

# Internal and Emergency Medicine

## Obstructive sleep apnea and blood pressure in young hypertensives: does it matter?

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## Obstructive sleep apnea and blood pressure in young hypertensives: does it matter?

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1 In the modern era, and in industrialized countries in particular, major health problems are frequently  
2 associated to the age period going from childhood to adulthood. This is highly due to bad lifestyles  
3 which may anticipate the further development of chronic diseases life-long.  
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5 Hypertension, the most common risk factor in the pathogenesis of cardiovascular (CV) disease, is  
6 not just an adult disorder. Young-onset hypertension increases all-cause mortality and results in  
7 subclinical organ damage early in its natural history. The exact prevalence of hypertension in young  
8 people is relatively difficult to assess, because studies differ according to age, ethnicity, selection  
9 criteria, methodology used for blood pressure (BP) measurements and number of BP determinations  
10 [1,2]. In the National Longitudinal Study of Adolescent Health in the United States, about 19 % of  
11 14,000 participants aged 24-32 years had high BP levels [2]. In 85,371 young subjects of the  
12 Chinese province of Shandong, Zhao and colleagues found that prevalence of hypertension  
13 increased from 1991 to 2007, from 4.4 to 14.1% in the age range 18-29 years, and from 7.9 to 28.5%  
14 in the age range 30-39 years [3].  
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17 The lifestyle of young generations includes several emerging factors that can cause or promote the  
18 development of hypertension, such as sedentary lifestyle, high salt diet, frequent assumption of junk  
19 food or energizing drinks, anabolizing or illicit drugs, use of stimulating or vasoconstricting drugs,  
20 reduced sleep time, excessive time spent with mobile phone, tablets, computers or psychiatric  
21 condition of the youth [4]. Moreover, the current epidemic of childhood obesity has a substantial  
22 impact on the prevalence of elevated BP in children and adolescents, as confirmed by cross-  
23 sectional studies [5-6]. In children, a stable relationship of blood pressure and body mass index  
24 (BMI) was found up to the 85<sup>th</sup> percentile of BMI; beyond this threshold the risk for elevated BP in  
25 children and adolescents markedly increased [7]. Thus, the risk for elevated BP is not limited to  
26 obese children (BMI >95<sup>th</sup> percentile) but also involves overweight children (BMI in the 85<sup>th</sup>-94<sup>th</sup>  
27 percentile).  
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30 The childhood obesity epidemic, with the associated increase in prevalence of elevated BP, predicts  
31 heightened risk for premature cardiovascular disease in adulthood. The International Childhood  
32 Cardiovascular Cohort Consortium on >6,000 individuals collected prospective data from childhood  
33 to young adulthood. Compared to individuals with normal BMI in both childhood and as adults,  
34 individuals with consistently high BMI in both childhood and adulthood showed an almost  
35 threefold risk of hypertension (relative risk [RR] 2.7, 95% CI 2.2-3.3). Additional metabolic risk  
36 factors further increased the risk in childhood. However, individuals with high BMI in childhood  
37 but normal BMI in adulthood had a RR similar to those with consistently normal BMI in both  
38 childhood and adulthood [8]. As for the health benefits of interventions on modifiable risk factors,  
39 early education, especially regarding weight control and recommendations for exercise, is  
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1 necessary, and control of lifestyle and BP at young age can have a major impact on subsequent  
2 cardiovascular disease [9].

3 Obstructive sleep apnea (OSA) is characterized by upper airway collapse during sleep, and clinical  
4 symptoms of snoring, poor sleep quality and excessive daytime sleepiness [10]. A strong  
5 relationship exists between OSA severity and hypertension, associated with sympathetic  
6 hyperactivity secondary to intermittent hypoxia during sleep [11]. Hypertension in OSA is often  
7 poorly responsive to treatment, and OSA treatment may improve BP control [12]. Little is known,  
8 however, on the potential role of OSA in the pathogenesis of hypertension at young age. The work  
9 by Jinchai et al. [13] is the first step towards filling such knowledge gap. In a large series of young  
10 hypertensive patients, secondary hypertension accounted for 80% of cases; in the remaining 20% of  
11 the patients, 89% showed OSA, that was moderate-severe in 60% of the sample. Similar to the  
12 findings in adult OSA patients, young hypertensive patients with OSA were mostly males, and on  
13 average more obese than patients without OSA. No differences were found in BP levels or anti-  
14 hypertensive medications in OSA compared to non-OSA young hypertensives, but onset of  
15 hypertension occurred at an older age in OSA than non-OSA subjects, suggesting a pathogenetic  
16 role of sleep disordered breathing. Prevalence of smoking and comorbidities, such as diabetes or  
17 gastroesophageal reflux disease, tended to be higher in patients with OSA. Only age and BMI  
18 predicted OSA, and a clear dose-response effect was evident for tiredness and daytime sleepiness  
19 when OSA severity was taken into account [13].

