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III Secondary hypertension D. Obstructive Sleep Apnea

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Introduction

Sleep disordered breathing includes obstructive and central sleep apnea (CSA), obesity hypoventilatory syndrome, snoring and Cheyne-Stokes breathing. Obstructive sleep apnea (OSA) is usually diagnosed via polysomnography (PSG) and quantified by the number of episodes of cessation (apnea) or reduction (hypopneas) of airflow, lasting ≥ 10 seconds per hour of sleep [1]. An apnea-hypopnea index (AHI) of ≥ 5 per hour is considered significant for OSA. A diagnosis of OSA syndrome (OSAS) is made when patients have OSA and symptoms. CSA has similar clinical features, but is due to reduced central drive vs OSA which is usually due to anatomical obstruction. PSG testing distinguishes between CSA and OSA.

Epidemiology

OSA prevalence varies across populations. In middle-aged adults in the Midwest, 25% of men and 10% of women have OSA. [2, 3] The prevalence in the general US population is approximately 4% (18 million) and predicted to increase in line with the rising obesity epidemic. Prevalence of hypertension (HTN) in those with OSA is 50–60% and is related to severity. 30–40% of hypertensives also have OSA. OSA is more prevalent in obese, young to middle-aged men and in those with resistant hypertension. Indeed, 70% or more of those with resistant hypertension will have OSA and secondary hyperaldosteronism. [4, 5]

Symptoms

These include daytime somnolence, fatigue, nocturia, and disruptive snoring. Witnessed apneas are highly predictive of OSA, snoring is suggestive, and daytime somnolence may be less evident in patients with cardiovascular co-morbidities such as heart failure and atrial fibrillation.

Signs

High BMI, short thick neck, macroglossia with crowded oropharynx, nocturnal hypertension or nondipping profile, and nocturnal bradyarrhythmias. Note that some populations, such as Southeast Asians, may have sleep apnea even in the context of what by Western standards is considered a normal BMI.

Diagnosing OSA

The gold standard for diagnosis of OSA is considered to be attended PSG, although home overnight oximetry and polygraphy (measures of oxygen saturation and indices of breathing and airflow), are increasingly being used for screening purposes. Screening questionnaires (STOPBANG, Berlin and Epworth) are also utilized; however, the sensitivity and specificity of these tests vary in different populations. Resistant hypertension (unachieved target BP despite 3 or more medications) and symptoms of OSA should prompt further investigation.

Sleep apnea and hypertension

OSA is accepted as an important independent risk factor for cardiovascular diseases in general, and in particular for hypertension. It is prominent in European and American guidelines as an identifiable and treatable cause of secondary hypertension.[6–8] It is difficult to tease out confounding variables and infer a direct causal relationship for OSA and hypertension. Nevertheless, a substantive body of evidence suggests a link, after adjusting for confounders. Importantly, treating OSA may improve hypertension and may translate into improved CV risk profile and patient outcomes. In a prospective cohort study, patients with BMI <27 and severe OSA had 3 fold higher odds of hypertension. [9] OSA is seen in 71% of those with resistant hypertension vs 38% of those with controlled hypertension. [10] The mechanisms by which OSA is thought to elicit hypertension include sympathetic activation, [11] endothelial dysfunction, increased endothelin, reduced nitric oxide, and systemic inflammation. [1] Note that an increased likelihood of hypertension has also been associated with restless legs syndrome[12] and reduced sleep duration, [13]independent of the presence of OSA. Furthermore, OSA has also been linked to diabetes, metabolic syndrome, heart failure, arrhythmia, depression, and erectile dysfunction.

Using ambulatory BP monitoring to diagnose hypertension in OSA

Making a diagnosis of hypertension in OSA may be more accurate using ambulatory blood pressure monitoring (ABPM) especially if ‘white-coat’ or pseudo-resistance (eg inappropriately sized cuff) is suspected. [6, 14] Nocturnal systolic BP may predict CV mortality and morbidity better than daytime BP.

