Published in final edited form as:

Heart Fail Rev. 2018 September ; 23(5): 701–709. doi:10.1007/s10741-018-9715-y.

Sleep-disordered breathing in hospitalized patients with congestive heart failure: a concise review and proposed algorithm

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Abstract

Congestive heart failure (CHF) is the most common cause of hospital admission in the USA costing the taxpayers billions of dollars. Sleep-disordered breathing (SDB) is a common co-morbid condition associated with CHF with prevalence estimated to be 60–70%. Despite substantial evidence supporting the negative impact of SDB on CHF, the condition is underrecognized and undertreated. Patients admitted to the hospital with CHF and SDB are prime candidates for intervention with positive airway pressure (PAP) therapy as they form a “captive audience,” and timely intervention and education may mitigate sub-optimal outcomes. In conclusion, this review explores emerging data on the cost effectiveness and outcome of early intervention with PAP in hospitalized CHF patients.

Keywords

Congestive heart failure; Sleep-disordered breathing; Hospitalized patients; Readmissions; Polysomnography

Introduction

Congestive heart failure (CHF) is a major public health problem and a leading cause of hospital admissions in the USA [1]. CHF-related admissions account for more than \$30 billion in direct and indirect medical costs and loss of productivity every year [2], and a major proportion of costs result from rehospitalizations. By conservative estimates, 20% of Centers for Medicare and Medicaid Services (CMS) enrollees are readmitted to the hospital

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Compliance with ethical standards

Conflict of interest Dr. Sharma has received unrestricted research grants from ResMed Inc.

within 30 days of discharge [3], and almost 50% are rehospitalized within 6 months [4, 5]. As part of the quality metrics under the Affordable Care Act, hospitals face major financial penalties if they are unable to decrease CHF readmissions [3]. It becomes imperative to examine independent predictors, including co-morbid conditions that increase readmissions in patients with CHF.

An estimated 40 to 70% of patients with CHF have sleep-disordered breathing (SDB), and more than three quarters of these patients have obstructive sleep apnea (OSA), with the rest being central sleep apnea (CSA) or mixed sleep apnea (OSA and CSA) [6–8]. Published data show that the prevalence is significantly higher in men and increases with age. Additional risk factors for SDB in CHF include obesity, atrial fibrillation, left ventricular ejection fraction (LVEF), and age [7]. However, its detection can be challenging since patients with CHF often do not have the hallmark symptom of SDB which is excessive daytime sleepiness [9]. Lack of daytime sleepiness may be due to a heightened adrenergic state in CHF patients [10, 11]. Because of the absence of the typical symptoms associated with OSA, administering screening questionnaires such as the Epworth Sleepiness Scale (ESS) [12] and the STOP-BANG questionnaire [13] independently has not been proven very helpful for detecting OSA in these patients [9]. However diagnostic algorithms including a clinical questionnaire and overnight pulse oximetry have been found to be more accurate with significantly reduced false positive rates [14, 15]. SDB remains largely underdiagnosed and undertreated. Overnight polysomnography, the gold standard for diagnosis, is expensive and not available or practical in a hospital setting, thus further contributing to this underdetection [16]. This paper will review appropriate screening tools for detecting SDB in hospitalized CHF patients, as well as outcomes of SDB treatment in this population. In addition, an algorithm is proposed for the screening, diagnosis, and treatment of SDB among acute decompensated heart failure patients to improve detection rates and outcomes.

Impact of sleep-disordered breathing in congestive heart failure

Sleep-disordered breathing is a known risk factor for adverse cardiovascular outcomes and excess mortality [17]. Epidemiology studies demonstrate that OSA, the most common type of SDB, is a risk factor for the development of CHF [18]. Congestive heart failure patients with OSA have a higher mortality rate compared to CHF patients without SDB [6, 19] even after adjusting for confounding factors (8.7 versus 4.2 deaths per 100 patient-years). Recent data suggest that the hypoxemic burden more than the frequency of SDB events may influence mortality in these patients [6]. Both OSA and CSA increase the risk for ventricular arrhythmias and automated defibrillator discharges [20].

In a recent study, the prevalence of congestive heart failure in hospitalized medical patients was found to be around 17% [21] and it was estimated that the prevalence of SDB was 18.7%. Since SDB is a risk factor for CHF, the prevalence of both CHF and SDB in hospitalized patients is likely to be high as well. Both OSA [22] and CSA [23] patients with CHF have higher hospital readmission rates than those without SDB, which underscores the importance of identifying and treating SDB in this patient population.