20 These findings are of major clinical relevance for the possible impact of OSA on cardiovascular  
21 (CV) variables in young hypertensive patients. To this end, obtaining 24-h BP profile in this  
22 population would be very important since OSA is associated with increased nocturnal BP [14].  
23 Recent research pointed to a detrimental role of nocturnal hypertension on CV risk [15], and the  
24 beneficial role of anti-hypertensive chronotherapy [16]. Therefore in the young HT group assessing  
25 the circadian profile of BP is recommended, in order to limit the detrimental effects of nocturnal  
26 hypertension which goes often unrecognized.

27 The paper by Jinchai et al. [13] does not provide data on end organ damage, such as  
28 echocardiography (i.e. left ventricular mass, diastolic dysfunction) or renal function (i.e.  
29 microalbuminuria). Future studies will have to assess the impact of OSA on these outcomes in  
30 young HT patients. In addition, the study does not report whether therapeutic measures, and in  
31 particular treatment of OSA with continuous positive airway pressure (CPAP) or interventions  
32 aiming at weight loss, were started. Although CPAP has minor effects on mean BP [17],  
33 BP variability decreases on CPAP, and OSA treatment helps normalize the BP profile especially at  
34 night [18]. Lifestyle interventions and CPAP improve the CV risk profile in adults [19], and a  
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1 similar approach should be used in young hypertensive OSA patients. Finally, as discussed in the  
2 manuscript, the study tested occurrence of OSA only in young hypertensives without recognized  
3 causes of hypertension. Given the strong relationship between OSA and high BP documented by a  
4 large amount of literature, occurrence of OSA in secondary hypertension of the young should also  
5 be studied.  
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10 Conflict of interest: The authors have no conflict of interest to declare regarding the current  
11 manuscript.  
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## 16 References 17

- 18 1. Perk J, De Backer G, Gohlke H, Graham I, Reiner Z, Verschuren M, Albus C, Benlian P, Boysen G, Cifkova  
19 R, Deaton C, Ebrahim S, Fisher M, Germano G, Hobbs R, Hoes A, Karadeniz S, Mezzani A, Prescott E,  
20 Ryden L, Scherer M, Syväne M, Scholte op Reimer WJ, Vrints C, Wood D, Zamorano JL, Zannad F;  
21 European Association for Cardiovascular Prevention & Rehabilitation (EACPR); ESC Committee for Practice  
22 Guidelines (CPG). European Guidelines on cardiovascular disease prevention in clinical practice (version  
23 2012). The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on  
24 Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by  
25 invited experts). *Eur Heart J*. 2012; 33(13):1635-1701.  
26
- 27 2. Nguyen QC, Tabor JW, Entzel PP, Lau Y, Suchindran C, Hussey JM, Halpern CT, Harris KM, Whitsel EA.  
28 Discordance in national estimates of hypertension among young adults. *Epidemiology* 2011; 22(4):532-541.  
29
- 30 3. Zhao Y, Lu F, Sun H, Liu Z, Zhao Y, Sun S, Wang S, Diao Y, Zhang H. Trends in hypertension prevalence,  
31 awareness, treatment, and control rates in Shandong Province of China. *J Clin Hypertens (Greenwich)*  
32 2012;14(9):637-643.
- 33 4. Battistoni A, Canichella F, Pignatelli G, Ferrucci A, Tocci G, Volpe M. Hypertension in Young People:  
34 Epidemiology, Diagnostic Assessment and Therapeutic Approach. *High Blood Press Cardiovasc Prev*  
35 2015;22(4):381-388.  
36
- 37 5. McNiece KL, Poffenbarger TS, Turner JL, Franco KD, Sorof JM, Portman RJ. Prevalence of hypertension and  
38 pre-hypertension among adolescents. *J Pediatr* 2007;150(6):640-644, 644.e1.
- 39 6. Falkner B, Gidding SS, Ramirez-Garnica G, Wiltrout SA, West D, Rappaport EB. The relationship of body  
40 mass index and blood pressure in primary care pediatric patients. *J Pediatr* 2006; 148(2):195-200.  
41
- 42 7. Tu W, Eckert GJ, DiMeglio LA, Yu Z, Jung J, Pratt JH. Intensified effect of adiposity on blood pressure in  
43 overweight and obese children. *Hypertension* 2011;5 8(5):818-824.
- 44 8. M, Magnussen CG, Berenson GS, Venn A, Burns TL, Sabin MA, Srinivasan SR, Daniels SR, Davis PH, Chen  
45 W, Sun C, Cheung M, Viikari JS, Dwyer T, Raitakari OT. Childhood adiposity, adult adiposity, and  
46 cardiovascular risk factors. *N Engl J Med* 2011; 365(20):1876-1885.  
47
- 48 9. Kawabe H, Azegami T, Takeda A, Kanda T, Saito I, Saruta T, Hirose H. Features of and preventive measures  
49 against hypertension in the young. *Hypertens Res* 2019;42(7):935-948.
- 50 10. Lévy P, Kohler M, McNicholas WT, Barbé F, McEvoy RD, Somers VK, Lavie L, Pépin JL. Obstructive sleep  
51 apnoea syndrome. *Nat Rev Dis Primers*. 2015; 1: 15015.  
52
- 53 11. Xia W, Huang Y, Peng B, Zhang X, Wu Q, Sang Y, Luo Y, Liu X, Chen Q, Tian K. Relationship between  
54 obstructive sleep apnoea syndrome and essential hypertension: a dose-response meta-analysis. *Sleep Med*  
55 2018;47:11-18.  
56
- 57 12. Oscullo G, Torres G, Campos-Rodriguez F, Posadas T, Reina-González A, Sapiña-Beltrán E, Barbé F,  
58 Martínez-García MA. Resistant/Refractory Hypertension and Sleep Apnoea: Current Knowledge and Future  
59 Challenges. *J Clin Med* 2019; 8(11). pii: E1872.  
60  
61  
62  
63  
64  
65

