Obstructive sleep apnea (OSA) is highly prevalent in the United States, with an estimated 1 in 4 Americans at risk for OSA. In recent years, there has been a large body of work assessing the role of OSA as an independent risk factor for hypertension. Certain patient characteristics, such as age and the type of elevated blood pressure, may confer increased likelihood that the hypertension is secondary to underlying sleep apnea. Furthermore, early diagnosis and treatment of OSA may be beneficial in the management of hypertensive patients, particularly in those with poorly controlled hypertension. The focus of this brief review is on recent developments in the characteristics and treatment of sleep apnea–associated hypertension. Because of space limitations, only limited references are provided.

Interdependence Between OSA and Hypertension

The seventh report of the Joint National Committee identified OSA as an important identifiable cause of hypertension. As many as half of all patients with sleep apnea may have underlying hypertension, and many patients with hypertension, particularly resistant hypertension, may have OSA. In fact, there seems to be an interaction between OSA severity and resistance to antihypertensive medications. Elevated nocturnal blood pressure and reduced blood pressure “dipping” during sleep also suggest a higher likelihood of underlying sleep apnea, even in normotensive patients. Whether hypertension contributes to OSA remains unknown.

Systolic and Diastolic Hypertension

OSA patients may not always exhibit elevated systolic pressures but may have a high prevalence of isolated diastolic hypertension. One study suggested that there was a significant association between the incidence of combined systolic and diastolic hypertension and the presence of sleep apnea in younger patients (<60 years of age) but not in older patients, and no significant association was seen between isolated systolic hypertension and sleep apnea in either age group. These studies suggest that the type of hypertension may need to be considered when studying epidemiologic interactions, pathophysiologic trends, and therapeutic options in sleep apnea–associated hypertension.

Effects of Gender

Sex differences in blood pressure responses to OSA remain to be fully elucidated. Population-based studies have not revealed any differential effect of gender on sleep apnea–associated hypertension prevalence in middle-aged subjects. The majority of studies have been limited primarily to men with OSA, but there is some evidence in rat models for a sex-dependent difference in response to intermittent hypoxic insults. Female rats subjected to intermittent hypoxic insults were less at risk for developing elevated blood pressure than their male or ovariectomized female counterparts. However, a recent study by Drager et al suggested that increasing age, body mass index, a family history of hypertension, and female gender independent of menopause and obesity may be risk factors for hypertension in patients with OSA. The apnea-hypopnea index has also been suggested to be associated more closely with impaired conduit and resistance vessel function in women than in men. Thus, whereas animal models suggest an attenuated hypertensive response to intermittent hypoxia in females, human studies regarding any association between female gender and sleep apnea–induced hypertension remains inconclusive.

Age

Age may also modulate the OSA-hypertension interaction. In a subgroup analysis of the Sleep Heart Health Study, patients <60 years of age with sleep apnea were more likely to demonstrate a significant relationship between minimum oxygen saturation and the development of hypertension. This particular study further demonstrated that it was only in younger patients that any significant association existed between blood pressure elevations and sleep-disordered breathing. Children with sleep apnea have higher daytime diastolic pressure and less nocturnal dipping of blood pressure than body mass–matched controls. Thus, younger patients with OSA may be more susceptible to consequent hypertension than the elderly.
Nocturnal Nondipping Blood Pressure Patterns

One of the characteristics of OSA is a nondipping nocturnal blood pressure profile. This likely results from heightened sympathetic drive during sleep, which is because of 4 main stimuli: (1) hypoxemia; (2) hypercapnia; (3) absence of lung inflation; and (4) microarousals at the end of apneic episodes. The cumulative effect of excess sympathetic activation, along with other vasoactive factors released in response to hypoxia (such as endothelin), may result in the daytime hypertension seen in these patients. However, even in the absence of daytime hypertension, sleep apnea patients may not exhibit the normal nocturnal dip in blood pressure during sleep because of apnea-induced sympathetic activation. Higher nocturnal blood pressure, independent of daytime hypertension, may play a significant role in the development of cardiovascular complications. Thus, even in normotensive patients, a nocturnal nondipping blood pressure profile may suggest increased cardiovascular risk. Further studies are needed to establish the prognostic role of elevated nocturnal blood pressures in sleep apnea.

Subclinical OSA and Prehypertension

Criteria for identification of early or subclinical manifestations of OSA and of hypertension have contributed to understanding their interaction. The seventh Joint National Committee report established guidelines for classification of patients as “prehypertensive.” These patients do not meet the clinical criteria for hypertension but are at higher risk of developing established hypertension and other cardiovascular disease. Similarly, subclinical syndromes suggestive of OSA but not meeting criteria have been identified, including snoring and upper airway resistance syndrome. Population-based studies have suggested an interaction between snoring and hypertension, although further investigation is needed to define the relationship. Thus, the relationship between OSA and hypertension could extend beyond OSA alone and may reflect a broader interaction between disturbed sleep and blood pressure.

