Hypertension Research (2023) 46:1606–1608
https://doi.org/10.1038/s41440-023-01268-0

COMMENT

# Clinical Question: Can CPAP suppress cardiovascular events in resistant hypertension patients with obstructive sleep apnea?

Shinobu Osanai[1]

Received: 20 February 2023 / Revised: 4 March 2023 / Accepted: 12 March 2023 / Published online: 4 April 2023


**Keyword** CPAP · Cardiovascular events · Obstructive sleep apnea · Resistant hypertension

Obstructive sleep apnea (OSA) is a common disease characterized by repetitive obstruction in the upper airway during sleep. The collapse in the upper airway induces intermittent hypoxia/hypercapnia, lead to autonomic dysfunction, increases intrathoracic pressure changes, and causes sleep fragmentation (Fig. 1). So far, it has been recognized that untreated OSA is an independent risk factor for various cardiovascular (CV) diseases, including hypertension, arrhythmias (atrial fibrillation), heart failure, coronary heart disease, stroke and pulmonary hypertension. Many clinical observations suggested that these mechanisms can activate several pathogenic pathways implicated in the development of CV diseases, including autonomic activation, systemic inflammation/atherosclerosis, endothelial dysfunction, hypercoagulability, metabolic dysregulation/disorders, hemodynamic changes, left atrial enlargement and sympathetic activation in OSA. These CV diseases can cause fatal or non-fatal cardiovascular events (see refs. [1–3] for comprehensive reviews and meta-analysis).

Continuous positive airway pressure (CPAP) is expected to reduce blood pressure and improve endothelial function and inflammatory status. It has also been demonstrated in observational cohort studies that CPAP treatment may reduce CV diseases and mortality risks. However, the effects of CPAP on CV diseases and mortality risks have not been confirmed in randomized controlled trials (RCTs) [4] and meta-analyses [5, 6]. Resistant hypertension (RHT) is a clinical condition which is uncontrolled office BP despite using at least three antihypertensive medications in full dosages, including a diuretic, or using ≥4 medications regardless of BP levels [7]. RHT is reported with a high prevalence of moderate/severe OSA, approximately 50 to 60% [8, 9]. Because of these clinical observations and the etiological mechanisms mentioned above, OSA is assumed to be one of the causes of RHT. CPAP treatment in these patients has been demonstrated to reduce ambulatory 24-hour blood pressure (BP) by -5/-4 mmHg [10]. However, a limited study evaluated the prognostic impact of CPAP treatment on CV outcomes in patients with RHT and moderate/severe OSA [11].

Cardoso and Salles studied to evaluate the prognostic impact of OSA severity and other polysomnography (PSG) -derived parameters for adverse cardiovascular and mortality outcomes in individuals with RHT [12]. They showed that patients with RHT had a high prevalence of severe OSA and very high CV risk. They demonstrated that neither moderate/severe nor severe OSA nor being untreated during follow-up was associated with significant excess risks for any outcome about the subgroup with no/mild OSA. Similarly, no other PSG-derived parameter predicted any adverse effect. CPAP treatment was associated with "non-significant" risk reductions of 37% for total CV events, 49% for major CV events and 63% for all-cause mortality among those who remained untreated during follow-up. Finally, they concluded that the presence/severity of OSA and its related PSG parameters were not associated with worse cardiovascular/mortality prognosis in patients with RHT; however, CPAP treatment might be protective in individuals with moderate/severe OSA.

The authors point out some limitations of this study: the study design, various unknown biases, and an insufficient number of patients examined. In addition, the observation of adherence in CPAP users needed to be improved. Based on these findings, we cannot deny the possibility that the

**Supplementary information** The online version contains supplementary material available at https://doi.org/10.1038/s41440-023-01268-0.

