



EVAGELISMOS GENERAL HOSPITAL OF ATHENS  
A' DEPARTMENT OF CARDIOLOGY

July 2013 • Volume 8 • No 3 (31)

ISSN: 1792-7919

e-ISSN: 1792-7927

## RHYTHMOS

*Editor-in-Chief: Antonis S. Manolis, MD*

*Editorial Staff: Spyridon Koulouris, MD, Sokratis Pastromas, MD, Ektor Anninos, MD, Effie Rouska, MD*

*Διευθύντρια Σύνταξης: Αντώνης Σ. Μανώλης*

*Μέλη: Σπυρίδων Κουλούρης, Σωκράτης Παστρομάς, Έκτωρ Άννινος, Έφη Ρούσκα*

*URL: <http://rhythmos.dyndns.org> / <http://rhythmos.info.tm> / <http://www.evangelismos.dom.gr>*

### EDITORIAL

#### **Evidence Linking Obstructive Sleep Apnea to Hypertension**

*Athanasios I. Triantafyllou, MD, Antonis S. Manolis, MD*

First Department of Cardiology, Evagelismos Hospital, Athens, Greece

Obstructive sleep apnea (OSA) has been linked to hypertension in several experimental, epidemiological, and clinical studies. Animal models of sleep apnea have provided strong evidence for a causal relationship with hypertension.<sup>1</sup> Studies in humans have demonstrated that patients with sleep apnea have an increased blood pressure and a higher incidence of hypertension.<sup>2-4</sup> The most compelling evidence linking OSA and hypertension was provided by data from the Wisconsin Sleep Cohort Study.<sup>5</sup> This study has demonstrated a dose-response association between sleep-disordered breathing at baseline and the presence of de novo hypertension 4 years later.<sup>5</sup> The odds ratios for the presence of hypertension at the 4-year follow-up study according to the apnea-hypopnea index (AHI) at base line were estimated after adjustment for baseline hypertension status, body mass index (BMI), neck and waist circumference, age, gender, and weekly use of alcohol and tobacco. Relative to the reference category of an AHI of 0 events per hour at baseline, the odds ratios for the presence of hypertension at follow-up were 1.42 (95% confidence intervals-CI 1.13-1.78) with an AHI of 0.1-4.9 events per hour at base

line as compared with none, 2.03 (95% CI 1.29-3.17) with an AHI of 5.0-14.9 events per hour, and 2.89 (95% CI 1.46-5.64) with an AHI of 15.0 or more events per hour. These findings suggest two important concepts. First, sleep-disordered breathing is a risk factor for hypertension in the general population. Second, even sleep apnea that is considered mild may also contribute significantly to overall blood pressure levels.

While the prevalence of sleep apnea increases with age, the link between sleep-disordered breathing and hypertension may be attenuated by aging.<sup>6</sup> A recent analysis of the Sleep Heart Health Study<sup>7</sup> has shown that OSA is independently associated with hypertension in middle-aged subjects but not in elderly subjects. Interestingly, isolated systolic hypertension was not associated with sleep-disordered breathing. In those aged <60 years, AHI was significantly associated with higher odds of systolic/diastolic hypertension [odds ratio-OR=2.38 (95% CI 1.30-4.38) for AHI 15-29; OR=2.24 (95% CI 1.10-4.54) for AHI≥30]. Thus, taking into account age and distinguishing between hypertensive subtypes reveals a stronger association between sleep-disordered breathing and hypertension for young and middle-aged subjects than previously reported.

The prevalence of hypertension is underdiagnosed in OSA patients if blood pressure is assessed by office readings only. Baguet et al.<sup>8</sup> have shown that ambulatory blood pressure monitoring might be of particular significance in the hypertension diagnosis of OSA patients. While 42% of their OSA patients demonstrated

office hypertension, 58% had daytime hypertension, and 76% had night time hypertension. Thus, OSA is characterised by a “non-dipping” pattern of hypertension, which itself has been associated with an adverse cardiovascular prognosis.<sup>9</sup>

Obstructive sleep apnea increases the prevalence of target organ damage in patients with hypertension, and is an independent risk factor for the development of left ventricular hypertrophy.<sup>10</sup> Furthermore, OSA affects functional and structural properties of large arteries contributing to hypertension and atherosclerosis progression. Middle-aged patients with OSA free of overt cardiovascular disease were shown to have increased pulse-wave velocity and increased intima-media thickness.<sup>11</sup> Marked increases in transmural pressure of the aorta wall during obstructive events may contribute to the increased risk of thoracic aorta dissection in hypertensive patients. Indeed Sampol et al.<sup>12</sup> have recently demonstrated a high prevalence of previously undiagnosed and frequently severe OSA in patients with thoracic aorta dissection.

