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EDITORIAL COMMENT

Seek and Treat Obstructive Sleep Apnea in Heart Failure*

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Obstructive sleep apnea (OSA) is a highly prevalent disorder. It affects 9% to 25% of the North American population (1–4). Intermittent cessation of breathing during sleep caused by occlusion of the upper airway followed by arousals from sleep defines OSA. The prevalence of OSA is even greater among patients with chronic heart failure (CHF). Approximately one-third to one-half of the 5 million Americans with CHF suffers from concomitant OSA, especially those with severe CHF (5–7). Notwithstanding the sheer number of patients with OSA and obesity as a common risk factor, repetitive episodes of hypoxia/reoxygenation, augmented intrathoracic pressure swings, and arousals from sleep promote arterial stiffness, hypertension, and increased sympathetic activity that account for the frequent coexistence of OSA and CHF (8–10). Patients with OSA are 2.2 times more likely to develop CHF than patients without OSA, and patients with CHF who develop OSA are thought to have a worse prognosis than patients with CHF alone (11).

See page 1625

In this issue of the *Journal*, Wang et al. (12) report their experience in the context of a single-center prospective observational study that compared the mortality of patients with coexistent CHF and OSA with that of patients with only CHF over an average period of 33 months. The mortality of patients with CHF and untreated OSA was nearly 2-fold greater than that of patients with CHF alone. In contrast, none of the patients with CHF and treated OSA died during the 39-month follow-up period.

These findings, although not unexpected and somewhat optimistic, are of great importance. Treatment with continuous positive airway pressure (CPAP) for 4 h per night does not improve survival in patients with CHF and central sleep apnea (CSA) (13). However, in contrast to CSA that is a consequence of CHF, OSA is on its own a risk factor for hypertension and stroke and is likely to impact negatively on left ventricular function (9,14). Patients with untreated severe OSA have a higher incidence of fatal cardiovascular events (1.06 vs. 0.35 per 100 person-years, $p = 0.0008$) and nonfatal cardiovascular events (2.13 vs. 0.64 per 100 person-years, $p < 0.0001$) than patients treated with CPAP after adjustment for pre-existing cardiovascular risk factors (15).

The observation by Wang et al. (12) that untreated OSA independently increases mortality in CHF is important because OSA remains frequently unrecognized in patients with CHF (7). The modest impact of OSA on subjective measurements of sleepiness or quality of life may explain why OSA is so often unrecognized in patients with CHF (16). To make things worse, even when recognized OSA remains often untreated, as was the case in the report by Wang et al. (12). Hopefully the positive findings in their report will encourage physicians and nurse practitioners who care for patients with CHF to be more vigilant about the diagnosis and treatment of OSA.

Wang et al. (12) contend that treatment with CPAP negates OSA-related increase in mortality in patients with CHF, but they do not definitively prove it. Patients with CHF and OSA were not randomly assigned to CPAP. Moreover, the majority of patients were not treated with CPAP for unclear reasons. Patients with CHF who are willing to comply with CPAP treatment may be more health conscious and thus more adherent to other treatment modalities and more likely to do well.

Treatment with CPAP has become the standard of care for moderate to severe OSA, and thus unbiased randomization of OSA patients to CPAP or no CPAP may no longer be feasible (17). Confronted with evidence that supports the use of CPAP in the management of OSA, physicians may not be willing to enroll patients with severe OSA into a randomized trial, thereby biasing the trial toward negative results. The use of a multivariate risk model to predict 1-, 2-, and 3-year mortality of patients with coexistent CHF and OSA who have accepted or refused treatment with CPAP may be a preferable and ethical approach for evaluating the effects of CPAP on clinical outcomes in this patient population (18).

Objective evaluation of the minimum CPAP adherence needed for reduction of mortality is also a worthwhile goal in patients with OSA and CHF. Wang et al. (12) reported CPAP adherence as self-reported "use" or "no use." Subjective or objective CPAP adherence data were not provided. Self reporting of CPAP adherence is notably unreliable (19). In a prospective study that covertly monitored objective CPAP adherence, 60% of patients claimed to use CPAP nightly; however, only 46% met criteria for regular use, and they overestimated CPAP use by more than 1 h

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(16). In the report by Wang et al. (12), the majority of patients with coexistent OSA and CHF did not receive CPAP treatment because they were not complaining of daytime sleepiness. Patients with moderate to severe OSA documented by nocturnal polysomnography should not be left untreated (17). One to three months of CPAP treatment increases left ventricular ejection fraction and improves quality of life in patients with coexistent CHF and OSA whether or not they complain of daytime sleepiness (20,21).

Lastly, CPAP therapy may not completely reverse the complications associated with OSA. Many patients with OSA continue to experience daytime sleepiness despite effective long-term CPAP therapy (22). Reduction of oxidative stress requires effective CPAP therapy for at least 3 months, whereas antioxidant defense remains partially impaired after 12 months of therapy in OSA patients (22–25). Adherence to treatment is hampered by the cumbersomeness of CPAP devices, and proper delivery of pressures is frequently impaired by ill-fitting facial interfaces and inadvertent leaks. Delayed diagnosis and poor adherence to CPAP treatment may contribute to the partial reversibility of OSA cardiovascular manifestations. Nevertheless, as observed in the study by Wang et al. (12), effective CPAP therapy may halt progression of the underlying cardiovascular condition. Therefore, early diagnosis of OSA and initiation of effective CPAP therapy are of paramount importance in patients with coexistent CHF and OSA. Future studies will establish the minimum duration of nightly CPAP therapy needed to offset the impact of OSA on morbidity and mortality in CHF.

In summary, the observational study by Wang et al. (12) points out the therapeutic usefulness of CPAP in patients with coexistent CHF and OSA. The findings of this observational study need to be confirmed by either a large randomized trial or a detailed registry of the use or lack of use of CPAP in patients with coexistent CHF and OSA. The latter approach seems preferable for ethical and practical reasons.

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