✉ Shinobu Osanai
shinobuo@asahikawa-med.ac.jp

[1] Cardiovascular, Respiratory and Neurology Division, Department of Internal Medicine, Asahikawa Medical University, Asahikawa, Japan

**Graphical Opinion**

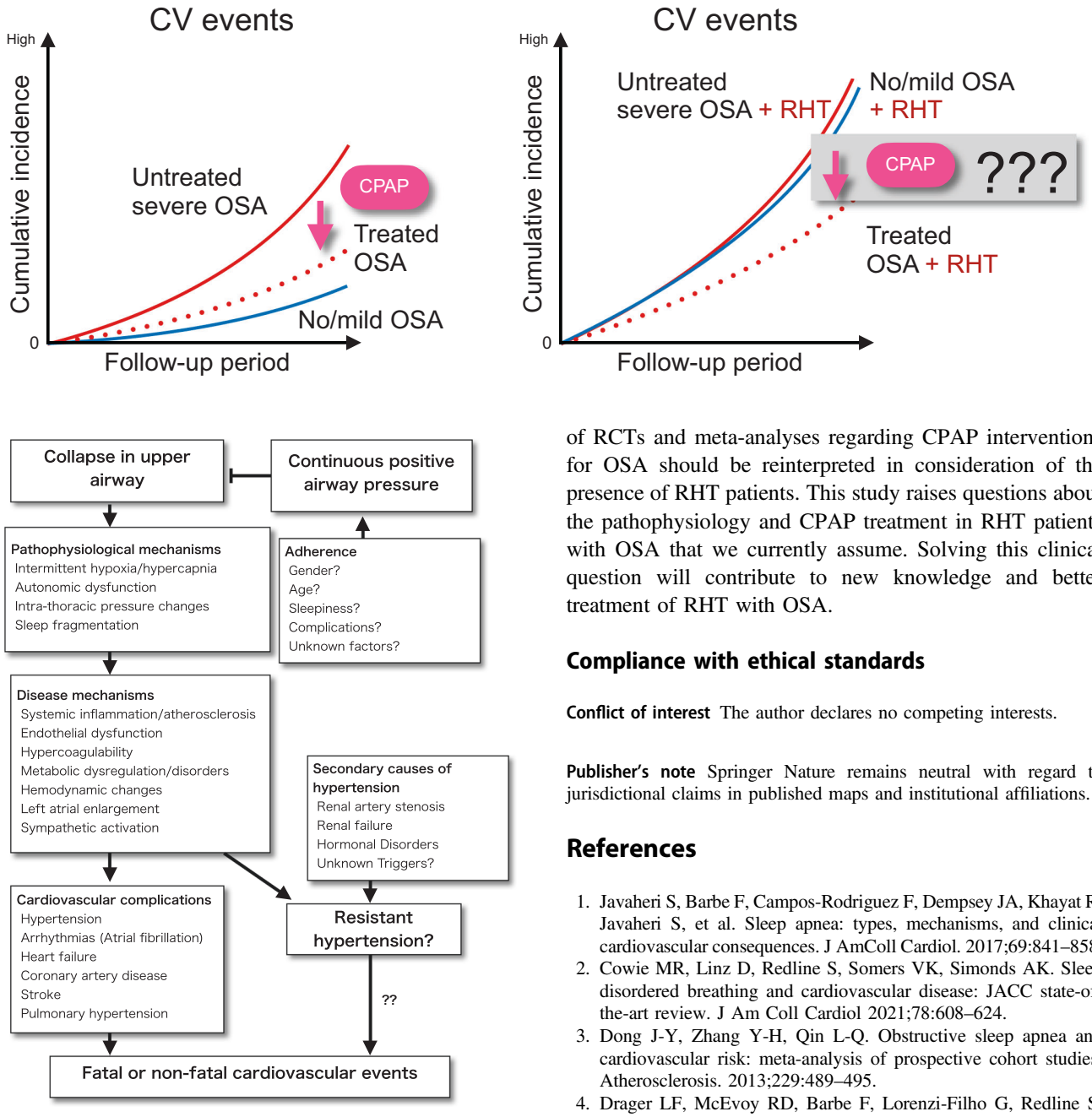


**Fig. 1** Pathophysiological relationship between obstructive sleep apnea, cardiovascular events and resistant hypertension

