Obstructive sleep apnea (OSA) is characterized by transient, repetitive partial or complete upper airway obstruction during sleep associated with sleep disturbance and chronic intermittent hypoxia (CIH). One in five Americans may have OSA, defined as an apnea-hypopnea index (AHI) of \( \geq 5 \) events/h (1). Male gender and obesity are strongly associated with the presence of OSA. Importantly, most individuals (approximately 80%) with clinically significant OSA have not received a diagnosis (2). Recently, clinical guidelines recommending the incorporation of OSA into routine health evaluations with subsequent comprehensive sleep evaluation if OSA is suspected have been published (3). Individuals included as “high risk” for OSA include those with diabetes and hypertension who are also at increased risk for chronic kidney disease (CKD).

OSA has been independently associated with cardiovascular disease including hypertension (5), coronary heart disease (6), heart failure and stroke (7,8). Furthermore, individuals with OSA have a peak in sudden death from cardiac causes during the sleeping hours (9). Several proposed mechanisms in addition to increased sympathetic activation include vascular endothelial dysfunction, increased oxidative stress, systemic inflammation, increased platelet aggregability, insulin resistance, and metabolic dysregulation. Similar factors are implicated in the initiation and progression of CKD (10).

High rates of OSA have been reported in individuals who have CKD and are on dialysis (11), but sleep disorders in earlier stages of CKD have been less studied (12). The Kaiser Permanente Southern California group reported the risk for OSA for individuals with estimated GFR (eGFR) of \(<90 \text{ ml/min per 1.73 m}^2\) to be elevated compared with normal kidney function, with odds ratios ranging from 1.22 to 1.42 for each 15-ml/min decrease. However, increase severity of CKD did not have a graded increase in odds ratio for OSA. In obese adults, increasing severity of OSA is associated with higher serum creatinine (13). In patients who have stages 3 through 5 CKD and are evaluated for OSA, a weak correlation of AHI with estimated creatinine clearance was found (14).

The most direct pathophysiologic mechanism by which long-standing OSA might contribute to CKD progression is by inducing chronic elevations in BP as a result of increased sympathetic nerve discharge, raising BP during episodes of upper airway occlusion, and sustained elevations in BP during the awake state (15,16). OSA is the leading cause for secondary hypertension. Multiple studies have shown an association between AHI and hypertension (5,17). There is a dose-response association between increasing AHI and hypertension 4 years later independent of age and body mass index (18).

The apneas/hypopneas and associated CIH contribute to an increase in sympathetic activity, renin-angiotensin system, and oxidative stress, which cause endothelial dysfunction (19). CIH for 28 days is associated with sympathetic activation and augmented vascular resistance in young, healthy adults (20). OSA is associated with systolic/diastolic hypertension in those who are younger than 60 years but not in those who are older than 60 years (21). As expected, there is no association between isolated systolic hypertension and OSA.

OSA has also been linked to glomerular hyperfiltration (22), but whether OSA is an independent predictor of proteinuria is still controversial (23,24). CIH itself could have a direct effect on the kidney independent of the mechanisms described already.

In this issue, Sagakuchi et al. (25) found that Japanese individuals with CKD had a high prevalence (65%) of AHI \( \geq 5 \) events/h, with one-third of the cohort classified as having moderate (AHI 15 to 29 events/h) or severe (AHI \( \geq 30 \) events/h) OSA. Every 10-ml/min per 1.73 m\(^2\) decrease in eGFR was associated with a 42% increased risk of the likelihood of OSA after adjustment for age, body mass index, and diabetes. As described in other Asian cohorts (26), the cohort was predominantly not obese.

Also, in this issue, Roumelioti et al. (27) report that OSA is common among individuals with severe CKD (mean eGFR 18.9 ± 7.6 ml/min per 1.73 m\(^2\)) and those on dialysis therapy compared with a community-based cohort (eGFR 91.8 ± 19.2 ml/min per 1.73 m\(^2\)). The dialysis group had significantly greater stage 1 (“light sleep”) and stages 3 to 4 sleep (“deep sleep”) and significantly less stage 2 and rapid eye movement sleep, whereas patients with CKD had significantly greater stages 3 to 4 sleep compared with the control subjects. Both CKD and hemodialysis groups were
more likely to have severe OSA and nocturnal hypoxemia.

Polysomnography was used for objective testing of OSA in both studies. However, they are cross-sectional, and causation cannot be established.

Inflammatory mediators decrease after continuous positive airway pressure (CPAP) treatment (28). In addition, CPAP therapy improves endothelial function (29), decreases the abnormally increased levels of circulating apoptotic endothelial cells (30), attenuates free radical production from neutrophils (31), increases vasodilator levels (32), and mediates a decline in vasoconstrictor levels in patients with sleep apnea (33). In a recent randomized trial of 340 Spanish individuals with newly diagnosed hypertension and AHI >15, there was a modest but significant reduction in BP parameters between individuals who were assigned to optimal CPAP compared with those who were assigned to sham CPAP for 12 weeks. The mean 24-hour ambulatory optimal CPAP compared with those who were assigned to

**References**


