Received: 3 September 2019 | Accepted: 18 September 2019

DOI: 10.1111/jch.13718

OPINION

WILEY

# Obstructive sleep apnea and left ventricular hypertrophy: More questions than answers

Cesare Cuspidi MD[1,2] | Carla Sala MD[3] | Marijana Tadic MD, PhD[4]

[1]Department of Medicine and Surgery, University of Milano-Bicocca, Milano, Italy

[2]Istituto Auxologico Italiano, IRCCS, Milano, Italy

[3]Department of Clinical Sciences and Community Health, University of Milano and Fondazione Ospedale Maggiore IRCCS Policlinico di Milano, Milano, Italy

[4]Department of Cardiology, Charité-University-Medicine Campus Virchow Klinikum, Berlin, Germany

**Correspondence**
Cesare Cuspidi, Istituto Auxologico Italiano IRCCS, Clinical Research Unit, Viale della Resistenza 23, 20036 Meda, Italy.
Email: cesare.cuspidi@unimib.it

Sleep-disordered breathing, in particular obstructive sleep apnea syndrome (OSAS), has been reported to unfavorably affect cardiovascular outcomes. Epidemiological studies support an association of OSAS with increased incidence rates of heart failure, coronary heart disease, sudden cardiac death, ventricular arrhythmias, atrial fibrillation, and stroke.[1] A recent retrospective analysis of the National Inpatient Sample (NIS), the largest national inpatient database in the United States, including 18.013.878 patients' hospital discharges, collected from 2012 to 2014, reports that a discharge diagnosis of OSAS (ICD-9 code 327.23) was present in 5.2% of the entire sample and, more importantly, a number of comorbidities were more frequently present in OSAS patients than in non-OSAS counterparts, including chronic heart failure (32% vs 14%), acute coronary syndrome (5% vs 4%), ventricular tachycardia (2% vs 1%), and ventricular fibrillation (0.3% vs 0.2%).[2] Numerous prospective studies conducted in different clinical settings (ie, general population, hypertension, type 2 diabetes, obesity, coronary heart disease, stroke) have documented that OSAS is an independent risk factor for both the first cardiovascular event and its recurrence.[3]

Multiple mechanisms associated with OSAS have been identified to adversely affect cardiovascular function and structure, leading to progressive cardiac and vascular remodeling and, ultimately, to overt cardiovascular disease. OSAS, indeed, is characterized by repetitive collapses of upper airways resulting in intermittent hypoxia, hypercapnia, impaired gas exchange, exaggerated sympathetic activity, and sleep disruption. In particular, OSAS-induced sympathetic activation promotes a wide array of hemodynamic and metabolic changes such as increased blood pressure (BP) and heart rate, oxidative stress, release of inflammatory substances, lipolysis, and insulin resistance. Since the early 1990s, an association between OSAS and subclinical target organ damage, an intermediate stage in the cardiovascular continuum linking unhealthy risk factors to cardiovascular disease and death, has been reported in both cross-sectional and longitudinal studies.[4]

As for subclinical cardiac damage, an increased incidence of left ventricular hypertrophy (LVH) in OSAS patients has been attributed to the synergistic effect of hypoxemia, catecholamine excess, BP elevation, non-dipping BP pattern, and intra-thoracic pressure swings affecting pre- and post-load as well as left atrial and ventricular transmural pressures.[5]

It should be emphasized, however, that available evidence targeting the association between OSAS and LVH, as assessed by echocardiography, is less consistent than expected considering the above-mentioned physio-pathological links between these conditions and the exponential growth of OSAS, nowadays the most frequent cause of resistant hypertension in the general population. The limits of the current literature in this research can be briefly summarized as follows.

One, in the last two decades less than fifty studies, including a few thousands of OSAS patients apparently free of heart disease, have provided findings on LV structure by assessing the prevalence of echocardiographic LVH or estimating LV mass indexed to body surface area, height or height to allometric power of 2.7 in subjects with and without OSAS. Two, prevalence rates of LVH markedly varied in OSAS patients and controls (from 8.0% to 88.0% and from 8.8% to 67.0%, respectively), this variability among published reports likely depending on differences in demographic/clinical features of selected patients, criteria defining OSAS and LVH phenotypes. Three, in some studies LVH prevalence and average LV mass index values have been reported similar in patients with OSAS as in non-OSAS controls. In contrast, other studies concluded for a more pronounced subclinical cardiac involvement in OSAS patients, in particular in subgroups with more severe forms. Four, these conflicting results may be related, among other reasons, to

  

the differences among studies in the criteria used for LVH definition (more or less restrictive diagnostic cutoffs), in methods for LV mass normalization, in adjustments for major confounders. Five, a further source of variability concerns the diagnosis of OSAS that was based on apnea-hypopnea index (AHI) ≥5 event/h in some studies and ≥15 event/h in others. As for the classification of hypopnea, this condition was variously defined as an airflow reduction from 30% to 50% for at least 10 seconds, with or without arousals and/or oxy-hemoglobin desaturation by 3%-4%. Finally, the differences in methods used to identify OSAS phenotypes (ie, unattended home sleep recordings versus in-hospital sleep recordings, polygraphy versus polysomnography) further impair the comparison of the results provided by current literature.[6]

In conclusion, available information on the role of OSAS in the development/progression of LVH remains scanty and is flawed by methodological differences in both OSAS and LVH phenotyping. This unsolved issue constitutes a challenge for precision medicine that is called to clarify the implications of a such association in order to reduce the impact of CV diseases in the community.

## CONFLICT OF INTEREST

The authors report no conflicts of interest.

## ORCID

*Cesare Cuspidi* https://orcid.org/0000-0002-7689-478X
*Marijana Tadic* https://orcid.org/0000-0002-6235-5152

## REFERENCES

1. Drager LF, McEvoy RD, Barbe F, et al; INCOSACT Initiative (International Collaboration of Sleep Apnea Cardiovascular Trialists). Sleep apnea and cardiovascular disease: lessons from recent trials and need for team science. *Circulation*. 2017;136:1840-1850.
2. Salama A, Abdullah A, Wahab A, et al. Is obstructive sleep apnea associated with ventricular tachycardia ? A retrospective study from the national inpatient sample and a literature review on the pathogenesis of obstructive sleep apnea. *Clin Cardiol*. 2018;41:1543-1547.
3. Brown DL, Shafie-Khorassani F, Kim S, et al. Sleep-disordered Breathing is associated with recurrent ischemic stroke. *Stroke*. 2019;50:571-576.
4. Hedner J, Ejnell H, Caidahl K. Left ventricular hypertrophy independent of hypertension in patients with obstructive sleep apnoea. *J Hypertens*. 1990;8:941-946.
5. Chami HA, Devereux RB, Gottdiener JS, et al. Left ventricular morphology and systolic function in sleep-disordered breathing: the sleep heart health study. *Circulation*. 2008;117:2599-2607.
6. Cuspidi C, Tadic M, Sala C, et al. Blood pressure non-dipping and obstructive sleep apnea syndrome: a meta-analysis. *J Clin Med*. 2019;8:1367.

**How to cite this article:** Cuspidi C, Sala C, Tadic M Obstructive sleep apnea and left ventricular hypertrophy:More questions than answers. *J Clin Hypertens*. 2019;21:1908–1909. https://doi.org/10.1111/jch.13718