Sleep Medicine Reviews 35 (2017) 51–61

Contents lists available at ScienceDirect

Sleep Medicine Reviews

journal homepage: www.elsevier.com/locate/smrv

CLINICAL REVIEW

Ventricular assist devices and sleep-disordered breathing

Bindu Akkanti [a], Richard J. Castriotta [a, *], Pavani Sayana [b], Emmanuel Nunez [b], Indranee Rajapreyar [b], Sachin Kumar [b], Sriram Nathan [b], Ruckshanda Majid [a]

[a] Divisions of Pulmonary, Critical Care and Sleep Medicine, University of Texas Health Science Center at Houston, McGovern Medical School, Houston, TX, USA
[b] Center for Advanced Heart Failure, University of Texas Health Science Center at Houston, McGovern Medical School, Houston, TX, USA

ARTICLE INFO

Article history:
Received 19 November 2015
Received in revised form
16 August 2016
Accepted 17 August 2016
Available online 25 August 2016

Keywords:
Congestive heart failure
Ventricular assist device
Central sleep apnea
Obstructive sleep apnea
Complex sleep apnea
Sleep-disordered breathing

SUMMARY

Congestive heart failure is one of the leading causes of morbidity and mortality in the United States, and left ventricular assist devices have revolutionized treatment of end-stage heart failure. Given that sleep apnea results in significant morbidity in these patients with advanced heart failure, practicing sleep physicians need to have an understanding of left ventricular assist devices. In this review, we summarize what is known about ventricular assist devices as they relate to sleep medicine.

Introduction

Congestive heart failure (CHF) is one of the leading causes of morbidity and mortality in the United States [1]. Based on 2009 to 2012 data from the National health and nutrition examination survey, an estimated 5.7 million Americans ≥20 years of age have CHF (National Heart, Lung, and Blood Institute tabulation). There are 870,000 new CHF cases annually, and projections show that the prevalence of CHF will increase 46% from 2012 to 2030, resulting in >8 million people ≥18 years of age with CHF [2]. Survival after CHF diagnosis has improved over time, as shown by data from the Framingham heart study and the Olmsted County study [3,4]. However, the death rate remains high: about half of those diagnosed with CHF will die within five years [4,5]. With the increasing burden of CHF, an understanding of its pathophysiology as it relates to sleep—not only the way that sleep-disordered breathing (SDB) can affect the progression of cardiac dysfunction, but also how heart failure (HF) itself can influence the constellation of disorders during sleep—is increasingly relevant to the practicing sleep physician.

In the expanding arena of CHF management, beyond the medical mediations and interventional procedures, ventricular assist devices (VADs) have emerged to further support cardiac function in advanced HF, and these devices add an additional layer to the effects of cardiac function on SDB in HF. This review briefly looks at HF and sleep and then reviews the current array of VADs to understand their effect on ventricular function and mechanics and their plausible interaction on sleep disturbances.

Heart failure and sleep

SDB characterized by apneas (cessation of breathing) and hypopneas (decrease in the amplitude of breathing associated with an oxygen desaturation and/or an electroencephalogram arousal) has been well described in patients with HF [6–9]. These events can be related to either a central etiology (lack of respiratory effort) or obstructive etiology (presence of respiratory effort). Often, both categories of SDB coexist in the same patient, which is known as complex sleep apnea (CompSA) [10]. In one of the largest studies done on systolic CHF, SDB was present in 76% of patients [11]. In this study, 700 patients with CHF (New York Heart Association [NYHA] class ≥2; left ventricular ejection fraction [LVEF] ≤40%) were

* Corresponding author. Division of Pulmonary and Sleep Medicine, University of Texas Health Science Center at Houston, McGovern Medical School, 6431 Fannin, MSB 1.270, Houston, TX 77030, USA.
E-mail address: Richard.J.Castriotta@uth.tmc.edu (R.J. Castriotta).

http://dx.doi.org/10.1016/j.smrv.2016.08.002
1087-0792/

Abbreviations

AHI	apnea-hypopnea index
APAP	auto titrating positive airway pressure
ASV	adaptive servo-ventilation in heart failure
BiVAD	biventricular assist device
BMI	body mass index
BNP	brain natriuretic peptide
CAI	central apnea index
CHF	congestive heart failure
CompSA	complex sleep apnea
CPAP	continuous positive airway pressure
CSA	central sleep apnea
CSR	Cheyne-Stokes respiration
EF	ejection fraction
EPAP	expiratory positive airway pressure
ESS	Epworth sleepiness scale
HF	heart failure
LVAD	left ventricular assist device
LVEF	left ventricular ejection fraction
NYHA	New York Heart Association
OSA	obstructive sleep apnea
PAP	positive airway pressure
pCO_2	partial pressure of carbon dioxide
PSG	polysomnography
RVAD	right ventricular assist device
RVSP	right ventricular systolic pressure
SDB	sleep-disordered breathing
SERVE-HF	servo-ventilation in heart failure
TST	total sleep time
VAD	ventricular assist device

prospectively screened for SDB using polysomnography. Of those found to have SDB, 40% had central sleep apnea (CSA) and 36% had obstructive sleep apnea (OSA). These patients were being medically optimized with concomitant HF medication, including β-blockers (≥85%), angiotensin-converting enzyme inhibitors and/or angiotensin II type 1 receptor blockers (≥94%), diuretics (≥87%), and spironolactone (≥62%). Despite optimal HF medication, the prevalence of SDB and in particular CSA remained remarkably high. This prevalence and distribution have been reproduced in other studies [12–14].

