


COMMENTARY

Epidemiology of obstructive sleep apnea: What is the contribution of hypertension and arterial stiffness?

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Funding information

National Institutes of Health, Grant/Award Numbers: R01-HL146691, R01-HL159062, R01-DK123259, R01-DK033823, T32-HL144456; American Heart Association, Grant/Award Number: AHA-22POST995561

1 | EPIDEMIOLOGY OF OBSTRUCTIVE SLEEP APNEA

Obstructive sleep apnea (OSA) is defined as brief and repeated interruptions of breathing due to upper airway obstructive events during the sleep¹; these recurrent interruptions could be complete (apneas) and/or partial (hypopneas), resulting in intermittent hypoxemia, autonomic fluctuation, and sleep fragmentation.² The apnea-hypopnea index (AHI) quantifies the episodes of apnea (cessation of airflow for at least 10 seconds) and hypopnea (reduction in airflow by at least 30% for at least 10 seconds with decrease in blood oxygen saturation). When defined as an AHI > 5 events per hour of sleep, the prevalence of OSA in the United States is ~15–30% in males and 10–15% in females; instead, if defined as AHI ≥5 events per hour plus symptoms or AHI ≥15 events per hour, the prevalence is approximately 15% in males and 5% in females.³ OSA is typical in adults; males, older, and obese individuals are at a higher risk.⁴ The prevalence of OSA may also be influenced by race: indeed, it is common in African-Americans, independent of body weight.^{5,6}

2 | OSA, HYPERTENSION, AND ARTERIAL STIFFNESS: MÉNAGE À TROIS?

Patients with OSA have an increased incidence of hypertension, even when asymptomatic.^{7–9}

Arterial stiffness is common in hypertension and is a sign of structural and functional alterations of the vascular wall, associated with organ damage.^{10,11} On the other side of the coin, patients with resistant hypertension have a high prevalence of OSA.^{12,13} Hence, hypertensive patients with arterial stiffness and OSA have many complications and adverse outcomes.¹⁴ Nonetheless, the complex relationship linking hypertension, arterial stiffness, and OSA is not fully clear (Figure 1). To elucidate this matter, Saeed and associates prospectively investigated a large population of 6408 participants with suspected OSA undergoing a standard respiratory polygraphy, and the results have been published in this issue of the *Journal of Clinical Hypertension*.¹⁵

The prevalence of hypertension was 70.8% in OSA patients (defined as AHI ≥15/h) and 46.7% in non-OSA controls ($P < .0001$).

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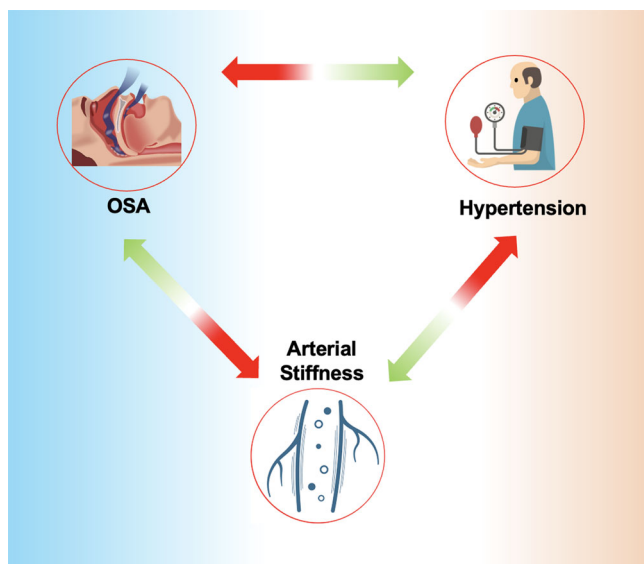


FIGURE 1 The complex relationship linking hypertension, arterial stiffness, and obstructive sleep apnea (OSA)

Hypertension and obesity were the most common modifiable cardiovascular risk factors among OSA patients; approximately one-fourth of OSA patients displayed an increased arterial stiffness, defined by a brachial pulse pressure (PP) ≥ 60 mmHg. Albeit in an unadjusted logistic regression model, OSA was associated with a 1.3-fold higher risk of having increased PP, in a multivariable-adjusted model, OSA did not retain its association with arterial stiffness, which was instead maintained by age, male sex, and history of hypertension. It is important to note that the Authors only used PP to quantify arterial stiffness and did not use PWV, generally considered the gold standard method; furthermore, the duration of antihypertensive treatment in the population was not known.

