Adaptive Servoventilation in Central Sleep Apnea

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KEYWORDS

• Adaptive servoventilation • Cheyne-Stokes respiration • Central sleep apnea
• Positive airway pressure

KEY POINTS

- There is increasing evidence that central sleep apnea and Cheyne-Stokes respiration are associated with a poor prognosis in patients with heart failure.
- Continuous positive airway pressure (CPAP), bilevel positive airway pressure (BPAP) and oxygen might reduce, but not normalize central sleep apnea/Cheyne-Stokes respiration CSA/CSR in heart failure.
- Optimal suppression of respiratory disturbances is crucial to improve outcome of patients with cardiovascular diseases.
- Adaptive servoventilation counterbalances ventilatory over- and undershoot and is superior to other PAP treatments or oxygen.
- Open questions include the influence of ASV on survival of heart failure patients and its use in other phenotypes of CSA.

INTRODUCTION

Since the description of effective treatment of the obstructive sleep apnea syndrome (OSAS) with continuous positive airway pressure (CPAP),[1] the awareness of sleep-related breathing disorders (SRBDs) has risen rapidly in the medical community. An increasing number of patients with severe underlying comorbidities, including cardiovascular diseases, renal failure, and neurologic disorders, are presenting to sleep laboratories. This trend has led to growing recognition obstructive phenotypes other than breathing disturbances during sleep. Obstructive sleep apnea (OSA) has to be separated from hypocapnic and hypercapnic central breathing disturbances. Whereas hypocapnic disturbances are characterized by hyperventilation resulting in a diminished arterial pressure of carbon dioxide ($Paco_2$), the respiratory drive is reduced in hypercapnia. Idiopathic central sleep apnea (ICSA) and Cheyne-Stokes respiration (CSR) are typical representations of hypocapnic central sleep apnea (CSA). Opioid-induced CSA and obesity-related hypoventilation represent hypercapnic central disturbances.[2,3]

As arousals, hypoxemia, and breathing effort can increase sympathoadrenal activity, SRBDs impair heart function. The left ventricular transmural pressure (ie, the afterload) is increased.[4,5] In addition, heart diseases induce central breathing disturbances. CSR is a marker of poor prognosis in patients with heart failure (HF).[6] On the other hand, optimal treatment of CSR significantly improves the survival of such patients.[7] Based on these findings, it is reasonable to screen HF patients systematically for SRBD, even if they do not suffer from daytime sleepiness or witnessed apneas. Because of the unfavorable consequences, specific treatment of CSR should be

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applied as soon as possible if breathing disorders still remain after optimizing cardiac medication and interventional therapy.[8]

Unfortunately, several therapeutic approaches have failed to sufficiently reduce CSR and other central breathing disturbances. There are conflicting results on the supplementation of oxygen during the night and on treatment with the carbonic anhydrase inhibitor acetazolamide.[9–13] Oxygen may reduce the apnea-hypopnea index (AHI; defined as the number of apneas and hypopneas per hour of sleep) by about 14 to 18 per hour in absolute figures in CSR.[14] However, this means only a 50% reduction in comparison with baseline, which is similar to the effect of CPAP. Oxygen improved the left ventricular ejection fraction (LVEF) in 1 of 3 studies.[14] Based on these limited data, the American Academy of Sleep Medicine has concluded that a trial may be reasonable.[14]

CPAP has demonstrated improvement in LVEF and survival in HF patients who suffer from CSR.[5,15] Although CPAP reduces the AHI by less than 50% according to several short-term and long-term studies,[16,17] it improves the increased work of breathing, the ventilation-perfusion relationship in the lungs, the oxygen demand and oxygen supply, and the left ventricular afterload and the cardiac index in HF patients.[5,15,18–28] Despite these encouraging findings, the CANPAP trial failed to confirm a benefit in survival under CPAP treatment.[16] However, a post hoc analysis of the study showed an improved survival in those patients whose SRBD were sufficiently reduced when compared with those with insufficient change. There are very limited data on the treatment of CSR using bilevel positive airway pressure (BPAP). Because of the small body of evidence BPAP should only be considered in individual cases.[14]

The most important conclusion from these data is that the prognosis of CSR patients essentially depends on the optimal suppression of SRBDs.[7] CPAP and BPAP mechanically influence preload and afterload of the heart, but this does not suffice. The fixed pressure support does not allow for counterbalancing the waxing and waning of the flow amplitude. Therefore, an approach more precisely addressing the complex pathophysiology would seem to be crucial in overcoming CSR and CSA and achieving optimal outcome.

PATHOPHYSIOLOGIC BACKGROUND

CSR is typically characterized by an alternation of apneas and/or hypopneas and prolonged hyperventilation in a crescendo-decrescendo pattern of the tidal volume.[2] Respiratory drive and consecutively breathing effort are reduced during central apneas. However, the hyperpneic periods are longer, and the increase and decrease of the ventilation less abrupt, in CSR in comparison with other forms of CSA. Thus, elevation and diminishment of ventilatory drive and consecutively ventilatory effort coexist in CSR. As a result, CSR is characterized by a net hyperventilation with reduced $Paco_2$. The pathophysiology includes several mosaic pieces leading to a vicious circle:

- Fluid overload in the lungs of HF patients stimulates vagal afferents, which increase breathing frequency.
- The reduction of cardiac output slows the blood flow to the chemoreceptors, leading to delayed reactions to changes of the CO_2.
- Hypersensitivity of peripheral and central chemoreceptors leads to overshooting or undershooting of the ventilation, and the hypoxic and hypercapnic ventilatory response is elevated.

As a result, respiration becomes unstable and the typical pattern of waxing and waning of the flow amplitude appears.[8]

ADAPTIVE SERVOVENTILATION

Devices and Algorithms

Adaptive servoventilation (ASV) has been developed to counterbalance the continuous shift between hyperventilation and hypoventilation and, therefore, to more effectively improve CSA/CSR. Moreover, ASV may also normalize the elevated apneic threshold that substantially contributes to the pathophysiology of CSR and CSA.

Three devices have been released that analyze the patient's breathing pattern (flow or minute ventilation) in a moving average throughout the night and modulate the pressure support anticyclically. If a predefined limit of the target parameter is not reached, additional pressure support is supplied. If the limit is overcome, pressure support is reduced. The algorithms are called Adaptive Servo-Ventilation (Resmed, Bella Vista, Australia), Auto Servo-Ventilation (Philips Respironics, Murrysville, PA, USA), and Anticyclic Modulated Ventilation (Weinmann, Hamburg, Germany). However, the term ASV is often used to generally describe the principle of treatment.

The devices commonly apply 2 pressure levels. The expiratory positive airway pressure (EPAP) serves to sustain upper airway patency. The difference between the actual inspiratory positive airway pressure (IPAP) and the expiratory pressure defines the pressure support, which is essential to overcome central hypopneas and CSR when required (**Fig. 1**).[8] Whereas BPAP devices apply