Management of OSA

These include postural measures, such as encouraging patients to sleep in a lateral position, since apnea is often worse sleeping supine, presumably due to the gravitational effects on the tongue and upper airway, promoting occlusion. Weight loss is very helpful, and

avoidance of alcohol and other neural-depressant medications before bedtime may be effective. Mandibular devices are used for milder OSA, and keep the lower jaw and tongue from “falling” backwards during sleep. The standard therapy is continuous positive airway pressure (CPAP). In those who cannot tolerate CPAP, pilot studies suggest a potential future role for hypoglossal nerve stimulation.[15] Severe and potentially life threatening OSA can be treated, at least in the short term, with tracheostomy. At present, there are no standard pharmacologic treatments for OSA.

Treatment of OSA – effects on blood pressure

Several meta-analyses and randomized trials demonstrate improved blood pressure with the use of positive airway pressure (continuous or bilevel). [16–18] A recent meta-analysis of 30 randomized trials pooled 1900 patients and showed a mean net reduction in BP of 2.5 mm Hg [16]. BP lowering effects are especially evident in those with more severe OSA. Even a modest BP reduction is of relevance when considered in the context of the 1 to 5 mmHg reduction in BP achieved by ACE inhibitors, which may reduce risk of stroke, major cardiovascular events and death between 20% to 25%. [19] Randomized trials suggest that treatment of OSA with mandibular devices can also lower BP. [20–22].

Whether other beneficial effects of OSA therapy, such as attenuation of nocturnal hypoxemia, sympathetic activation, and systemic inflammation, confer further benefit beyond blood pressure reduction remains to be determined. Currently, no class of antihypertensive is best suited to treat OSA-related hypertension. Aldosterone antagonists may be beneficial in those with resistant hypertension and OSA, but randomized data are unavailable. A recent meta-analysis suggests renal denervation may prove to be beneficial as an adjunct for patients with OSA and hypertension.[23]

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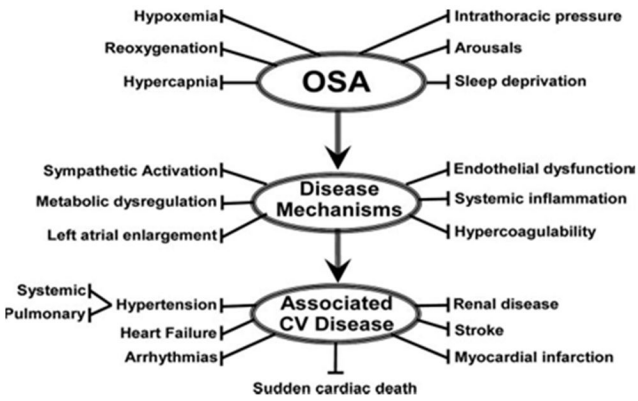

Figure 1.

Schematic outlining proposed pathophysiological components of OSA, activation of cardiovascular disease mechanisms, and consequent development of established cardiovascular disease. Reprinted from Somers VK et al [1] with permission from Lippincot Williams & Wilkins. Copyright 2008, American heart Association.

Table 1

Obstructive sleep apnea

Signs, symptoms, and risk factors	Disruptive snoring
	Witnessed apnea or gasping
	Obesity and/or enlarged neck size
	Hypersomnolence (not common in children or in heart failure)
	Other signs and symptoms include male gender, crowded-appearing pharyngeal airway, increased blood pressure, morning headache, sexual dysfunction, behavioral changes (especially in children)
Screening and diagnostic tests	Questionnaires (STOPBANG, Berlin, Epworth)
	Holter (24h ECG) monitoring
	Overnight oximetry
	Home-based/ambulatory unattended polysomnography
	In-hospital attended overnight polysomnography
Treatment Options	Positional therapy
	Weight loss
	Avoidance of alcohol and sedatives
	Positive airway pressure
	Oral appliances
	Surgery
	Radiofrequency ablation of the soft palate
	Uvulopalatopharyngoplasty
	Tonsillectomy
	Tracheostomy

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