Pathophysiology of sleep-disordered breathing in congestive heart failure

Several mechanisms have been proposed to explain the deleterious effects of untreated SDB in CHF patients, including intermittent hypoxemia, elevated sympathetic activity secondary to recurrent arousals, and baroreflex inhibition [24–27]. Sleep-disordered breathing can cause chronic intermittent hypoxia leading to oxidative damage. This finding has been supported in animal models by observing the development of increased sympathetic activity and hypertension on exposure to intermittent hypoxia [28]. Increased sympathetic activity can result in higher myocardial oxygen requirements mediated by elevations in systemic vascular resistance and consequent left ventricular afterload [29]. Hypercapnia accompanying apneic episodes may also contribute to sustained sympathetic activation [30]. Additionally, acute collapse of the pharynx during obstructive events results in important hemodynamic consequences. Sudden negative intra-thoracic pressure leads to elevations in left ventricular transmural pressure and consequent increased afterload. Negative intra-thoracic pressure also increases right filling pressure due to increased venous return, resulting in elevated right sided pressures. This shifts the interventricular septum leftward, reduces left ventricular filling, and decreases cardiac output. Through these mechanisms, SDB negatively impacts cardiac function and may contribute to worsening heart failure [31].

Identification of sleep-disordered breathing in hospitalized patients

Polysomnography

Overnight multi-channel polysomnography (PSG), also commonly known as a sleep study, is the gold standard for detecting SDB. The PSG recording includes electroencephalogram (EEG) monitoring to determine sleep stages and physiological parameters such as oxygen saturation, heart rate and rhythm, air flow, respiratory effort, and sound (i.e., snoring), as well as eye and leg movements. The diagnosis of SDB requires detection and calculation of the frequency of apneas and hypopneas. Although PSGs are ideally performed in a dedicated sleep laboratory, they also can be done in a hospital room. However, they require a trained technician for set up and monitoring, are expensive, use relatively non-portable equipment, and are burdensome for ill patients. Use of PSGs in hospitalized patients is generally cost prohibitive and not feasible as a diagnostic procedure in the inpatient setting.

Portable sleep study testing

Another practical tool to consider for evaluation of SDB in hospitalized patients is portable sleep testing. Portable sleep testing (PST) records a limited number of respiratory parameters (depending on type of study), usually at a minimum of pulse oximetry, airflow, and respiratory effort to evaluate SDB [32]. Not all portable sleep monitors have the ability/algorithm to differentiate between obstructive and central apneas; however, certain PSTs (type 2, a few type 3) may help screen obstructive versus central events. In a recent study, all patients admitted to the hospital for decompensated systolic CHF (ejection fraction (EF) < 45%) were administered type 2 PST (with ability to distinguish between obstructive and central events) on the first or second night of hospitalization. The prevalence of CSA (defined as central events > 50% of the total respiratory events) was 21% and prevalence of OSA (defined as AHI ≥ 15/h) was 51%. CSA was an independent predictor of 6-month

hospital readmission, as was severe OSA (defined as AHI >30/h) [33]. All PSTs require specialized expertise for study interpretation and considerable logistical support for effective implementation. In addition, portable devices compared to high-resolution pulse oximetry (vide infra) have been shown to require higher rate of repeat testing [34]. Currently, PSTs are not recommended by the American Academy of Sleep Medicine (AASM) for the diagnosis of central sleep apnea [35]. However, it may provide useful information as a screening tool in guiding therapy for hospitalized patients with CHF. Future studies of hospital outcomes, based on PST-directed interventions, may help determine its utility in patients with acute decompensated heart failure (ADHF). Also, studies using other forms of PST such as Watch PAT (peripheral arterial tonometry) may be informative in this setting.

High-resolution pulse oximetry

High-resolution pulse oximetry (HRPO) has recently been shown to be effective for SDB screening in hospitalized settings [19, 36, 37]. A readily available technology, HRPO is a relatively simple, low-cost, and comfortable tool to determine the oxygen desaturation index (oxygen desaturations of 4% per event per hour) and time in hypoxemia (minutes and percentage of sleep with oxygen saturations below 90%). HRPO is available in most hospitals. While pulse oximetry was once unreliable for detecting SDB, significant advances have occurred [38] to improve the plethysmographic signal, reducing averaging time, motion artifacts, and false alarms [39].

