Sleep apnoea in acute heart failure: fluid in flux

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This editorial refers to ‘Sleep-disordered breathing and post-discharge mortality in patients with acute heart failure’, by R. Khayat et al., on page 1463.

The present management of acute heart failure (AHF) suffers from a paucity of evidence-based treatment. Could this be because the pathophysiology that places such patients at greatest risk of death has yet to be identified or addressed?

In the present issue of the journal, Khayat et al. report the findings of a prospective cohort study involving patients admitted to their hospital with the primary diagnosis of AHF between January 2007 and December 2010. Stable patients with left ventricular ejection fraction (LVEF) ≤45% were offered in-hospital overnight cardiopulmonary monitoring but without polysomnographic documentation of sleep. Of 1375 such studies, 1117 yielded interpretable data. Only 36 of those patients had de novo AHF; the rest had previously documented chronic heart failure with reduced ejection fraction (HFrEF). Applying a calculated apnoea–hypopnoea index (AHI) of 15 ≥ events/h, Khayat et al. categorized 525 patients (47%) as having primarily central sleep apnoea (CSA) and 344 (30%) obstructive sleep apnoea (OSA). The AHI was <15/h in only 22% (248) of these patients. The 1096 who survived to hospital discharge were followed for a median of 3 years. Post-discharge mortality rates were determined from vital statistic databases. In multivariable analyses, adjusting for known covariates of risk, both CSA and OSA were associated independently with increased mortality [hazard ratio for CSA, 1.61, 95% confidence interval (CI) 1.1–2.4, P = 0.02; for OSA, 1.53, 95% CI 1.1–2.2, P = 0.02], whereas mortality risk was not increased in those who were offered and who accepted non-randomized and unblinded sleep apnoea treatment.

These data, which represent the largest published prospective series of this kind, highlight both the high prevalence and the prognostic importance of sleep-related breathing disorders in patients with AHF. Neither finding should surprise, since the combined prevalence of OSA and CSA in stable outpatients with chronic HFrEF is ~50%, and since virtually all subjects included in the present report had been diagnosed with HFrEF prior to their decompensation and index admission. Importantly, in the majority of such patients, who do not complain of daytime sleepiness, the presence of a moderate or severe sleep-related breathing disorder is undiagnosed. It is known from previous observational studies in chronic stable HFrEF outpatients that untreated CSA and OSA, but not treated OSA, fore-shorten survival. Thus, the prevalence and prognostic data of Khayat et al. essentially confirm the findings of those previous publications.

The higher prevalence of CSA and OSA in the present AHF series compared with that reported in chronic HFrEF is entirely consistent with: (i) our current understanding of the pathophysiology of sleep-related breathing disorders in fluid-retaining states; (ii) the postulated pathophysiology of acute decompensation, involving relatively sudden transfer of intravascular volume from capacitance vessels to the thorax and jugular veins; and (iii) the conventional in-hospital management of AHF, which incorporates prolonged bed rest. When ambulatory HFrEF patients sleep, fluid that has accumulated in the legs while upright over the day, due to gravity and high venous pressure, shifts rostrally. Overnight, redistribution of fluid into the jugular veins and peri-pharyngeal soft tissues will narrow the pharynx, render it more collapsible, and exacerbate OSA. Similarly, rostral fluid shift from the legs to the lungs will stimulate pulmonary vagal irritant receptors to elicit reflex hyperventilation that forces PaCO₂ below the apnoea threshold and initiates cyclical oscillations of Cheyne–Stokes respiration with central apnoeas. One would anticipate that supine bed rest in hospital will exacerbate these stimuli to OSA and CSA (Figure 1). Conversely, relief of congestion through diuresis has been shown to attenuate OSA.

Several caveats limit these authors’ findings and interpretations. It can be assumed from prior literature that undiagnosed sleep apnoea was present in the majority of these patients before their index admission. Without knowledge of its prior prevalence in their particular cohort, the authors are unable to determine definitively whether HF decompensation causes de novo sleep apnoea. Calculation of the AHI requires knowledge of sleep time as its denominator, but the ‘attended sleep study’ did not include electroencephalography for sleep staging. The authors do not indicate how they derived the AHI without acquiring objective sleep data. Importantly, the polygraphic recording involved only a single respiratory belt and thus cannot discriminate with certainty central from obstructive apnoeas and hypopnoeas. Despite this significant technical limitation, the authors elected to present independent hazard ratios for CSA.
Figure 1 Fluid shift in the pathogenesis of obstructive (OSA) and central sleep apnoea (CSA) in heart failure. Upper panel: chronic stable heart failure. Fluid accumulation in the leg and splanchnic veins while upright during the day shifts to the neck and thorax during recumbent sleep. Jugular fluid distention and fluid accumulation in peri-pharyngeal tissue decreases upper airway cross-sectional area (UA-XSA) and increases the likelihood of upper airway (UA) obstruction and OSA. An increase in pulmonary capillary wedge pressure (PCWP) and pulmonary congestion stimulates irritant receptors, causing reflex hyperventilation. An acute reduction in PCO2 below the apnoea threshold triggers central apnoea. Metabolic CO2 production causes PCO2 to rise during apnoea until it reaches the ventilator threshold, provokes hyperventilation, and initiates Cheyne–Stokes respiration. Augmented chemoreflex gain increases risk for CSA. As indicated by the bottom double-headed arrow, the predominant type of sleep apnoea can change over time in response to changes in PCWP. Lower panel: with acute decompensation, fluid reserved in capacitance vessels of the splanchnic circulation and legs redistributes rapidly to the neck and thorax in response to an inciting event, increasing the likelihood of both OSA and CSA, and their severity.
and OSA rather than taking the safer approach of calculating the hazard ratio for sleep apnoea vs. no sleep apnoea.

If the authors’ intent is to initiate treatment, definitive determination of the sleep apnoea phenotype is essential. Although there are no randomized trial data demonstrating that treating OSA in HFrEF improves cardiovascular outcome, observational studies report a strong tendency towards lower mortality in continuous positive airway pressure- (CPAP) treated, than in untreated OSA and also in patients with either type of sleep apnoea who were treated and complied with some form of positive airway pressure therapy. More importantly, for CSA in patients with HFrEF, the largest randomized clinical trial published to date demonstrated no beneficial effect of CPAP on heart transplant-free survival. Post-largest randomized clinical trial published to date demonstrated no beneficial effect of CPAP on heart transplant-free survival.13

Conflict of interest: This study was funded by the Heart Failure Association (HFA) of the ESC. Eur Heart Fail 2012;14:803–869.

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