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The effect of adaptive servo ventilation (ASV) on objective and subjective outcomes in Cheyne-Stokes respiration (CSR) with central sleep apnea (CSA) in heart failure (HF): A systematic review

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ABSTRACT

To summarize the current evidence for adaptive servo ventilation (ASV) in Cheyne-Stokes respiration (CSR) with central sleep apnea (CSA) in heart failure (HF) and advance a research agenda and clinical considerations for ASV-treated CSR-CSA in HF. CSR-CSA in HF is associated with higher overall mortality, worse outcomes and lower quality of life (QOL) than HF without CSR-CSA. Five databases were searched using key words ($n = 234$). Randomized controlled trials assessed objective sleep quality, cardiac, and self-reported outcomes in adults ($\geq$18 years) with HF ($n = 10$). ASV has a beneficial effect on the reduction of central sleep apnea in adult patients with CSR-CSA in HF, but it is not be superior to CPAP, bilevel PPV, or supplemental oxygen in terms of sleep quality defined by polysomnography, cardiovascular outcomes, subjective daytime sleepiness, and quality of life. ASV is not recommended for CSR-CSA in HF. It is important to continue to refer HF patients for sleep evaluation to clearly discern OSA from CSR-CSA. Symptom management research, inclusive of objective and subjective outcomes, in CSR-CSA in HF adults is needed.

Introduction

Heart failure (HF) is considered as a major public health problem because of steadily increasing prevalence, high morbidity, early mortality, and significant health care and quality of life costs.[1] In spite of advancements in the medical treatment of HF, morbidity and mortality among adults with HF continues to escalate and the overall prevalence of HF is increasing in the U.S.[2–4] HF is commonly accompanied by sleep-related breathing disorders (SRBD); it is estimated that at least 45% of adults who have a LVEF of less than 45% also have SRBD.[5]

SRBD are characterized by abnormal respiratory patterns during sleep, including obstructive sleep apnea (OSA) and two centrally-mediated disorders of respiratory control, central sleep apnea (CSA) and Cheyne-Stokes respiration (CSR).[6] Approximately 25–50% of patients with HF have CSR-CSA,[7,8] a cyclic breathing pattern characterized by a crescendo-decrescendo pattern of tidal volume interposed with periods of 20–30 s of hyperventilation followed by 10–40 s hypopneas or apneas.[9] The presence of CSR-CSA in HF indicates respiratory instability, observed as hyperventilation that results from pulmonary vagal irritant receptor stimulation due to pulmonary congestion in combination with prolonged circulation time and enhanced chemoreceptor sensitivity.[10,11] The physiologic pathway of CSR-CSA in HF is an adverse prognostic indicator.[12]

The detrimental sequelae of CSR-CSA in HF include sympathetic over-activity, hemodynamic impairment, and poor event-free survival.[13–16] CSR-CSA increases the risk of sudden cardiac death in adults with HF.[13,17] Previous studies show that mortality or cardiac transplantation is positively correlated with CSR-CSA, the apnea-hypopnea index (AHI), arousal index (ArI), and the amount of stage N1 and N2 sleep and adversely related to total sleep time.[18] When compared to HF without CSR-CSA, HF with CSR-CSA is also associated with lower LVEF, higher brain natriuretic peptide (BNP), higher urinary and plasma norepinephrine concentration, and increased sympathetic activation.[19–22]

Although excessive daytime sleepiness and decrements in health-related quality of life (HRQoL) may be consequences of SRBD in HF (Fig. 1), evidence to data about these relationships is inconsistent. Several studies reported that subjective daytime sleepiness had no relationship with CSR-CSA,[23,24] whereas in other studies CSR-CSA was related to daytime sleepiness and poorer HRQoL among patients with HF.[25,26] Although treatment trials are often aimed at addressing non-inferiority or superiority in terms of

