Editorial

Sleep Apnea and Cardiovascular Diseases

**Rodolfo Álvarez-Sala,^{1,2} Francisco García-Río,^{1,2} Félix Del Campo,³
Carlos Zamarrón,⁴ and Nikolaus C. Netzer⁵**

¹ Department of Pneumology, La Paz University Hospital, Madrid, Spain

² Instituto de Investigación Sanitaria del Hospital Universitario La Paz (IdiPAZ), Autónoma de Madrid University, Madrid, Spain

³ Department of Pneumology, Río Hortega Hospital, Valladolid University, Valladolid, Spain

⁴ Department of Pneumology, Santiago de Compostela Hospital, Santiago de Compostela Universidad, A Coruña, Spain

⁵ Hermann Buhl Institute for Hypoxia and Sleep Medicine Research, Research Program of the Paracelsus Medical University and Clinic Gherzburg for Geriatric Rehabilitation, Bad Aibling, Germany

Correspondence should be addressed to Rodolfo Álvarez-Sala; ralvarezw.hulp@salud.madrid.org

Received 12 November 2013; Accepted 12 November 2013; Published 5 February 2014

Copyright © 2014 Rodolfo Álvarez-Sala et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Obstructive sleep apnea (OSA) is a common respiratory disease characterized by abnormal collapse of the pharyngeal airway during sleep, causing repetitive arousals and falls in the oxygen saturation [1]. This disorder, when not correctly treated, has been associated with higher fatal and nonfatal cardiovascular events [2]. Also, OSA has been related to many cardiovascular diseases (CVD) such as heart failure [3], arrhythmias [4], pulmonary hypertension [5], and coronary artery disease (CAD) [6]. Moreover, in recent years OSA has emerged as a major public health problem due to its profound impact on patients' health. By this reason, we have proposed this special issue about the relationship between sleep disordered breathing (SDB) and CVD. We have suggested different topics such as potential mechanisms linking OSA to CVD, acute cardiovascular effects of OSA, impact of OSA on natural history of CVD, cardiovascular effects of continuous positive airway pressure (CPAP) treatment, and therapeutic cardiovascular efficacy of emerging treatment for OSA and central sleep apnea (CSA).

Several mechanisms are involved in the association between OSA and CVD. In fact, enhanced sympathetic activity, oxidative stress, systemic inflammation, and endothelial dysfunction contribute to this association and promote atherogenesis. Moreover, cyclic decreases in blood oxygen saturation during recurrent episodes of apnea produce chronic intermittent hypoxia and contribute to the development of atherosclerosis. Some hypoxia-induced transcription

factors as hypoxia-inducible factor-1 and nuclear factor- κ B are activated during intermittent hypoxia and contribute to the generation of inflammation and expression of proinflammatory cytokines such as tumor necrosis factor- α and interleukin-8.

It seems that these mechanisms could have an important impact in the occurrence of ischemic cardiac events. Hence, CAD in OSA patients probably precludes the activation of multiple mechanisms, such as atherosclerosis, hypertension, and endothelial dysfunction. Likewise, OSA may influence outcomes in patients with acute or chronic CAD, but this effect remains controversial as results obtained from studies have yielded discrepant data. In this way, Yumino et al. [7] observed a higher incident of cardiac death, reinfarction, or new revascularization in OSA patients with CAD and compared to subjects without OSA, after a mean follow-up period of 7 months. Nevertheless, Hagenah et al. [8] found that OSA did not increase the risk of mortality and cardiovascular complications in 50 patients with stable CAD after 10 years of follow-up period. Moreover, concerning treatment of OSA patients with CAD, CPAP may have beneficial effects in recurrence of ischemic cardiac disease and necessity of new revascularization procedures but higher-evidence studies are necessary to investigate the effect of CPAP in these subjects.

Regarding heart failure, a high prevalence of OSA and CSA in this disorder has been observed. Also, different therapeutic strategies such as oxygen therapy, CPAP, bilevel

positive airway pressure (BIPAP), and adaptive servoventilation (ASV) have been proposed to treat OSA in heart failure patients. In this way, in OSA heart failure subjects, CPAP may improve survival, left ventricular ejection fraction, and quality of life [9–11]. Nevertheless, in heart failure CSA patients, CPAP probably is not effective as ASV to abolish the apnea-hypopnea index to <15 events·h⁻¹ [12]. So far, it is evident that SDB treatment has showed consistent improvements in heart function, quality of life, and respiratory events in patients with heart failure. However, it is necessary to evaluate the impact of these respiratory treatments in randomized-controlled, long-term longitudinal studies.