Furthermore, OSA has been linked with *resistant hypertension*, defined as hypertension refractory to at least three antihypertensive medications, one of which is a diuretic.<sup>13-15</sup> Resistant hypertension has been reported in ~12% among the hypertensive population.<sup>15</sup> In a recent prospective study of 204 patients (mean age 48 years) with ambulatory daytime mean blood pressure >135/85 mm Hg, the frequency of OSA was evaluated.<sup>15</sup> Mild, moderate and severe OSA were present in 55 (27.0%), 38 (18.6%) and 54 (26.5%) patients, respectively. Importantly, three comorbidities, OSA, metabolic syndrome and primary aldosteronism, were the most frequent conditions encountered. Fortunately, treatment of OSA with use of continuous positive airway pressure (CPAP) has a beneficial effect not only in lowering blood pressure but also in ameliorating additional concomitant risk factors.<sup>16</sup> Thus, OSA with its intermittent hypoxia should be sought and considered as a potentially modifiable risk factor in patients with hypertension, and particularly in those with resistant hypertension.

AHI = apnea-hypopnea index (events per hour: 5-15 mild, 15-30 moderate, >30 severe); OSA = obstructive sleep apnea

## REFERENCES

- Brooks D, Horner RL, Kozar LF, Render-Teixeira CL, Phillipson EA. Obstructive sleep apnea as a cause of systemic hypertension. Evidence from a canine model. *J Clin Invest* 1997; 99:106-109.
- Bixler EO, Vgontzas AN, Lin HM, et al. Association of hypertension and sleep-disordered breathing. *Arch Intern Med* 2000; 160:2289-2295.
- Young T, Peppard P, Palta M, et al. Population-based study of sleep-disordered breathing as a risk factor for hypertension. *Arch Intern Med* 1997; 157:1746-1752.
- Nieto FJ, Young TB, Bonnie KL, et al, for the Sleep Heart Health Study. Association of sleep-disordered breathing, sleep apnea and hypertension in a large community-based study. *JAMA* 2000; 283:1829-1836.
- Peppard PE, Young T, Palta M, Skaturd J. Prospective study of the association between sleep-disordered breathing and hypertension. *N Engl J Med* 2000; 342:1378-1384.
- Grote L, Hedner J, Peter JH. Sleep-related breathing disorder is an independent risk factor for uncontrolled hypertension. *J Hypertens* 2000; 18:679-685.
- Haas DC, Foster GL, Nieto FJ, et al. Age-dependent associations between sleep-disordered breathing and hypertension: importance of discriminating between systolic/diastolic hypertension and isolated systolic hypertension in the Sleep Heart Health Study. *Circulation* 2005; 111:614-21.
- Baguet JP, Hammer L, Levy P, et al. Night-time and diastolic hypertension are common and underestimated conditions in newly diagnosed apnoeic patients. *J Hypertens* 2005; 23:521-527.
- Pickering TG, Kario K. Nocturnal non-dipping: what does it augur? *Curr Opin Nephrol Hypertens* 2001; 10:611-616.
- Kraiczi H, Peker Y, Caidahl K, Samuelsson A, Hedner J. Blood pressure, cardiac structure and severity of obstructive sleep apnea in a sleep clinic population. *J Hypertens* 2001; 19:2071-2078.
- Drager LF, Bortolotto LA, Lorenzi MC, Figueiredo AC, Krieger EM, Lorenzi-Filho G. Early signs of atherosclerosis in obstructive sleep apnea. *Am J Respir Crit Care Med* 2005; 172:613-618.
- Sampol G, Romero O, Salas A, et al. Obstructive sleep apnea and thoracic aorta dissection. *Am J Respir Crit Care Med* 2003; 168:1528-1531.
- Khan A, Patel NK, O'Hearn DJ, Khan S. Resistant hypertension and obstructive sleep apnea. *Int J Hypertens* 2013; 2013:193010. doi: 10.1155/2013/193010.
- Phillips CL, O'Driscoll DM. Hypertension and obstructive sleep apnea. *Nat Sci Sleep* 2013 May 10; 5:43-52. doi: 10.2147/NSS.S34841.
- Florczak E, Prejbisz A, Szwench-Pietrasz E, et al. Clinical characteristics of patients with resistant hypertension: the RESIST-POL study. *J Hum Hypertens* 2013 May 23. doi: 10.1038/jhh.2013.32. [Epub ahead of print]
- Litvin AY, Sukmarova ZN, Elfimova EM, et al. Effects of CPAP on "vascular" risk factors in patients with obstructive sleep apnea and arterial hypertension. *Vasc Health Risk Manag* 2013; 9:229-35. doi: 10.2147/VHRM.S40231. Epub 2013 May 10.