Obstructive Sleep Apnea in Heart Failure

Subjects: Others

Contributor: Shahrokh Javaheri, Sogol Javaheri

Obstructive sleep apnea (OSA) is characterized by repetitive upper airway closure due to soft tissue collapse and genioglossus muscle relaxation in the upper airway resulting in apneas (cessation of breathing for 10 s or longer) and hypopneas (reductions in breathing coupled with desaturation and/or arousal). OSA is highly prevalent among patients with asymptomatic left ventricular systolic and diastolic dysfunction and congestive heart failure, and if untreated may contribute to the clinical progression of heart failure (HF).

Keywords: obstructive sleep apnea ; heart failure ; continuous positive airway pressure

1. Introduction

According to the American Heart Association 2022 Statistics [1], over 8 million people 18 years or older will have heart failure (HF) in 2030. Despite treatment advances, the prevalence, burden, and costs of HF continue to increase. The healthcare costs associated with HF exceed 30 billion dollars annually and over 50% of these costs are associated with hospitalizations [1]. Obstructive sleep apnea (OSA) is highly prevalent in, and may contribute to the progression of, both HF with reduced ejection fraction (HFrEF) and HF with preserved ejection fraction (HFpEF), potentially reflecting an important modifiable risk factor. The prevalence of OSA ranges from 20% to up to 60% among the HF population, with rates of OSA typically running higher among those with HFpEF as compared with HFrEF [2][3][4][5][6]. Observational data has shown that OSA is independently associated with poor quality of life, excess rehospitalization, and premature mortality among patients with HF [5]. Notably, multiple observational studies have demonstrated that effective treatment of OSA may decrease hospital readmission rates and improve survival [7][8][9]. To date, there are no randomized controlled trials assessing continuous positive airway pressure (CPAP) therapy in an HF with comorbid OSA population. Prior RCTs using CPAP to treat OSA have shown no benefit on secondary prevention of cardiovascular diseases but have shown improvement in quality-of-life measures.

2. Obstructive Sleep Apnea (OSA) and Heart Failure (HF) Pathophysiology

OSA is characterized by repetitive upper airway closure due to soft tissue collapse and genioglossus muscle relaxation in the upper airway resulting in apneas (cessation of breathing for 10 s or longer) and hypopneas (reductions in breathing coupled with desaturation and/or arousal). Obesity and rostral fluid shifts both contribute to upper airway narrowing and collapse. Like the general population, obese individuals with HF are also more prone to upper airway closure related to fat deposition in the upper body, including visceral fat and tongue and throat fat [10]. At the same time, fluid retention and edema, particularly during HF decompensation, can contribute to upper airway closure in the supine position. Translocation of fluid from the lower extremities to the neck may cause vascular congestion and edema of the pharyngeal area [11]. Regardless of the contributing factors, the downstream effects include intermittent hypoxia and hyper-hypocapnia, repetitive arousals, and large negative intrathoracic pressure swings. Hypoxia, hypercapnia, and arousals lead to autonomic dysregulation with heightened sympathetic activity and reduce parasympathetic tone as well as hypothalamic pituitary axis dysregulation. Intermittent hypoxia reoxygenation leads to production of oxygen free radicals, oxidative stress, and upregulation of inflammatory cascades such as NF kb and TNF-alpha. Finally, negative intrathoracic pressure swings may result in increased atrial stretch (facilitating atrial fibrillation), left ventricular transmural pressure and afterload, and myocardial oxygen demand [5][11].

3. Epidemiology

Multiple observational studies suggest that OSA is independently associated with excess hospital readmission [9][10] and that treatment may lower the rate of readmissions [7][8][9]. Specifically, severe OSA has been independently associated with 1.5 times higher readmission of HF patients when compared with those without OSA [9]. Observational studies also suggest OSA is independently associated with premature mortality in individuals with comorbid HF [7][8][9][12][13] and that

treatment of OSA attenuates this risk [7][9][12][13]. In the largest study, among 30,000 Medicare beneficiaries newly diagnosed with HF, the treatment of SDB was associated with decreased readmission, health care cost, and mortality [7]. Two other studies have shown that effective treatment of OSA with CPAP improves survival in patients with comorbid HF, particularly in those who are compliant with CPAP [9][12]. Long-term randomized control trials (RCTs) in this population are not available, but there is a critical need to assess how effective treatment of OSA affects the clinical course of HF and hard outcomes.

4. Acute Decompensated Heart Failure

Multiple observational studies have shown a high prevalence of SDB, particularly OSA in patients admitted to the hospital for HF decompensation. In a multi-center study from Brazil, consecutive patients with confirmed acute cardiogenic pulmonary edema (ACPE) underwent polygraphy following clinical stabilization [14]. Approximately 100 patients were included in the final analysis, of whom 79 had HFpEF with LVEF greater than or equal to 50%. A total of 61% of the patients had OSA defined as an apnea-hypopnea index (AHI) greater than or equal to 15 events/h based on polygraphy. The mean follow-up was 1 year and the primary outcome was ACPE recurrence. Higher incident rates of ACPE recurrence (25 vs. 6 episodes; $p = 0.01$) and myocardial infarction (15 vs. 0 episodes; $p = 0.0004$) were observed in patients with OSA compared with those without OSA. All 17 deaths occurred in the OSA group ($p = 0.0001$). In a Cox proportional hazards regression analysis, OSA was independently associated with ACPE recurrence (hazard ratio (HR), 3.3 [95% CI, 1.2–8.8], $p = 0.01$), incidence of myocardial infarction (HR, 2.3 [95% CI, 1.1–9.5]; $p = 0.02$), cardiovascular death (HR, 5.4 [95% CI, 1.4–48.4]; $p = 0.004$), and total death (HR, 6.5 [95% CI, 1.2–64.0]; $p = 0.005$). Among the patients with OSA who presented with ACPE recurrence or who died, AHI and hypoxemic burden and rates of sleep-onset ACPE were significantly higher [14].

Given the high prevalence of OSA in HFpEF and HFrEF and supportive observational data, OSA may represent a modifiable risk factor. This is particularly important as HFpEF remains highly prevalent and thus far pharmacological trials have not shown a drug therapy that could improve survival as the primary outcome, though a recent sodium–glucose co-transporter 2 (SGLT-2) inhibitor trial has demonstrated improved survival in the composite endpoint of hospital admission and mortality [15].

One RCT in acute decompensated HF randomized 150 patients with HFrEF who were diagnosed with OSA during hospitalization to a CPAP therapy arm ($n = 75$) or control arm ($n = 75$). All participants received guideline-directed therapy for HF decompensation. Exploratory analysis revealed that 6 months after discharge, there was over a 60% decrease in readmissions for patients who used PAP > 3 h/night compared with those who used PAP < 3 h/night ($p < 0.02$) and compared with controls ($p < 0.04$) [13].

5. Conclusion

OSA is commonly comorbid with HF. The pathophysiological consequences of OSA has deleterious effects on the cardiovascular system and based on multiple observational studies is independently associated with poor quality of life, excess rehospitalization and premature mortality. Notably, multiple observational studies have demonstrated that effective treatment of OSA decreases hospital readmission and improves survival but ultimately RCTs are needed using a more targeted population of HF patients with symptomatic OSA and ideally with higher CPAP adherence to determine whether effective treatment of OSA can improve hard outcomes beyond quality of life.

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