Sleep and Breathing in Congestive Heart Failure

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KEYWORDS

• Heart failure • Sleep apnea • Obstructive sleep apnea • Central sleep apnea
• Cheyne-Stokes respiration • Sleep-disordered breathing • CPAP • BPAP

KEY POINTS

- Sleep apnea is a common and underdiagnosed comorbidity of heart failure.
- Untreated sleep apnea is an independent risk factor for increased mortality in heart failure.
- Heart failure and sleep apnea are interrelated in that one disease can cause the other and vice versa.
- Noninvasive positive pressure ventilation is the mainstay of therapy for sleep apnea in heart failure.

INTRODUCTION

Heart failure (HF) is one of the most prevalent and costly diseases in the United States.[1] Sleep apnea (SA) is now recognized as a common, yet underdiagnosed, comorbidity of HF.[2] Much investigation on the relationship between these two disorders has occurred already to help elucidate why they frequently occur together, what effect their coexistence has on patients' morbidity and mortality, and how to best manage them when they coincide. This article discusses the unique qualities that SA has when it occurs in HF and explains the underlying pathophysiology that illuminates why SA and HF frequently occur together. The authors provide an overview of the treatment options for SA in HF and discuss the relative efficacies of these treatments. Of note, because of a paucity of data on SA in HF with preserved ejection fraction (HFpEF), the authors' discussion of HF only refers to HF with reduced EF unless otherwise specified. In addition, the term *SA* is used as a broad term referring to any of its subtypes, be it central SA (CSA), obstructive SA (OSA), or the occurrence of both together.

SLEEP CHARACTERISTICS IN HF WITHOUT SA

Irrespective of the presence of a primary sleep disorder, nocturnal symptoms of HF alone can interfere with sleep quality. Cough is a well-established cause of sleep dysfunction[3] and can be a manifestation of HF-related pulmonary edema. In addition, angiotensin-converting enzyme (ACE) inhibitors are a class I recommended medication for the treatment of HF[4]; 10% to 20% of patients treated with this medication will develop an ACE inhibitor–induced cough.[5] Orthopnea and nocturia are common symptoms of HF, and they also cause sleep dysfunction. The effect of these symptoms on sleep quality was objectively measured by Javaheri[6] in a single-center prospective study of patients with HF in whom polysomnography was obtained without screening for symptoms of SA. In the subset of patients with no SA (n = 32, mean

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apnea-hypopnea index [AHI] = 2/h), the percentage of light sleep (N1) was elevated at 34% of the total sleep time. There was complete absence of deep sleep (N3, or slow wave sleep); the arousal index was elevated at 15/h. These patients also corroborated that the sleep measured on the night of their polysomnogram (PSG) was typical of a night's sleep at home. In 2003, Arzt and colleagues[7] compared polysomnography data in a HF cohort with a non-HF community sample cohort. In the subgroup of patients with HF with an AHI less than 5, they had statistically significantly increased sleep-onset latency and wake after sleep onset as compared with the control group. They also had significantly reduced rapid-eye-movement sleep and sleep efficiency, with an average of 1.2 hours less sleep per night.

DIAGNOSIS OF SA

To diagnose SA, patients must undergo a PSG. It typically includes measurements of various activities during sleep, including heart rate, pulse oximetry, abdominal movement, chest wall movement, airflow through the nose and mouth, electroencephalographic activity, and leg movements. These measurements allow for the detection of hypoxemia during sleep and apneas and hypopneas, among other things. An apnea or hypopnea is defined as the complete or partial cessation of airflow for 10 seconds or more, respectively. Apneas and hypopneas are further characterized into central and obstructive subtypes. An obstructive apnea (OA) or hypopnea occurs when there is pharyngeal obstruction to airflow caused by collapse of the pharyngeal muscles at some point along the upper airway. The PSG will indicate persistent or increasing thoracoabdominal effort despite the lack of airflow. In contrast, a central apnea or hypopnea occurs when there is an absence or decrease of respiratory effort along with the cessation of airflow.[8] The total number of apneas and hypopneas that occur during a PSG are added together and divided by the total amount of time patients slept during the PSG to give the AHI. The AHI indicates the average number of respiratory events that occur per hour. SA is diagnosed when there is an abnormally high AHI. An AHI less than 5 is normal, between 5 and 14 indicates mild SA, between 15 and 29 is moderate SA, and 30 or more is severe SA. When most of the respiratory events are caused by obstruction of airflow, the SA is called OSA. When most of the respiratory evens are caused by a lack of breath initiation, the SA is called CSA.[8] AHI and hypoxemia are not only helpful in diagnosing and categorizing SA but their resolution with therapy can help also objectively determine treatment response.

SA IN THE SETTING OF HF

Epidemiology and Mortality of CSA in HF

In the general population, CSA is rare in that its prevalence in the general population is less than 1%,[9] which is starkly different than the prevalence of OSA. However, in the HF population, CSA prevalence can range from 21%[10] to 37%.[11] There is uncertainty as to whether CSA incurs a mortality risk in HF. There are several studies that argue for[12,13] and against[14,15] this assertion, though they are limited in that they are single centered with small sample sizes and there is no uniformity between them in how they diagnose CSA, define CSA, and in their inclusion/exclusion criteria (for example, whether patients with CSA on noninvasive positive pressure ventilation [NIPPV] are allowed in the study).[16] Nevertheless, most studies indicate an independent association of CSA with increased mortality in HF.

CSA and Cheyne-Stokes Respiration in HF

CSA is actually a broad term that encompasses several different disorders. The condition that causes CSA in patients with HF is called Cheyne-Stokes respiration (CSR).[17] It is a periodic breathing pattern whereby hyperpneic breaths gradually decrease into hypopneas and/or apneas in a crescendo-decrescendo fashion. This cycle of breathing periods lasts anywhere from 30 seconds to 2 minutes.

CSR occurs in HF via several derangements to homeostatic processes. Pulmonary congestion will stimulate vagal nerve fibers in the alveolar wall called J receptors, which cause a hyperventilatory response.[18] In addition, for reasons unknown, the apneic threshold remains close to the resting P_{CO_2} in HF. Therefore, any slight decrease in P_{CO_2} can bring it to less than the apneic threshold and cause an apnea. Once the apnea occurs, it continues until peripheral and central chemoreceptors can sense the P_{CO_2} has returned to an appropriate level. As a result of reduced cardiac output, the circulation time is increased. Therefore, the peripheral and central P_{CO_2} chemoreceptors incur a lag in sensing changes in P_{CO_2}.[19] This lag partially explains why peripheral and central chemoreceptors will overshoot in their hyperventilatory response to a high P_{CO_2} or undershoot their hypoventilatory response to a low P_{CO_2}[20] and, thus, perpetuate the cycle. Aside from J receptor stimulation, other events that may initiate the CSR cycle include hyperventilatory responses from hypoxemia[21] or upper airway