next 4 years. The Sleep Heart Health Study helped link sleep apnoea with stroke. It found that men in the highest quartile of AHI (>19) had a HR of 2.86 for having stroke and even in the mild moderate sleep apnoea category (AHI 5–25), each 1 unit increase in AHI increased the risk of stroke by 6%. In women, the same study found an increase in risk of stroke only in the severe sleep apnoea group[11]. In a study by Marin *et al*, severe OSA significantly increased the risk of fatal and non-fatal cardiovascular events while CPAP treatment reduced the risk. In the Wisconsin sleep cohort study, there was a significant, high cardiovascular mortality risk with untreated SDB, independent of age, sex and body mass index (BMI). The American Heart Association recommends screening for OSA for stroke prevention and suggests that treatment might be reasonable[12].

**Sleep apnoea in acute stroke**

Respiratory changes are seen acutely after stroke and can be divided into sleep–wake cycle and SDB. The changes may vary with the location of the stroke. As mentioned in an earlier section, OSA is part of SDB which includes central sleep apnoea. About 50–70% of patients with stroke have SDB as defined by AHI≥10/hour with OSA being the most common pathology.Some studies indicate that during the first 5 days poststroke central sleep apnoea predominates[12].The frequency of OSA itself has been reported to be between 38% when measured as AHI>20/hour to 72% when measured as AHI>5/hour in a meta-analysis performed by Johnson and Johnson only 7% of SDB was central apnoea1[3]. Males had a higher percentage of SDB (AHI>10) than females (65% vs 48%, respectively). Patients with recurrent strokes had higher percentage of SDB than patients with first stroke (74% vs 57% respectively). A small study involving patients in an acute stroke rehabilitation unit demonstrated AHI >10 in 91% of the studied population with a mean AHI of 32/hour[13]. Worsening of OSA may also be found after acute stroke due to impairment of respiratory muscle coordination. In some studies, presence of dysphagia was found to predict the development of OSA in patients with acute stroke, while another suggests that presence of prestrokeleucoencephalopathy predicts a more severe OSA[14]. BMI and neck circumference have also been found to predict the presence of OSA in poststroke patients.

**Effect of treating sleep apnoea in patients with acute stroke**

In addition to its effect on the cardiovascular system, an arterial blood flow steal phenomenon has been described in patients with acute stroke. The affected tissue in ischaemic stroke is supplied by maximally or nearly maximally dilated arterioles with decreased vasomotor reactivity of the blood vessels. Studies have found severely impaired cerebral vasoreactivity and increased arterial stiffness in patients with PSG confirmed severe OSA,even during wakefulness[15]. During episodes of apnoea, development of hypercapnia results in selective vasodilation of blood vessels supplying normal brain tissue,

resulting in a steal phenomenon away from the ischaemic vasoparalysed region depriving it of critical oxygen. The term 'reverse Robin Hood syndrome' has been used for this phenomenon[16].

## CONCLUSION

It is concluded that sleep apnoea causes pathological increase in sympathetic activity, contributing to autonomic dysregulation. This dysautonomia probably contributes to worsening of the cardiovascular risk profile in patients with sleep apnoea, and may be responsive to treatment with positive airway pressure ventilation and other sleep apnoea therapies. The worsening of cardiovascular profile is well known to increase the risk of stroke. Early diagnosis and treatment of sleep apnoea should reduce the risk of stroke

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