OSA is associated with a marked increase in sympathetic activity during sleep, which influences heart rate and blood pressure.¹⁶ This augmented sympathetic activity in OSA patients is most likely a result of intermittent hypoxemia, hypercapnia, and sleep fragmentation.^{14,17,18} In a controlled trial, 318 patients with moderate-to-severe OSA were randomized to either sleep education (control arm) or continuous positive airway pressure (CPAP), or nocturnal supplemental oxygen, for a period of 12 weeks; CPAP was associated with a 2.8 mmHg greater reduction in mean arterial pressure compared to controls, whereas supplemental oxygen alone did not significantly reduce blood pressure.¹⁹

A recent large clinical trial conducted in 31 309 patients undergoing overnight polysomnography revealed that patients with more severe OSA as measured by the AHI are more likely to have incident venous thromboembolism; however, adjusted analyses suggest that this association is explained due to confounding by obesity.²⁰ Indeed, OSA patients have been shown to have higher circulating levels of leptin compared to controls, and these levels are positively correlated with the AHI.²¹ Instead, the strong association between OSA and coronary

and cerebral vascular disease appears to be independent of shared risk factors including adiposity.²²

3 | OSA, HYPERTENSION, AND COGNITIVE DYSFUNCTION

Hypertension is one of the main determinants of endothelial dysfunction, particularly in the aging population.²³ Cognitive dysfunction is a well-known complication of hypertension and other cardiovascular diseases^{24,25} and several reports have highlighted the relationships between arterial stiffness and cognition in hypertensive patients.^{26–28} Furthermore, OSA sleep-disordered breathing has been associated with an increased risk of cognitive impairment.^{17,29} A recent study³⁰ evidenced a significant correlation ($r: 0.30$; $P: .002$) between arterial stiffness and executive function-processing speed performance in patients with OSA and chronic obstructive pulmonary disease (COPD). Therefore, it should be interesting to investigate the relationship between arterial stiffness and cognitive dysfunction in hypertensive patients with OSA.

4 | PERSPECTIVES: DIAGNOSING MORE, TREATING BETTER

OSA remains too often underdiagnosed and undertreated in cardiovascular practice, despite its high prevalence in patients with cardiovascular disease and the vulnerability of cardiac patients to OSA-related stressors. A recent scientific statement of the American Heart Association recommends screening for OSA in patients with resistant (or poorly controlled) hypertension, pulmonary hypertension, and recurrent atrial fibrillation after either cardioversion or ablation.²

ACKNOWLEDGEMENTS

The Santulli's Lab is supported in part by the National Institutes of Health (NIH: R01-HL146691, R01-HL159062, R01-DK123259, R01-DK033823, and T32-HL144456, to G.S.), by the Irma T. Hirschl and Monique Weill-Caulier Trusts (to G.S.), and by the Diabetes Action Research and Education Foundation (to G.S.); F.V. holds a postdoctoral fellowship from the American Heart Association (AHA-22POST995561).

CONFLICTS OF INTEREST

The authors have no competing interests.