Studies have evaluated the utility of HRPO signals versus gold standard full PSG. These studies identified a good correlation between HRPO and PSG, with 80–94% agreement [36, 37]. Based on these findings and sensitivity analyses, an oxygen desaturation index (ODI, the number of oxygen desaturations per hour of sleep) of > 5/h was observed to have an area under the curve (AUC) of 0.82 and thus has been proposed as a diagnostic cut-off. In a recent prospective study on 105 consecutive patients admitted for acute heart failure, HRPO and PST were performed simultaneously for one night. There was significant agreement between the ODI derived from HRPO versus PST with an AUC of 0.89 for >5 events/h. More significantly, 88% of patients identified as having moderate to severe SDB by PST were correctly classified by HRPO. This finding provides further support for the utility of HRPO as a cost-effective screening tool in hospitals where resources are limited [34]. Based on pre-discharge overnight HRPO, SDB was identified as a significant independent predictor of hospital readmission and mortality over 14.2 months of follow-up [40]. This clinical observation is consistent with a recent large study by Oldenburg and colleagues demonstrating that the severity of nocturnal hypoxemia was an independent risk factor for mortality in stable heart failure patients [19]. Thus, several lines of evidence indicate that an HRPO-derived ODI may be a cost-effective tool to identify hospitalized patients with decompensated CHF for SDB.

Potential limitations of HRPO include inability to differentiate between central and obstructive events and the possibility of false negatives due to poor sleep efficiency. Performing the study early during the hospitalization (decompensated state) may overestimate the severity of ongoing SDB. When used appropriately, this low-cost strategy may

function as screening tool for SDB in hospitalized patients [37] especially in centers where PST is not available.

Intervention with positive airway pressure

Treatment with positive airway pressure (PAP) therapy has been shown to reduce high blood pressure and daytime sleepiness and improve ejection fraction in HFrEF patients with SDB [17], but it is greatly underutilized, especially in heart failure patients. One study found that only 2% of CMS patients with CHF were diagnosed and treated for SDB [41].

Recent data [42, 43] have specifically evaluated the role of PAP therapy in decreasing readmissions among CHF patients. In a non-randomized evaluation of SDB among more than 100 patients hospitalized for heart failure, arrhythmias, and myocardial infarction, Kautz et al. [42] found that none with adequate PAP adherence were readmitted to the hospital or visited the emergency department (ED) within 30 days after discharge compared to 30% readmissions among those with partial or non-adherence to PAP therapy.

Another recent study [43] of consecutively admitted patients with decompensated CHF indicated that early recognition and treatment of SDB in hospitalized CHF patients may reduce hospital readmissions and ED visits over a 6-month period of time. In that study, consecutively admitted patients with acute CHF were screened for SDB in the hospital and underwent PSG with subsequent PAP therapy after discharge if SDB was clinically suspected. Subsequent hospital readmissions and ED visits were documented in both PAP therapy-compliant and non-compliant patients. Change in clinical events (number of ED visits and hospital readmissions) pre- and 6 months post-intervention were calculated for each patient, and the mean change for each clinical event was compared between the two groups. Of the 70 patients with SDB, 37 (53%) were compliant with PAP therapy (≥ 4 h usage on 70% or more nights). Both groups experienced a decrease in total readmissions (hospitalizations plus ED visits), although compliant patients had a significantly greater reduction (mean ± SE 1.5 ± 0.2 clinical in events versus 0.2 ± 0.3) ($p < 0.0001$). This was the first study to evaluate the longterm benefit (6-month) of early intervention for SDB in hospitalized CHF patients. However, studies comparing adherent with non-adherent groups are complicated by the healthy user effect, emphasizing the need for randomized trials to draw rigorous conclusions.

Recent experience of the largest screening and intervention program in hospitalized patients is also supportive of a positive impact of PAP intervention [22]. This study screened 5062 patients using a combination of the STOP or STOP-BANG questionnaire and HRPO. Those patients confirmed to have SDB were offered treatment with PAP therapy. Long-term clinic follow-up of these patients showed that patients who were compliant with PAP therapy had a survival benefit. The PAP adherence in the first 3 months was also found to be a predictive marker of improved survival [22] (Fig. 1).

A recent study of the association between OSA risk and rapid response events (RRE) provides additional evidence supporting the use of PAP therapy in hospitalized CHF patients [44]. In that study, high-risk OSA patients, many whom had CHF, had increased rates of RRE. However, event rates were reduced if the patients were compliant with PAP therapy.

