Geriatric Nursing xx (2017) 1–7

Contents lists available at ScienceDirect

Geriatric Nursing

journal homepage: www.gnjournal.com

Feature Article

Sleep disordered breathing in older adults with heart failure with preserved ejection fraction

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ARTICLE INFO

Article history:
Received 27 March 2017
Received in revised form
28 June 2017
Accepted 1 July 2017
Available online xxx

Keywords:
Heart failure
Heart failure with preserved ejection fraction
Sleep-disordered breathing
Sleep apnea syndrome
Adaptive servo-ventilation
Positive airway pressure

ABSTRACT

Heart failure in older adults is frequently accompanied by sleep disordered breathing (SDB). Treatment of SDB in persons with heart failure with preserved ejection fraction (HFpEF) is unclear because most data is on heart failure with reduced ejection fraction (HFrEF). The purpose of this paper was to evaluate studies that report on the effects of positive airway pressure on patient outcomes in older adults with HFpEF and comorbid SDB. A search of the literature found six data-based studies (N = 36 to 126). Treatment with positive airway pressure reduced nighttime SDB symptoms and improved daytime functional status in persons with HFPEF and SDB (New York Heart Association Functional Class: effect sizes = −0.67 to −1.60). Limitations (i.e. only two studies were randomized controlled trials, small sample sizes, and women were under-represented) suggest that additional evidence is needed to guide treatment of SDB in older adults with HFpEF.

Introduction

According to the American Heart Association, in 2014 over 6.5 million adults in the U.S. had heart failure. The prevalence of heart failure is expected to increase by 46% by 2030 to over 8 million.[1] Heart failure is associated with significant decreases to health-related quality of life (HRQoL), daytime dysfunction, fatigue, dyspnea, and increased mortality.[2] The total cost of heart failure in 2012 was estimated as almost 31 billion dollars; this cost is projected to increase to 70 billion dollars by 2030.[3] Although cardiac disease is not part of healthy aging, older adults have a disproportionate risk. The prevalence of heart failure is less than 2% of adults under 60 years old, it increases to 6% in the 60 to 79 year-old age group and is greater than 13% in persons over 80 years old.[1]

Heart failure is characterized as either heart failure with reduced ejection fraction (HFrEF; left ventricular ejection fraction [LVEF] ≤ 40%) or as heart failure with preserved ejection fraction (HFpEF; LVEF ≥ 50%).[4] Half of all patients with heart failure present with a preserved LVEF[1]; these patients have a unique phenotype from HFrEF. Patients with HFpEF are frequently older (often in the 8th decade of life), more likely to be female, without a myocardial infarction, and have a history of hypertension, coronary artery disease, obesity compared to patients with HFrEF.[1,5–7] The prevalence of HFpEF relative to HFrEF is increasing at a rate of 1% per year and may become the predominant form of heart failure in the developed world.[2] Unlike HFrEF, there are no established therapies to improve mortality and morbidity in patients with HFpEF.[8] There are differences in the etiology of morbidity and mortality between HFrEF and HFpEF, with morbidity in HFpEF influenced more by non-heart failure related conditions.[2,9] Thus, therapy in HFpEF is aimed at treating the more prevalent comorbidities that coexist in persons with HFpEF in order to reduce symptom burden and to improve HRQoL.[2]

Sleep disordered breathing (SDB) is a highly prevalent comorbidity in adults with HFpEF, estimated to range from 50% to over 80% when compared to persons who have no history of heart failure.[10–14] According to the American Academy of Sleep,[15] SDB refers to a number of breathing disruptions that occur during sleep that include:

Conflicts of interest: none.

This research was supported by the T32, Technology: Research in Chronic and Critical Illness (2T32 NR008857) at the University of Pittsburgh, School of Nursing (L. Baniak).

This research was supported by the NINR: K24 NR016685 (E. Chasens).

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http://dx.doi.org/10.1016/j.gerinurse.2017.07.001

- obstructive apneas (cessation of airflow for 10 s or longer because of an obstruction in airflow in the upper pharynx with continued respiratory effort)
- hypopneas (a decrease in airflow by 50% from baseline accompanied by a decrease of 3% in oxygen saturation),
- central apneas (absence of a central nervous system signal to breath with a cessation in breathing for at least 10 s)
- mixed apneas (an apnea that starts as an obstructive event but converts to a central apnea, or vice versa), and
- Cheyne-Stokes respirations (a cyclic pattern of waxing and waning airflow with respirations).

Data from previous research suggests that SDB results in sympathetic activation, sleep fragmentation, and intermittent hypoxia that is associated with a variety of adverse consequences in older adults including excessive daytime sleepiness,[16] depression,[16] cognitive decline,[17,18] reduced functional status,[19] cardiovascular disease,[20,21] and increased mortality.[21]

In patients with heart failure, the choice of treatment for SDB depends on the severity and type of breathing disturbance, symptom presentation (i.e. presence of snoring or excessive daytime sleepiness), and the type of cardiovascular disease present.[22–24] Positive airway pressure (e.g., *continuous positive airway pressure* [CPAP], *bi-level positive airway pressure* [bi-PAP], or *adaptive servo-ventilation* [ASV]) is the mainstay treatment of SDB.[22] CPAP involves wearing a mask that delivers a steady stream of air to prevent airway collapse and obstructive apneas. Unlike CPAP, Bi-PAP machines have two pressure settings with a higher pressure for inhalation and a lower pressure for exhalation. Bi-PAP is useful for patients who find it difficult to exhale against positive pressure, require a high positive pressure setting to prevent airway obstruction, require oxygen, have a neuro-muscular disorder, or who have HFrEF. ASV is a further refinement as a type of positive airway pressure that uses an algorithm based on the detection of apneas to the level of pressure required to maintain respiration with inspiratory support to treat central apneas.[25,26] ASV is used for patients with more complex SDB consisting with mixed obstructive and central apneas and Cheyne-Stokes respirations.