Only in recent years have studies systematically explored any potential causal relationship between these conditions. One of these studies demonstrated a direct correlation between the severity of sleep-disordered breathing and the presence of incident hypertension 4 years later, independent of other factors. Although treatment of OSA may improve blood pressure control, whether early identification and treatment of OSA or sleep-disordered breathing contributes to long-term prevention of hypertension and other cardiovascular complications remains to be determined.

Sleep Duration and Hypertension

In patients with sleep apnea, sleep quality is decreased secondary to frequent nocturnal arousals. The effects of sleep duration on hypertension have been described recently in a large cohort of patients from the First National Health and Nutrition Examination Survey. Sleep duration of <5 hours per night was shown to significantly increase risk for hypertension in patients <60 years of age, even after controlling for obesity and diabetes. These findings are supported by results from the Sleep Heart Health Study, which suggest that sleep duration above or below a median of 7 to 8 hours per night is associated with a higher prevalence of hypertension. Thus, improving duration and quality of sleep in sleep apnea patients may conceivably help decrease the risk of developing hypertension.

Mechanisms Mediating OSA-Associated Hypertension

The mechanisms by which cardiovascular complications may develop in patients with OSA have been extensively discussed in other recent reviews. Hypertension because of OSA may be multifactorial in origin and may depend on systemic inflammation, oxidative stress, endogenous vasoactive factors, endothelial dysfunction, increased sympathetic activation, and metabolic dysregulation. The underlying maladaptive physiology contributing to hypertension may include increased atherosclerosis, vascular injury, inappropriate vasoconstriction, and heightened adrenergic tone.

Hypertension, OSA, and Changes in Cardiac Structure and Function

A growing body of evidence suggests that obesity and sleep apnea, in part via effects on blood pressure and also via direct effects on the heart, may have long-term effects on cardiac structure and function in adults and in children. Even after controlling for blood pressure, OSA may be an independent risk factor for the development of left ventricular hypertrophy and atrial enlargement. Sleep apnea has also been associated with impaired right ventricular systolic and diastolic function independent of hypertension. Cardiac structural changes are evident even in children with OSA. The effect of OSA on left ventricular systolic function and right ventricular myocardial performance index, systolic function, and free wall diameter have also been shown to improve with continuous positive airway pressure (CPAP) therapy. These data suggest that OSA may have a significant impact on cardiac structure and function that is partly reversible with CPAP therapy.

Management

The first-line treatment for OSA-induced hypertension is treatment of OSA and antihypertensive medications as indicated. The most effective methods of treatment of OSA include CPAP, postural adjustments, and weight control. Tracheostomy is considered a last resort in difficult-to-treat, medically complicated OSA. Whether any specific antihypertensive drug class has superior blood pressure control in OSA is unclear.

Sleep apnea treatments, including positional therapy, oral appliances, and bariatric surgery, have been suggested to improve hypertension in OSA patients. Presumably, the primary antihypertensive effect is achieved via relief of concomitant OSA.

CPAP

The mainstay of therapy for sleep apnea patients is CPAP, administered during sleep via a face mask or nasal mask. CPAP treatment of OSA may attenuate several of the mech-
CPAP can acutely decrease systemic blood pressure at night and seems to also lower daytime blood pressure in hypertensive patients but less so in normotensive patients. However, the antihypertensive effect may depend on the type of CPAP therapy and on the degree of improvement in OSA. In fact, a reduction of >50% in the apnea-hypopnea index may be needed to decrease blood pressure. Furthermore, CPAP may improve blood pressure by mechanisms other than improving oxyhemoglobin saturation, as suggested in a study comparing nocturnal supplemental oxygen therapy with CPAP (Figure 1). The data regarding the antihypertensive effect of CPAP therapy, however, are not entirely consistent, with some studies not showing any antihypertensive effect. Several recent meta-analyses suggested that CPAP has only very modest effects, lowering blood pressure by ~2 mm Hg, although certain subgroups may have more robust responses. Blood pressure was reduced more in those patients with more severe OSA and better effective nightly CPAP use (Figure 2). Thus, further study is needed into the role of CPAP therapy and the effectiveness of different devices in treatment of OSA-associated hypertension, as well as to determine the clinical significance of this magnitude of blood pressure reduction in the context of OSA.

Clinical Perspectives

Although OSA has been associated with a range of cardiovascular diseases, it has been etiologically linked most convincingly to hypertension. There is also considerable evidence that treatment of sleep apnea lowers blood pressure acutely and in the long-term, both at night and during the day. These effects of blood pressure lowering seem to be most marked in more severe hypertensive subjects. Resistant hypertensive patients seem to have a high prevalence of sleep apnea, and their OSA should be treated along with the treatment of hypertension.

It would be reasonable to expect that attenuation of nocturnal hypoxemia, along with blood pressure lowering, both of which could be expected to result from treatment of sleep apnea, would decrease cardiac and vascular events. Nevertheless, definitive evidence based on longitudinal randomized control studies clarifying whether treatment of OSA is accompanied by decreased cardiac and vascular events is lacking. Whether treatment of obstructive apnea decreases cardiovascular events secondary to blood pressure lowering also remains to be determined.

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References