Despite encouraging data from studies of CHF cohorts where OSA was the primary manifestation of SDB, the impact of PAP therapy among CHF patients with central sleep apnea remains controversial. Investigators from the CANPAP trial (Canadian Positive Airway Pressure Trial for Heart Failure Patients with Central Sleep Apnea) showed that although CPAP improved CSA, nocturnal oxygenation, ejection fraction, and distance walked in 6 min, it did not affect survival in patients who had CSA and heart failure. There was no effect from PAP therapy on the number of hospitalizations or quality of life indices [45]. The post hoc subgroup analysis from the CANPAP trial indicated that patients whose AHI was reduced to < 15 events per hour by PAP therapy had significant improvement in ejection fraction and transplant-free survival compared to controls [46]. This finding suggests that a subset of patients with CSA, with reduced systolic function, may respond favorably to PAP therapy.

Adaptive servo-ventilation (ASV) is an advanced PAP device which automatically adjusts the level of pressure support ventilation to an individual patient's ventilation requirements. Early studies indicated that ASV would be beneficial in treatment of CSA in the setting of CHF [47, 48].

The SERVE-HF (Adaptive Servo-Ventilation for Central Sleep Apnea in Systolic Heart Failure) study revealed that ASV produced no significant improvement on the primary endpoint [all-cause mortality, lifesaving cardiovascular intervention (cardiac transplantation, implantation of a ventricular assist device, resuscitation after sudden cardiac arrest, or appropriate lifesaving shock), or unplanned hospitalization for worsening heart failure] [49]. In the patient population with LVEF < 45%, an increase in cardiovascular mortality was noted (10.0% of the ASV group experienced a cardiovascular death each year compared to 7.5% of the control group, representing a statistically significant 33.5% relative increased risk). This finding translated into a 2.5% annual absolute increase in cardiovascular mortality for those randomized to ASV therapy compared to the control group [49]. Hence, there is a moratorium on use of ASV in patients with an LVEF < 45% until further data is available.

There is little data available concerning the impact of implementing PAP therapy for SDB in CHF hospitalized patients. In a pilot study, patients with acute decompensated heart failure and moderate to severe OSA were randomly assigned to standard care versus standard with additional auto titrating bi-level PAP therapy [50]. The group receiving PAP therapy had an absolute 4.4% increase in LVEF while the control group had a 0.2% decrease. The impact of PAP on long-term outcomes was not assessed. However, PAP therapy has been shown to improve outcomes such as the need for intubation, ICU transfer, and mortality in patients admitted with acute pulmonary edema and hypoxemia [19, 51–53]. While none of the subjects in these studies had a confirmed diagnosis of SDB, based on its high prevalence, it is reasonable to infer that some of the salutary effects of PAP therapy may be due to its impact on underlying unrecognized SDB [51]. Use of PAP therapy in unselected non-surgical hospitalized SDB patients has not been observed to improve hospital length of stay [54–56].

SDB screening, evaluation, and treatment protocol in hospitalized CHF patients

In a protocol devised and instituted at Thomas Jefferson University, all patients admitted to the heart failure service were screened for SDB by a trained respiratory therapist using a validated simple clinical questionnaire, the STOP or STOP-BANG. Patients with known history of OSA and on therapy were excluded. If a patient screened positive for SDB (2/4 positive for STOP and 3/8 for STOP-BANG), the admitting team was informed of the high-risk status of the patient. If they determined that an in-house evaluation of the patient was necessary, the hospital pulmonary sleep medicine team performed a consult. They performed a comprehensive sleep evaluation in the context of the patient's admitting diagnosis, made both short-term and longterm recommendations, and determined when to perform HRPO (see Table 1).

Overnight pulse oximetry was performed in relatively stable conditions, either on room air or a maximum of 2 l per minute of nasal oxygen. A board-certified sleep specialist reviewed the overnight pulse oximetry tracing and data the subsequent day. An ODI of $\geq 5/h$ was considered presumptive of SDB, and an ODI of $\geq 15/h$ with major oxygen desaturations (defined as saturations $< 89\%$ for more than 5 min cumulative) was considered high risk and a potential candidate for initiation of therapy in the hospital (Fig. 1).

Since there is no currently published algorithm or guidelines for PAP intervention in the treatment of hospitalized CHF patients with SDB, we propose the following criteria, developed from our experience at a tertiary care academic center (Thomas Jefferson University, Philadelphia) [21, 34].