incidence of CV events in CPAP-using patients was inaccurate. On the other hand, the presence or absence of OSA did not affect CV events or mortality, leading to the hypothesis that OSA does not significantly affect the prognosis of RHT. Large randomized controlled trials will be needed to test this hypothesis. Suppose it is shown that CPAP treatment does not suppress CV events in patients with severe OSA and RHT. In that case, the previous results of RCTs and meta-analyses regarding CPAP interventions for OSA should be reinterpreted in consideration of the presence of RHT patients. This study raises questions about the pathophysiology and CPAP treatment in RHT patients with OSA that we currently assume. Solving this clinical question will contribute to new knowledge and better treatment of RHT with OSA.

## Compliance with ethical standards

**Conflict of interest** The author declares no competing interests.

**Publisher's note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

## References

1. Javaheri S, Barbe F, Campos-Rodriguez F, Dempsey JA, Khayat R, Javaheri S, et al. Sleep apnea: types, mechanisms, and clinical cardiovascular consequences. J AmColl Cardiol. 2017;69:841–858.
2. Cowie MR, Linz D, Redline S, Somers VK, Simonds AK. Sleep disordered breathing and cardiovascular disease: JACC state-of-the-art review. J Am Coll Cardiol 2021;78:608–624.
3. Dong J-Y, Zhang Y-H, Qin L-Q. Obstructive sleep apnea and cardiovascular risk: meta-analysis of prospective cohort studies. Atherosclerosis. 2013;229:489–495.
4. Drager LF, McEvoy RD, Barbe F, Lorenzi-Filho G, Redline S, 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;136:1840–50.
5. Yu J, Zhou Z, McEvoy RD, Anderson CS, Rodgers A, Perkovic V, et al. Association of positive airway pressure with cardiovascular events and death in adults with sleep apnea: a systematic review and meta-analysis. JAMA. 2017;318:156–66.
6. Labarca G, Dreyse J, Drake L, Jorquera J, Barbe F. Efficacy of continuous positive airway pressure (CPAP) in the prevention of cardiovascular events in patients with obstructive sleep apnea: Systematic review and meta-analysis. Sleep Med Rev. 2020;52:101312.
7. Calhoun DA, Jones D, Textor S, Goff DC, Murphy TP, Toto RD, et al. Resistant hypertension: diagnosis, evaluation, and treatment.

A scientific statement from the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research. Hypertension. 2008;51:1403–19.
8. Pedrosa RP, Drager LF, Gonzaga CC, Sousa MG, de Paula LK, Amaro AC, et al. Obstructive sleep apnea: the most common secondary cause of hypertension associated with resistant hypertension. Hypertension. 2011;58:811–7.
9. Muxfeldt ES, Margallo VS, Guimarães GM, Salles GF. Prevalence and associated factors of obstructive sleep apnea in patients with resistant hypertension. Am J Hypertens. 2014;27:1069–78.
10. Lei Q, Lv Y, Li K, Ma L, Du G, Xiang Y, et al. Effects of continuous positive airway pressure on blood pressure in patients with resistant hypertension and obstructive sleep apnea: a systematic review and meta-analysis of six randomized controlled trials. J Bras Pneumol. 2017;43:373–9.
11. Navarro-Soriano C, Martínez-García MA, Torres G, Barbé F, Sánchez-de-la-Torre M, Caballero-Eraso C, et al. Long-term effect of CPAP treatment on cardiovascular events in patients with resistant hypertension and sleep apnea. Data from the HIPARCO-2 study. Arch Bronconeumol. 2021;57:165–71.
12. Cardoso, C.R.L., Salles, G.F. Prognostic importance of obstructive sleep apnea and CPAP treatment for cardiovascular and mortality outcomes in patients with resistant hypertension: a prospective cohort study. Hypertens Res 2023;46:1020–30.