13. Jinchai J, Khamsai S, Chattakul P, Limpawattana P, Chindaprasirt J, Chotmongkol V, Silaruks S, Senthong V, Sawanyawisuth K. How common is obstructive sleep apnea in young hypertensive patients? *Intern Emerg Med* 2020 Jan 22.
14. Cuspidi C, Tadic M, Sala C, Gherbesi E, Grassi G, Mancia G. Blood Pressure Non-Dipping and Obstructive Sleep Apnea Syndrome: A Meta-Analysis. *J Clin Med* 2019; 8(9). pii: E1367.
15. Hermida RC, Crespo JJ, Otero A, Domínguez-Sardiña M, Moyá A, Ríos MT, Castiñeira MC, Callejas PA, Pousa L, Sineiro E, Salgado JL, Durán C, Sánchez JJ, Fernández JR, Mojón A, Ayala DE; Hygia Project Investigators. Asleep blood pressure: significant prognostic marker of vascular risk and therapeutic target for prevention. *Eur Heart J* 2018; 39(47): 4159-4171.
16. Hermida RC, Crespo JJ, Domínguez-Sardiña M, Otero A, Moyá A, Ríos MT, Sineiro E, Castiñeira MC, Callejas PA, Pousa L, Salgado JL, Durán C, Sánchez JJ, Fernández JR, Mojón A, Ayala DE; Hygia Project Investigators. Bedtime hypertension treatment improves cardiovascular risk reduction: the Hygia Chronotherapy Trial. *Eur Heart J* 2019 Oct 22. pii: ehz754.
17. Patil SP, Ayappa IA, Caples SM, Kimoff RJ, Patel SR, Harrod CG. Treatment of Adult Obstructive Sleep Apnea With Positive Airway Pressure: An American Academy of Sleep Medicine Systematic Review, Meta-Analysis, and GRADE Assessment. *J Clin Sleep Med* 2019; 15(2): 301-334.
18. Marrone O, Bonsignore MR. Blood-pressure variability in patients with obstructive sleep apnea: current perspectives. *Nat Sci Sleep* 2018; 10: 229-242.
19. Chirinos JA, Gurubhagavatula I, Teff K, Rader DJ, Wadden TA, Townsend R, Foster GD, Maislin G, Saif H, Broderick P, Chittams J, Hanlon AL, Pack AI. CPAP, weight loss, or both for obstructive sleep apnea. *N Engl J Med* 2014; 370(24):2265-2275.

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