Sleep-Disordered Breathing in Patients with Heart Failure

Robert J. Mentz, MD*, Mona Fiuzat, PharmD

KEYWORDS

• Comorbidities • Sleep apnea • Heart failure • Clinical trials • Outcomes • Adaptive servoventilation • Positive airway pressure

KEY POINTS

- Sleep-disordered breathing is prevalent in patients with heart failure, and is associated with increased morbidity and mortality.
- Sleep-disordered breathing is proinflammatory, with nocturnal oxygen desaturations and hypercapnia playing a role in the development of oxidative stress and sympathetic activation.
- Attention to the diagnosis and management of sleep-disordered breathing in patients with heart failure may improve outcomes.

INTRODUCTION

Although there have been important successes in the development of therapies for chronic heart failure (HF) in recent decades, most recent HF trials have failed to show added benefit from new therapies,[1–3] and rates of adverse events remain high. In particular, there has been little progress in the development of new therapies for acute HF.[4] This lack of progress suggests the need for a critical reappraisal of treatment strategies in HF, including the treatment of comorbidities.

The presence of comorbidities in HF patients has been associated with significantly increased morbidity and mortality.[5] The risk of hospitalization markedly increases with the number of noncardiovascular chronic conditions.[6] Rehospitalization rates following acute HF are nearly as high for noncardiovascular causes as for HF.[7] Comorbid pulmonary and renal dysfunction, along with sleep-disordered breathing (SDB), complicates the management of HF patients. This article summarizes the impact of SDB on the characteristics, treatment, and outcomes of HF patients. Data investigating the treatment of SDB in HF patients are reviewed, and areas for future research identified.

EPIDEMIOLOGY AND DEFINITIONS

SDB is common in patients with HF.[8] It occurs in up to 50% to 80% of HF patients[9] and is highly prevalent in both those with preserved ejection fraction (EF) and reduced EF. Two primary types of SDB occur in HF patients: obstructive sleep apnea (OSA) and central sleep apnea/Cheyne-Stokes respiration (CSA/CSR). The prevalence of SDB in HF patients is substantially higher than in the general community, where approximately 18% of subjects have OSA (2:1 male predominance) and less than 1% have CSA.[10]

OSA involves repeated collapse of the pharynx that triggers apneas during sleep (**Box 1**).[9,11] Apnea is defined as a greater than 90% reduction in tidal volume lasting 10 seconds or longer, and hypopnea is a reduction in tidal volume of 50% to 90% lasting 10 seconds or longer, accompanied by a 3% or greater decrease in oxyhemoglobin

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Duke University Medical Center, Duke Clinical Research Institute, 2301 Erwin Road, Durham, NC 27710, USA
* Corresponding author. Duke University Medical Center, 2301 Erwin Road, Durham, NC 27710.
E-mail address: robert.mentz@duke.edu

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Box 1
Definitions of sleep-disordered breathing

Apnea

- A greater than 90% reduction in tidal volume lasting 10 seconds or longer

Hypopnea

- A reduction in tidal volume of 50% to 90% that lasts 10 seconds or longer
- Accompanied by a 3% or more decrease in oxyhemoglobin saturation (Sao_2) or termination by arousal from sleep

Sleep Breathing Disorder

- Five or more episodes of apnea or hypopnea per hour of sleep
- Accompanied by either hypersomnolence or at least 2 episodes of choking or gasping during sleep, recurrent awakenings, unrefreshing sleep, daytime fatigue, or impaired concentration or memory

Obstructive Sleep Apnea

- Repeated collapse of the pharynx that triggers apneas during sleep
- Reduction in the tidal volume with apneas and/or hypopneas in the setting of typical breathing efforts

Central Sleep Apnea

- Apneas for 10 seconds or longer without typical breathing efforts

saturation or termination by arousal from sleep. A sleep breathing disorder is defined as the presence of 5 or more episodes of apnea or hypopnea per hour of sleep (ie, apnea-hypopnea index [AHI]), which is accompanied by either hypersomnolence or at least 2 episodes of choking or gasping during sleep, recurrent awakenings, unrefreshing sleep, daytime fatigue, or impaired concentration or memory. The AHI is used to grade severity as mild (6–14 episodes/h), moderate (15–29 episodes/h), or severe (≥30 episodes/h). OSA involves reduction in the tidal volume in the setting of typical breathing efforts, whereas CSA involves apnea for 10 seconds or longer without typical efforts as diagnosed on polysomnography. CSA and OSA rarely occur together in normal subjects, but commonly coexist in HF patients, although one pattern usually predominates.[12]

One study of 700 stable HF outpatients with reduced EF (HFrEF) and symptoms of New York Heart Association (NYHA) functional class II and higher demonstrated that 76% of patients exhibited SDB with a breakdown of CSA and OSA in 40% and 36% of patients, respectively.[13] In particular, CSA seemed to be a marker of HF severity given the association with worse NYHA functional class and lower EF. However, the prevalence of SDB is high even in those with milder HF symptoms.[14] SDB has been shown to be at least as common in acute HF patients as in chronic HF patients.[15] Strikingly in one study of acute HF patients nearly all hospitalized patients had evidence of SDB with a mean AHI of 41 and approximately 50% of total sleep time in CSR.[16] Acute treatment of HF also did not appear to consistently improve SDB. Women with HF may be less likely than men to have SDB, and the severity of SDB may be lower.[17] HF with preserved EF (HFpEF) patients have a similarly high prevalence of SDB compared with those with HFrEF.[18,19] However, the breakdown between the predominant type of SDB in HFpEF may favor OSA rather than CSA, as in HFrEF patients.[20]

Risk factors for the development of SDB in HF patients include male sex and increased age for both types of SDB (Table 1).[21,22] Elevated body mass index (BMI) is an additional risk factor for OSA (perhaps only in men), while atrial fibrillation, hypocapnia during wakefulness (partial pressure of carbon dioxide <38 mm Hg), and severe left ventricular impairment increase the likelihood of CSA.[8,21]

OSA has been associated with increased morbidity and mortality in the general population.[23–25] In acute HF patients, SDB is an independent predictor of cardiac readmission.[26] In chronic HF patients, untreated moderate to severe OSA was associated with increased mortality on multivariable analysis in a small study of 164 patients

Table 1
Risk factors for sleep-disordered breathing

Both Obstructive and Central Sleep Apnea	Obstructive Sleep Apnea	Central Sleep Apnea
Male sex	Elevated body mass index (possibly males only)	Atrial fibrillation
Increased age		Hypocapnia during wakefulness
		Severe left ventricular impairment