Finally, respecting the association between atrial arrhythmia and OSA, it has been described that cardiac remodeling, sympathetic activity, and systemic inflammation may lead to the development of arrhythmias in these patients. Moreover, hypoxemia and hypercapnia have an important role in the pathogenesis of this association. However, it is necessary to investigate the effect of CPAP treatment in atrial arrhythmias of OSA patients.

In conclusion, sleep apnea is a high prevalence disease that has an important relationship with cardiovascular disease. In this special issue, we have tried to make an extensive review about mechanisms involved in the association between ischemic cardiac disease, heart failure, and arrhythmias with OSA. Nevertheless, we know that despite multiple reports about OSA and cardiovascular disease, it is yet necessary to perform higher grade evidence studies to explore mechanisms involved in this association and the impact of CPAP treatment in these subjects.

Rodolfo Álvarez-Sala
Francisco García-Río
Félix Del Campo
Carlos Zamarrón
Nikolaus C. Netzer

References

- [1] P. Lloberes, J. Durán-Cantolla, M. Á. Martínez-García et al., “Diagnosis and treatment of sleep apnea-hypopnea syndrome. spanish society of pulmonology and thoracic surgery,” *Archivos De Bronconeumologia*, vol. 47, no. 3, pp. 143–156, 2011.
- [2] J. M. Marin, S. J. Carrizo, E. Vicente, and A. G. N. Agustí, “Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study,” *Lancet*, vol. 365, no. 9464, pp. 1046–1053, 2005.
- [3] E. Shahar, C. W. Whitney, S. Redline et al., “Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the sleep heart health study,” *American Journal of Respiratory and Critical Care Medicine*, vol. 163, no. 1, pp. 19–25, 2001.
- [4] S. Javaheri, T. J. Parker, J. D. Liming et al., “Sleep apnea in 81 ambulatory male patients with stable heart failure: types and their prevalences, consequences, and presentations,” *Circulation*, vol. 97, no. 21, pp. 2154–2159, 1998.
- [5] M. Alchanatis, G. Tourkouritis, S. Kakouros, E. Kosmas, S. Podaras, and J. B. Jordanoglou, “Daytime pulmonary hypertension in patients with obstructive sleep apnea: the effect of continuous positive airway pressure on pulmonary hemodynamics,” *Respiration*, vol. 68, no. 6, pp. 566–572, 2001.
- [6] C.-H. Lee, S.-M. Khoo, B.-C. Tai et al., “Obstructive sleep apnea in patients admitted for acute myocardial infarction: prevalence, predictors, and effect on microvascular perfusion,” *Chest*, vol. 135, no. 6, pp. 1488–1495, 2009.
- [7] D. Yumino, Y. Tsurumi, A. Takagi, K. Suzuki, and H. Kawanishi, “Impact of obstructive sleep apnea on clinical and angiographic outcomes following percutaneous coronary intervention in patients with acute coronary syndrome,” *American Journal of Cardiology*, vol. 99, no. 1, pp. 26–30, 2007.
- [8] G. C. Hagenah, E. Gueven, and S. Andreas, “Influence of obstructive sleep apnoea in coronary artery disease: a 10-year follow-up,” *Respiratory Medicine*, vol. 100, no. 1, pp. 180–182, 2006.
- [9] D. R. Mansfield, N. C. Gollogly, D. M. Kaye, M. Richardson, P. Bergin, and M. T. Naughton, “Controlled trial of continuous positive airway pressure in obstructive sleep apnea and heart failure,” *American Journal of Respiratory and Critical Care Medicine*, vol. 169, no. 3, pp. 361–366, 2004.
- [10] Y. Kaneko, J. S. Floras, K. Usui et al., “Cardiovascular effects of continuous positive airway pressure in patients with heart failure and obstructive sleep apnea,” *The New England Journal of Medicine*, vol. 348, no. 13, pp. 1233–1241, 2003.
- [11] H. Wang, J. D. Parker, G. E. Newton et al., “Influence of obstructive sleep apnea on mortality in patients with heart failure,” *Journal of the American College of Cardiology*, vol. 49, no. 15, pp. 1625–1631, 2007.
- [12] T. D. Bradley, A. G. Logan, R. J. Kimoff et al., “Continuous positive airway pressure for central sleep apnea and heart failure,” *The New England Journal of Medicine*, vol. 353, no. 19, pp. 2025–2033, 2005.