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Central Sleep Apnea in Heart Failure: Marker, Mediator, or Therapeutic Target?

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Central sleep apnea (CSA), particularly when accompanied by Cheyne–Stokes respiration (CSR), is a distinctive manifestation of cardiorespiratory instability in heart failure (HF). Rather than representing an isolated sleep disorder, CSA reflects the interaction between impaired cardiac function and an unstable ventilatory control system. Increased chemosensitivity, reduced carbon dioxide reserve, and prolonged circulatory delay promote ventilatory overshoot below the apneic threshold, generating periodic breathing. This instability can be conceptualized through loop gain, which may also predict suppression of CSR by continuous positive airway pressure (CPAP) independently of HF severity[1].

Sleep-disordered breathing is highly prevalent across the HF spectrum, whereas CSA is particularly associated with heart failure with reduced ejection fraction (HFrEF)[2]. Importantly, CSA is associated with increased mortality, including in large real-world populations, raising a clinically relevant dilemma: is CSA merely a marker of advanced HF, a contributor to disease progression, or a modifiable therapeutic target?[3] Growing evidence suggests that the answer may depend on phenotype. Respiratory characteristics beyond the conventional apnea–hypopnea index may provide clinically relevant information. Distinct hyperpneic patterns during CSR have been associated with differences in cardiac function[4], while the FACE cohort demonstrated substantial heterogeneity among HF patients with CSA and suggested that prognosis and response to adaptive servo-ventilation (ASV) may differ across clinical phenotypes[5,6]. These observations challenge a "one-size-fits-all" approach and support more precise physiological and clinical phenotyping of CSA in HF.

Optimization of HF therapy remains the cornerstone of management. Additional treatment options include CPAP, oxygen, ASV and, in selected patients, transvenous phrenic nerve stimulation. Earlier evidence demonstrated effective suppression of sleep-disordered breathing with ASV[7], but its role underwent major reassessment following the safety concerns raised by SERVE-HF[8,9]. More recently, ADVENT-HF demonstrated effective control of sleep-disordered breathing without an identified safety signal, although cardiovascular morbidity and mortality were not reduced[10]. Contemporary recommendations therefore emphasize careful patient selection and individualized treatment rather than a uniform therapeutic approach[11].

CSA in HF should not be viewed solely as a risk marker or simply as an abnormal apnea–hypopnea index. It represents a heterogeneous physiological phenotype in which the failing heart and unstable breathing interact. The future challenge is not merely to suppress central events, but to identify which patient, with which phenotype, is most likely to benefit from targeted therapy.

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