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REFERENCES

1. Dopp JM, Reichmuth KJ, Morgan BJ. Obstructive sleep apnea and hypertension: mechanisms, evaluation, and management. *Curr Hypertens Rep.* 2007;9(6):529–534. <https://doi.org/10.1007/s11906-007-0095-2>

2. Yeghiazarians Y, Jneid H, Tietjens JR, et al. Obstructive Sleep Apnea and Cardiovascular Disease: a Scientific Statement From the American Heart Association. *Circulation*. 2021;144(3):e56. <https://doi.org/10.1161/CIR.0000000000000988>
3. McNicholas WT. COPD-OSA Overlap Syndrome: evolving Evidence Regarding Epidemiology, Clinical Consequences, and Management. *Chest*. 2017;152(6):1318-1326. <https://doi.org/10.1016/j.chest.2017.04.160>
4. Carneiro G, Zanella MT. Obesity metabolic and hormonal disorders associated with obstructive sleep apnea and their impact on the risk of cardiovascular events. *Metabolism*. 2018;84:76-84. <https://doi.org/10.1016/j.metabol.2018.03.008>
5. Redline S, Tishler PV, Hans MG, Tosteson TD, Strohl KP, Spry K. Racial differences in sleep-disordered breathing in African-Americans and Caucasians. *Am J Respir Crit Care Med*. 1997;155(1):186-192. <https://doi.org/10.1164/ajrccm.155.1.9001310>
6. Kapur VK, Auckley DH, Chowdhuri S, et al. Clinical Practice Guideline for Diagnostic Testing for Adult Obstructive Sleep Apnea: an American Academy of Sleep Medicine Clinical Practice Guideline. *J Clin Sleep Med*. 2017;13(3):479-504. <https://doi.org/10.5664/jcsm.6506>
7. Tam W, Ng SS, To KW, Ko FW, Hui DS. The interaction between hypertension and obstructive sleep apnea on subjective daytime sleepiness. *J Clin Hypertens (Greenwich)*. 2019;21(3):390-396. <https://doi.org/10.1111/jch.13485>
8. Konecny T, Kara T, Somers VK. Obstructive sleep apnea and hypertension: an update. *Hypertension*. 2014;63(2):203-209. <https://doi.org/10.1161/HYPERTENSIONAHA.113.00613>
9. Vgontzas AN, Li Y, He F, et al. Mild-to-moderate sleep apnea is associated with incident hypertension: age effect. *Sleep*. 2019;42(4):zsy265. <https://doi.org/10.1093/sleep/zsy265>
10. Guo X, Li Y, Yang Y, et al. Noninvasive markers of arterial stiffness and renal outcomes in patients with chronic kidney disease. *J Clin Hypertens (Greenwich)*. 2021;23(4):823-830. <https://doi.org/10.1111/jch.14185>
11. Wilson S, Mone P, Jankauskas SS, Gambardella J, Santulli G. Chronic kidney disease: definition, updated epidemiology, staging, and mechanisms of increased cardiovascular risk. *J Clin Hypertens (Greenwich)*. 2021;23(4):831-834. <https://doi.org/10.1111/jch.14186>
12. Sapina-Beltran E, Torres G, Benitez I, et al. Prevalence, Characteristics, and Association of Obstructive Sleep Apnea with Blood Pressure Control in Patients with Resistant Hypertension. *Ann Am Thorac Soc*. 2019;16(11):1414-1421. <https://doi.org/10.1513/AnnalsATS.201901-053OC>
13. Martinez-Garcia MA, Navarro-Soriano C, Torres G, et al. Beyond Resistant Hypertension. *Hypertension*. 2018;72(3):618-624. <https://doi.org/10.1161/HYPERTENSIONAHA.118.11170>
14. Mansukhani MP, Covassin N, Somers VK. Apneic Sleep, Insufficient Sleep, and Hypertension. *Hypertension*. 2019;73(4):744-756. <https://doi.org/10.1161/HYPERTENSIONAHA.118.11780>
15. Saeed S, Romarheim A, Mancia G, et al. Characteristics of hypertension and arterial stiffness in obstructive sleep apnea: a Scandinavian experience from a prospective study of 6408 normotensive and hypertensive patients. *J Clin Hypertens (Greenwich)*. 2022;24(4):385-394.
