No cardiovascular benefit with CPAP use in patients with OSA

In patients with cardiovascular disease and comorbid moderate-to-severe obstructive sleep apnoea (OSA), continuous positive airway pressure (CPAP) therapy did not prevent cardiovascular events, but improved mood, work productivity, and quality-of-life measures. This finding was presented at the ESC Congress 2016 in Rome, Italy by the SAVE investigators, and simultaneously published in *The New England Journal of Medicine*.

OSA affects 40–60% of patients with cardiovascular disease. Previous observational studies have reported that CPAP therapy can reduce cardiovascular-related morbidity and mortality, particularly in patients who are adherent to treatment, but data from large randomized trials are needed to confirm these findings. McEvoy *et al.* now report findings from the SAVE study, “a secondary prevention trial that was designed to evaluate the effectiveness of CPAP in reducing the rate of cardiovascular events among patients with [OSA].”

The SAVE trial was an international, multicentre, randomized, open-label study that enrolled patients with moderate-to-severe OSA (defined as oxygen desaturation index ≥ 12). Patients were randomly assigned to receive either CPAP therapy plus usual care (CPAP group) or usual care only (usual-care group). The primary end point was a composite of cardiovascular death, myocardial infarction, stroke, heart failure hospitalization, acute coronary syndrome, or transient ischaemic attack. Prespecified safety end points included serious adverse events, self-reported injuries sustained while driving or at work, or any accidents that resulted from the participant falling asleep.

The mean age of the patients included in the primary analysis was 61 years, and 81% were male. In total, 1,284 patients in the CPAP group and 1,256 in the usual-care group were followed

through to the final follow-up visit (mean follow-up of 3.7 years). A primary end point event occurred in 17.0% of the participants ($n = 229$) in the CPAP group and 15.4% ($n = 207$) in the usual-care group (HR with CPAP 1.10, 95% CI 0.91–1.32, $P = 0.34$). No differences were detected in any cause-specific cardiovascular outcome or composite secondary cardiovascular end point in the primary analysis. However, the prespecified secondary end points of daytime sleepiness, mood, and health-related quality of life were all improved in patients receiving CPAP therapy compared with those receiving usual care only. In addition, patients in the CPAP group took fewer days off from work owing to sickness than the usual-care group. No differences were observed in the prespecified safety end points between the two treatment groups. “This study was not powered to provide definitive answers regarding the effects of CPAP on secondary cardiovascular end points, but there was no indication of a significant benefit with respect to any cause-specific cardiovascular outcome,” explain the investigators.

In an accompanying editorial, Babak Mokhlesi and Najib Ayas question whether the negative outcome was the result of inadequate CPAP duration. “In the SAVE trial, the mean duration of CPAP adherence was only 3.3 h per night, which is probably less than half the time patient was asleep,” they explain. “This dose of CPAP may not be adequate to prevent cardiovascular events.” They also highlight the importance of future studies aimed at improving CPAP technology to maximize adherence, and identifying novel strategies that allow for better adherence.

Karina Huynh

ORIGINAL ARTICLE McEvoy, R. D. *et al.* CPAP for prevention of cardiovascular events in obstructive sleep apnea. *N. Engl. J. Med.* <http://dx.doi.org/10.1056/NEJMoa1606599> (2016)

FURTHER READING Parati, G. *et al.* Heart failure and sleep disorders. *Nat. Rev. Cardiol.* **13**, 389–403 (2016)