PAP therapy is recommended if

- HRPO or PST shows ODI/AHI $> 15/h$
- There is ODI $\geq 5/h$ and oxygen desaturations $< 89\%$ for more than 5 min over the entire study (see Fig. 2)

Initiating PAP therapy

Patient hospitalization presents a unique opportunity for education and acclimation to PAP therapy given the close monitoring, access to the healthcare team, and lack of additional adherence barriers. A dedicated respiratory therapist team that is well versed with SDB and the various PAP therapy options can be a huge asset in delivering care to hospitalized patients. At Thomas Jefferson University, patients are educated about the cardiovascular implications of untreated SDB, provided HRPO results, and given the opportunity to discuss the potential impact on their current conditions with the sleep specialist. Patients are then given an acclimation trial, which typically includes discussions concerning the appropriate interface and pressure, and a trial of masks to assess comfort. Once patients are comfortable with their choice, the PAP device pressure is initiated at 5 cm of H₂O pressure and gradually increased to maximum of 9 cm of H₂O pressure during the acclimation trial. The interface is tested for leaks. After a successful acclimation trial, the patient is scheduled for nightly PAP therapy.

We prefer CPAP for patients with heart failure or pulmonary edema, and we avoid pressures of more than 10 cm of H₂O since unexpected drops in blood pressure can occur in dehydrated CHF patients [57]. A repeat HRPO on the initial setting is sometimes ordered if a need for supplemental oxygen is suspected. CPAP set at a fixed pressure is interrogated the next morning for any residual events (AHI), and pressures are adjusted based on the residual AHI and patients' comfort. If central apnea is suspected (CPAP shows worsening apneas/hypopneas), nightly PAP therapy is discontinued and a clinical decision is initiated to consider oxygen supplementation, close cardio-pulmonary monitoring, and aggressive heart failure management. Medical management of heart failure has been shown to improve central apnea in prior studies [31, 58, 59]. The role of ASV in the inpatient setting is evolving but would be reasonable to consider in select patients. Patients suspected and treated for SDB in the hospital are discharged with a strong recommendation to undergo an outpatient confirmatory sleep study and given an appointment at an accredited sleep disorders center for follow-up (Fig. 1).

Based on our data, the 3-month PAP adherence among CHF patients diagnosed in the hospital setting was 52%, and compliance at 3 months was associated with better prognosis at the 3-year follow-up [60]. We believe that the inpatient education and acclimation process are substantial contributors to this outcome. Earlier data in CHF patients with SDB also found an association between good PAP adherence and a reduction in 6-month readmission [43].

Conclusion

Sleep-disordered breathing is a highly prevalent condition in patients with CHF and it has a major impact on clinical outcomes. The condition remains underdiagnosed and undertreated. The ideal treatment of SDB (especially CSA) in patients with CHF remains controversial. In patients with heart failure and obstructive sleep apnea, CPAP therapy may improve cardiac function, blood pressure, exercise capacity, and quality of life [17, 61–66]. However, large randomized controlled trials assessing hard outcomes such as mortality are lacking. The present body of evidence is limited because most studies evaluated the impact of SDB therapy on surrogate outcomes (e.g., blood pressure, catecholamine levels, cardiac function) and did not measure clinically important hard outcomes (e.g., quality of life, hospitalizations, mortality, functional class).

When patients are hospitalized, there is an opportunity to screen and recognize this condition. This has been made easier by reliable and cost-effective screening strategies. While preliminary data suggest that early intervention of SDB in hospitalized CHF patients can improve outcomes and mitigate readmissions, no randomized controlled trials yet demonstrate these findings conclusively. The data on the impact of PAP on OSA in CHF align in the direction of positive clinical benefit and physiological plausibility; however, optimal treatment of CSA in CHF patient management is far from clear.

Acknowledgments

Dr. Quan has served as a consultant for Jazz Pharmaceuticals.

Dr. Malhotra is PI on NIH RO1 HL085188, K24 HL132105, and T32 HL134632 and co-investigator on R21 HL121794, RO1 HL 119201, and RO1 HL081823. As an Officer of the American Thoracic Society, Dr. Malhotra has relinquished all outside personal income since 2012. ResMed, Inc. provided a philanthropic donation to the UC San Diego in support of a sleep center. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

Drs. Ankit and Dr. Oldenburg have no conflicts of interest or financial ties to disclose.

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Fig. 1.
Kaplan-Meier survival curves for patient's compliance with PAP therapy versus non-compliance

Fig. 2.

Algorithm for early diagnosis and intervention of SDB in hospitalized CHF patients

Table 1

Relative contra-indications fo overnight pulse-oximetry

High oxygen requirements (> 2 L/min)
Hemodynamically unstable
Severe insomnia or psychosis
Severe restless leg symptoms
Anticipating frequent medications (i.e., nebulizers, pain medications)
Frequent tests (i.e., lab draws, trips for imaging)