While the prevalence of SDB is similar between the populations of HFrEF and HFpEF, whether the predominant type of sleep apnea (e.g. obstructive versus central sleep apnea) is similar remains unclear.[14,27] Central sleep apnea is more common in persons with heart failure compared to the general population.[12] The prevalence of central sleep apneas has been shown to increase significantly ($p < .05$) with increasing heart failure severity.[27,28] In general, patients with HFpEF tend to have more obstructive apneas in comparison with patients with HFrEF.[14] In a prospective study of both HFpEF and HFrEF, OSA was the predominant type of SDB in the HFpEF patients (62%) but not in HFrEF patients.[14] A larger study of 244 persons with only HFpEF also found more OSA (40%) versus central sleep apnea (30%) in those identified with SDB.[27] However, several studies suggest that the pattern of central apneas, Cheyne-Stokes respirations, obstructive apneas, and hypopneas changes on a night-to-night basis further complicating the delineation of SDB between persons with HFrEF and HFpEF as well as the management of SDB in each population.[26,29]

A growing body of evidence over the past decade supports positive airway pressure (e.g., CPAP, bi-PAP, or ASV) as effective methods to treat SDB with demonstrated improvements to nocturnal respiratory function and daytime sleepiness.[30–32] The impact of positive airway pressure on cardiac function and mortality is less clear.[30–33] For example, the *Sleep Apnea Cardiovascular Endpoints* (SAVE) study.[33] was a randomized control trial to evaluate the effectiveness of CPAP in reducing adverse cardiovascular events among patients with cardiovascular disease and comorbid moderate-to-severe OSA (apnea + hypopnea index [AHI] $\geq$ 15).[33] Those patients randomized to CPAP ($n = 1346$) had significant improvements in daytime sleepiness, respiratory function, and quality of life measures but not in mortality or the recurrence of myocardial infarction when compared to the usual-care group ($n = 1341$).

Additionally, adverse results occurred in a second study the *Treatment of Sleep-Disordered Breathing with Predominant Central Sleep Apnea by Adaptive Servo-Ventilation in Patients with Heart Failure* (SERVE-HF).[25] The SERVE-HF study, a large randomized controlled trial ($N = 1325$) of subjects with HFrEF (LVEF $\leq$ 45%) and comorbid moderate-to-severe central sleep apnea (AHI $\geq$ 15), prompted healthcare professionals to question the safety of using ASV in persons with heart failure. The SERVE-HF trial was prematurely stopped because of a statistically significant increase in the primary end-point of all-cause mortality and cardiovascular deaths in those participants randomized to ASV ($p < .01$). Although the results from the SERVE-HF study cannot be generalized to persons with HFpEF, both the SAVE and SERVE-HF trials have rendered the treatment of SDB among heart failure patients a controversial topic regardless of treatment type.

While the negative prognostic impact of HFpEF is similar to that of HFrEF,[34] each type of heart failure represents a different clinical syndrome that should be studied and treated separately.[35] Important differences exist between HFpEF and HFrEF with respect to the extent of myocardial dysfunction, patterns of cardiac remodeling in heart chambers, and in the response to therapeutic interventions.[35] Additionally, OSA in older adults greater than 65 years has a distinctly different physiological phenotype in old versus young individuals.[36] As a result of these differences, outcomes during positive airway pressure therapy in patients with HFpEF, typically persons greater than 65 years with comorbid SDB, would be expected to be different from the samples in both the SERVE-HF and SAVE trials.

Previous studies on the treatment of SDB in adults with heart failure have historically focused on middle aged adults, featured samples for which the type of heart failure was not identified, or where the majority of the participants had symptoms suggestive of HFrEF. Therefore, the effect of positive airway therapy on patient-centered and clinical outcomes in older adults with HFpEF is poorly understood. The purpose of this paper is to evaluate the studies that report on the effects of positive airway pressure on patient-centered and clinical outcomes in older adults with HFpEF and comorbid SDB.

Methods

Search and data abstraction

In June 2017, a systematic all-field and no-date-limit literature search using PubMed, OVID, and Web of Science was conducted. Two investigators, working independently, used the following combination of search terms: *sleep apnea*, or *sleep apnea—obstructive,* or *sleep apnea—central,* or *sleep apnea—mixed*; AND *continuous positive airway pressure,* or *CPAP,* or *adaptive servo ventilation, or ASV,* or *bi-level positive airway pressure, or BiPAP*; AND *heart failure*, or *heart failure—diastolic*, or *heart failure—preserved ejection fraction*, or *HFpEF.* The identified articles were analyzed using the protocol below.

The search identified 279 publications (i.e., articles in peer-reviewed journals); 71 were excluded from further analysis because they were written in languages other than English or were not data-based research articles. The titles and abstracts of the