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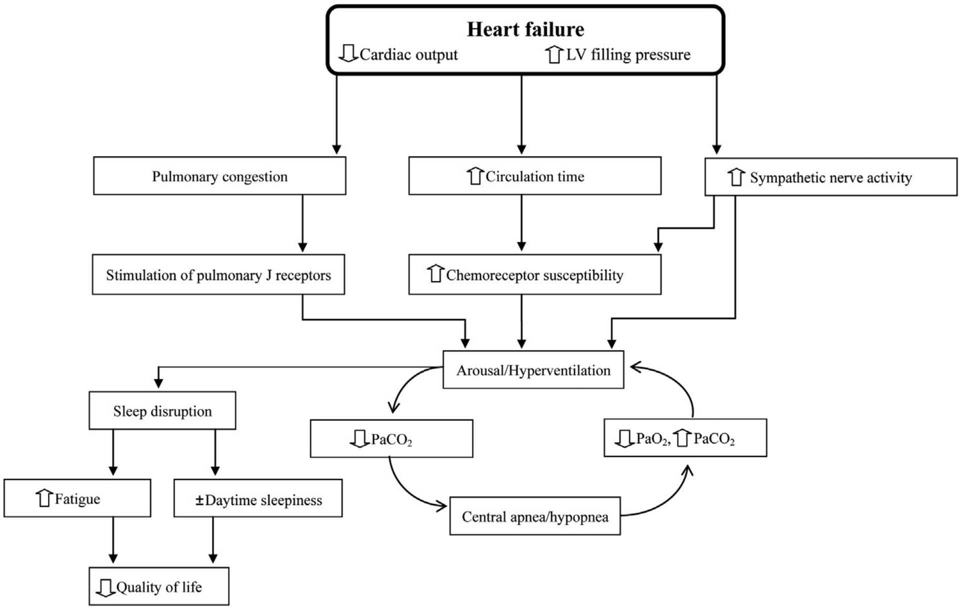

Fig. 1. Pathophysiology of CSR-CSA with HF.

biophysiologic responses, it is also important to address patient-centered outcomes of treating CSR-CSA in HF (Table 1).

Treatment of CSR-CSA in HF

The treatment options for CSR-CSA in HF include: 1) positive airway pressure such as adaptive servo ventilation (ASV), bilevel positive pressure ventilation (bilevel PPV), and continuous positive airway pressure (CPAP); 2) oxygen therapy; and 3) and respiratory stimulant therapy such as 3% CO_2 inhalation and theophylline.[9,27] ASV is a novel therapy that provides expiratory positive airway pressure (EPAP) and inspiratory positive airway pressure (IPAP), that is servo-controlled based on the detection of CSR-CSA. ASV adjusts the IPAP in response to the patient's respiratory effort and EPAP eliminates upper airway collapse during the hyperventilation phase of CSR-CSA.[18] Bilevel PPV provides assisted ventilation with a fixed lower level of EPAP and a higher level of IPAP during spontaneous breathing and a preset respiratory rate, or backup respiratory rate, can be set for apneic phases.[28] CPAP provides a single level of air pressure above atmospheric pressure.[29]

Table 1
Abbreviation list.

Abbreviation	Description
ASV	Adaptive servo ventilation
CPAP	Continuous positive airway pressure
Bilevel PPV	Bilevel positive pressure ventilation
SRBD	Sleep-related breathing disorders
CSA	Central sleep apnea
CSR	Cheyne-Stokes respiration
OSA	Obstructive sleep apnea
AHI	Apnea hyponea index
CAI	Central apnea index
PBI	Periodic breathing Index
CSAI	Cheyne-Stokes apnea index
CSRI	Cheyne-Stokes respiration index
ODI	Oxygen desaturation index
RDI	Respiratory disturbance index
ArI	Arousal index
TST	Total sleep time
SWS	Slow wave sleep
REM sleep	Rapid eye movement sleep
NREM sleep	Non-rapid eye movement sleep
HFrEF	Heart failure with reduced ejection fraction
LVEF	Left ventricular ejection fraction
NYHA	New York heart association functional classification
DCMP	Non-ischemic dilated cardiomyopathy
ICMP	Ischemic dilated cardiomyopathy
BNP	Brain natriuretic peptide
HRQoL	Health-related quality of life

Evidence suggests that ASV treatment of CSR-CSA is efficacious for eliminating CSR-CSA in HF.[30,31] Previously published systematic reviews and meta-analyses of ASV for CSR-CSA in HF have predominantly included cardiac function (e.g., LVEF) and objectively measured CSR-CSA (e.g., measured by apnea-hypopnea index [AHI]); yet, subjective daytime sleepiness and HRQoL of ASV in CSR-CSA in HF have been less well-described in prior reviews and meta-analyses. Previous systematic reviews of ASV in HF have not specifically focused on CSR-CSA, but have focused more broadly on measures of the apnea-hypopnea index rather than more specific measures of central apnea (e.g., the central apnea index) and CSR.[32] Therefore, a systematic evaluation of studies that have examined specific measures of CSR-CSA and subjective outcomes of ASV treatment of CSR-CSA in HF is necessary to better define opportunities for future inquiries, and develop clinical recommendations for the management of CSR-CSA in HF. The objectives of this study are to examine the effects of ASV on (1) subjective outcomes, including daytime sleepiness and HRQoL, and (2) sleep-related breathing disorder outcomes, cardiovascular function, polysomnography defined sleep quality outcomes, and event-free survival among adults who have chronic HF and CSR-CSA.

Methods

Search strategy

The search strategy included publicly-available, online databases which are repositories of scientific publications that address