16. Venkataraman S, Vungarala S, Covassin N, Somers VK. Sleep Apnea, Hypertension and the Sympathetic Nervous System in the Adult Population. *J Clin Med*. 2020;9(2):591. <https://doi.org/10.3390/jcm9020591>
17. Prabhakar NR, Peng YJ, Nanduri J. Hypoxia-inducible factors and obstructive sleep apnea. *J Clin Invest*. 2020;130(10):5042-5051. <https://doi.org/10.1172/JCI137560>
18. Somers VK, Dyken ME, Clary MP, Abboud FM. Sympathetic neural mechanisms in obstructive sleep apnea. *J Clin Invest*. 1995;96(4):1897-1904. <https://doi.org/10.1172/JCI118235>
19. Gottlieb DJ, Punjabi NM, Mehra R, et al. CPAP versus oxygen in obstructive sleep apnea. *N Engl J Med*. 2014;370(24):2276-2285. <https://doi.org/10.1056/NEJMoa1306766>
20. Genuardi MV, Rathore A, Ogilvie RP, et al. Incidence of venous thromboembolism in patients with obstructive sleep apnea: a cohort study. *Chest*. 2021. In press. <https://doi.org/10.1016/j.chest.2021.12.630>
21. Li X, He J. The Association Between Serum/Plasma Leptin Levels and Obstructive Sleep Apnea Syndrome: a Meta-Analysis and Meta-Regression. *Front Endocrinol (Lausanne)*. 2021;12:696418. <https://doi.org/10.3389/fendo.2021.696418>
22. Gottlieb DJ. Sleep Apnea and Cardiovascular Disease. *Curr Diab Rep*. 2021;21(12):64. <https://doi.org/10.1007/s11892-021-01426-z>
23. Torngren K, Rylance R, Bjork J, et al. Association of coronary calcium score with endothelial dysfunction and arterial stiffness. *Atherosclerosis*. 2020;313:70-75. <https://doi.org/10.1016/j.atherosclerosis.2020.09.022>
24. Mone P, Gambardella J, Pansini A, et al. Cognitive Impairment in Frail Hypertensive Elderly Patients: role of Hyperglycemia. *Cells*. 2021;10(8):2115. <https://doi.org/10.3390/cells10082115>
25. Mone P, Gambardella J, Pansini A, et al. Cognitive dysfunction correlates with physical impairment in frail patients with acute myocardial infarction. *Aging Clin Exp Res*. 2021. In press. <https://doi.org/10.1007/s40520-021-01897-w>
26. Hanon O, Haulon S, Lenoir H, et al. Relationship between arterial stiffness and cognitive function in elderly subjects with complaints of memory loss. *Stroke*. 2005;36(10):2193-2197. <https://doi.org/10.1161/01.STR.0000181771.82518.1c>
27. Rensma SP, Stehouwer CDA, Van Boxtel MPJ, et al. Associations of Arterial Stiffness With Cognitive Performance, and the Role of Microvascular Dysfunction: the Maastricht Study. *Hypertension*. 2020;75(6):1607-1614. <https://doi.org/10.1161/HYPERTENSIONAHA.119.14307>
28. Marfella R, Paolisso G. Increased Arterial Stiffness Trumps on Blood Pressure in Predicting Cognitive Decline in Low-Risk Populations. *Hypertension*. 2016;67(1):30-31.
29. Leng Y, McEvoy CT, Allen IE, Yaffe K. Association of Sleep-Disordered Breathing With Cognitive Function and Risk of Cognitive Impairment: a Systematic Review and Meta-analysis. *JAMA Neurol*. 2017;74(10):1237-1245. <https://doi.org/10.1001/jamaneurol.2017.2180>
30. Luehrs RE, Moreau KL, Pierce GL, et al. Cognitive performance is lower among individuals with overlap syndrome than in individuals with COPD or obstructive sleep apnea alone: association with carotid artery stiffness. *J Appl Physiol (1985)*. 2021;131(1):131-141. <https://doi.org/10.1152/jappphysiol.00477.2020>

How to cite this article: Mone P, Kansakar U, Varzideh F, et al. Epidemiology of obstructive sleep apnea: what is the contribution of hypertension and arterial stiffness? *J Clin Hypertens*. 2022;24:395-397. <https://doi.org/10.1111/jch.14426>