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COMMENTARY

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Hypertension is the crucial link between obstructive sleep apnea and arterial stiffness

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In the present issue of the Journal of Clinical Hypertension, Saeed and associates examined the data of a large sample size consisting of 6408 individuals with suspected obstructive sleep apnea (OSA) who were referred for further evaluation.[1] Specifically, the investigators assessed the interplay between OSA and arterial hypertension and their cumulative association with arterial stiffness measured by the noninvasive, readily available pulse pressure.[1]

OSA and arterial hypertension are well-described factors associated with increased risk of adverse cardiovascular events.[2] OSA as a risk factor for arterial hypertension has been extensively studied previously.[3] The prevalence of arterial hypertension in this cohort was estimated at 70.8% for patients with moderate/severe OSA (apnea-hypopnea index ≥15/h), in line with the landmark Sleep Heart Health study.[4] The pathophysiology of this interaction is based on the dysregulated activity of the sympathetic nervous system and the renin-angiotensin-aldosterone system (Figure 1).[3] Moreover, as a low-grade, sterile inflammatory disease, OSA may propagate endothelial dysfunction, a hallmark of arterial hypertension pathogenesis.[3,5] Moreover, potent associations of OSA with resistant and refractory hypertension have been described.[6] Surprisingly, elevated clinic blood pressure was equally observed in treated hypertensive individuals with and without OSA in this Scandinavian patient population. However, the lack of specific information regarding antihypertensive medication limits the ability to elucidate the relevance of this finding, which warrants further investigation.

Another aspect examined by the researchers concerned the association of OSA with arterial stiffness. Specifically, they noted higher pulse pressure values and a higher prevalence of increased pulse pressure, using a cut-off value of 60 mmHg, in those with OSA. However, the prevalence of arterial hypertension was nearly two-fold higher in the OSA group. After the multivariate regression analysis, this finding was predictive of abnormal arterial stiffness, together with older age and male sex. This observation is of particular interest since it adds to the existing evidence supporting an indirect relationship of OSA with arterial stiffness and arterial hypertension acting as the crucial link (Figure 1). It is critical, however, to take into account several factors, such as the multitude of methods used for arterial stiffness assessment [central or peripheral pulse pressure, carotid-femoral or ankle-brachial pulse wave velocity (PWV), augmentation index] that might be responsible for the discrepancies in the reported conclusions of each study. Moreover, the prognostic value of the markers mentioned above may differ significantly.[7,8] Despite these marker-related limitations, the supported hypothesis has been validated in a recent meta-analysis of Joyeux-Faure and associates, who showed that carotid-femoral PWV, the most commonly used marker of arterial stiffness, was independently associated with older age, systolic blood pressure, and type 2 diabetes mellitus.[9] Several contemporary studies also failed to document independent associations between OSA and arterial stiffness.[10–12]

The lack of direct association between OSA and arterial stiffness may also become evident from the inability of its therapeutic options to induce an improvement in this parameter. When examining the therapeutic effect of continuous positive airway pressure (CPAP), a first-line treatment approach in moderate/severe OSA, on PWV, a plethora of randomized trials were unable to detect an independent benefit of CPAP.[13–15] It appears that a potential positive effect of CPAP on arterial stiffness may be mediated by an improvement of blood pressure,[13,15] since CPAP has been proven to be efficient in the management of OSA-associated hypertension.[16,17] Moreover, meta-analytic data from Chalerge and associates highlighting a beneficial

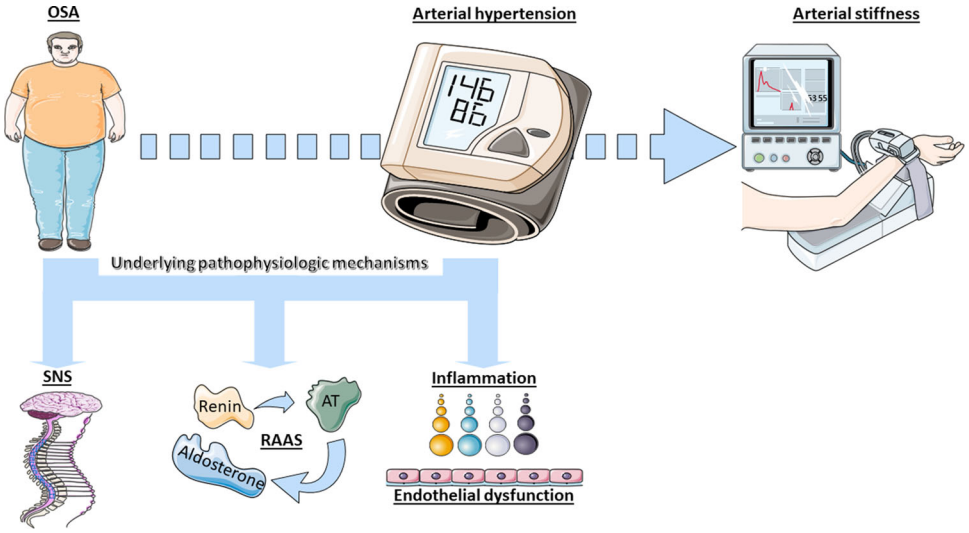

FIGURE 1 Arterial hypertension is the crucial intermediate of obstructive sleep apnea (OSA)-associated increased arterial stiffness. SNS, sympathetic nervous system; RAAS, renin-angiotensin-aldosterone system; AT, angiotensin

effect of CPAP on PWV should be interpreted with caution since the possible influence of CPAP on blood pressure control as a confounding factor could not be taken into account.[18]

Another provocative hypothesis generated by Saeed and associates was the association of smoking with a lower prevalence of abnormally increased arterial stiffness, which represented a secondary aim of the study.[1] The detrimental effect of smoking on cardiovascular health is unequivocal since it constitutes a traditional risk factor for major adverse cardiovascular events, and its cessation ranks high among the preventive goals in this direction.[19] This fact, together with the lack of additional data on smoking, including but not limited to smoking duration, smoking intensity, type of smoking, and exposure to passive smoking should raise skepticism towards this observation. According to the available evidence, however, numerous previous reports pointed to an increase in blood pressure and arterial stiffness proportional to chronicity and intensity of the exposure.[20–22] Contrary to those findings, Li and associates detected ameliorated blood pressure parameters and lower pulse pressure in current smokers.[23] At the same time, they noted an association of smoking cessation with a higher incidence of hypertension.[23] The recently reported CARDIA longitudinal study also deserves an honorable mention since the investigators found no differences in systolic blood pressure between smokers and never smokers on a large population base of young black and white individuals. In contrast, white smokers had lower diastolic blood pressure values than never smokers in a span of 30 years.[24] Pulse pressure was also elevated in both racial groups.[24]

In conclusion, the study of Saeed and associates, based on impressive sample size, provides further confirmation on the pivotal role of arterial hypertension, among other risk factors, on arterial stiffness. Moreover, it crucially depicts the central role of hypertension in OSA-associated arterial stiffness despite the inherent limitations of the cross-sectional design (causation, lack of mechanistic evidence). This study provides the rationale for intensifying hypertension management in patients with OSA, while the use of CPAP could be encouraged in this regard. However, the reported controversial effects of smoking on blood pressure and arterial stiffness need to be investigated further.

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CONFLICT OF INTEREST

The authors have no competing interests.

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