The role of OSA in the pathophysiology of cardiovascular morbidity and mortality has been extensively studied. It has been found, for instance, that the increased sympathetic activity seen in patients with OSA has deleterious effects on the cardiovascular system. This effect is thought to be a consequence of the intermittent hypoxemia and re-oxygenation associated with each event, especially during apnea, when the inhibitory contribution of the pulmonary afferents on the sympathetic tone is eliminated [15–18]. The result is vasoconstriction, increases in heart rate, and heightened peripheral vascular resistance [19]. In addition, due to the repeated occlusion of the upper airway in the face of continued respiratory effort (similar to a Mueller maneuver), the intrathoracic pressures drop, often dramatically, causing an increase in the systolic transmural pressure and an increase in the left ventricular afterload. The result is a drop in the cardiac output, which over time can lead to the development of left ventricular systolic and diastolic dysfunction [20–23]. OSA is also a well-recognized independent risk factor for hypertension and coronary artery disease, which can lead to CHF [24,25]. Thus, OSA may exacerbate CHF through a variety of mechanisms.

Hunter–Cheyne–Stokes breathing or Cheyne–Stokes respiration (CSR) is a marker of poor outcome in patients with CHF, with higher mortality and shorter transplant-free survival [26–28]. The poorer outcomes may be due in part to the sympathetic activation resulting from the arousals and hypoxemia associated with recurrent apneas [29–31]. CSA in CHF is thought to be predominantly caused by the instability of the ventilatory control systems. Patients with CSA-CSR have increased peripheral and central chemoresponsiveness with concomitant facilitation of hyperventilation and hypocapnia [32–35]. In addition, the pulmonary venous congestion seen in CHF (the result of left ventricular volume overload) augments the CHF-associated chronic hyperventilation by stimulating the pulmonary vagal irritant receptors [36–38]. Patients with CSA-CSR in CHF also have an abnormal cerebrovascular reactivity to carbon dioxide and are more likely to develop an abnormal ventilatory overshoot in response to a greater degree of alkalosis than normal. This drives the arterial partial pressure of carbon dioxide (pCO_2) below the apneic threshold, causing a decrease in central respiratory drive and ultimately central apnea [39]. The exaggerated ventilatory response to carbon dioxide (i.e., increased controller gain) may be key to the development of CSA in CHF [40]. A low baseline pCO_2 may predispose to the development of secondary CompSA with the emergence of CSA in those with pre-existing OSA upon application of positive airway pressure (PAP) [41].

Heart failure and positive airway pressure

It remains unclear whether targeted treatment of CSA or OSA in the setting of CHF is of any benefit, be it medical management (beyond optimization of the CHF) or positive airway pressure (PAP) therapy. In a meta-analysis of randomized controlled trials comparing the effect of nocturnal continuous positive airway pressure (CPAP) therapy on LVEF in patients with stable systolic CHF and OSA, the pooled odds ratio for improvement in LVEF after CPAP therapy was 7.3 [42]. Only a few studies have examined the long-term mortality benefits when treating OSA with CPAP in ASV-treated subjects with CHF. In a prospective study involving 164 CHF patients (LVEF $\leq$ 45%) with a mean follow-up period of 2.9 ± 2.2 years and a maximum follow-up of 7.3 years, the death rate was significantly higher in the 37 untreated OSA patients than in patients with mild or no OSA (8.7 vs. 4.2 deaths per 100 patient-years, $p = 0.029$). None of the patients with OSA and treated with CPAP died, but patients whose OSA was treated by CPAP did not have a significantly different mortality rate than untreated OSA patients ($p = 0.070$) [43]. A subsequent study found that CPAP reduced the risk of death in CHF patients with OSA treated with CPAP, but only if they were adherent with 6 h/night usage [44]. With regard to the use of CPAP in CSA, the results of the Canadian continuous positive airway pressure for patients with central sleep apnea and heart failure trial (CANPAP) are most important. When investigating treatment of CSA with CPAP in this trial, Bradley et al. found an early increase in mortality in the CPAP-treated group—related to those with inadequate control of their CSA or nonresponse of CSA to CPAP [45]. Later survival was better for CPAP-treated subjects whose CSA resolved with CPAP, but worse in those treated with CPAP whose CSA did not resolve. In a *post hoc* analysis, the patients whose CSA was suppressed below 15 events/hour with CPAP treatment experienced a greater increase in LVEF and had better transplant-free survival at three months compared