COMMENTARY

Role of Adaptive Servo-ventilation in Sleep-disordered Breathing: An Updated Evidence

Satish Kumar Kumawat[1], Pranav Ish[2], Rohit Kumar[3], Nitesh Gupta[4], Manu Madan[5]

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Dear Editor,

Sleep-disordered breathing (SDB) is an umbrella term including many disorders. However, the majority fall into one of three categories: Obstructive sleep apnea (OSA), central sleep apnea (CSA), and sleep-related hypoventilation.[1] Positive airway pressure (PAP) is the therapy of choice for patients who are suffering from moderate to severe OSA and is also prescribed to those patients with mild OSA who have symptoms or associated comorbidities. Although there are multiple PAP devices available, continuous PAP i.e., CPAP remains the treatment of choice for most patients of OSA. Other advanced modes including bilevel pap (BPAP), adaptive servo-ventilation (ASV), and volume assured modes have certain features that may help in certain patient profiles.

A large study found that 50–75% of patients with heart failure and reduced ejection fraction (HFrEF) have SDB.[2] This is a high prevalence and helps conclude that heart failure patients are more likely than the general population to experience OSA. Up to forty percent of these HFrEF cases have CSA, which can present as Cheyne-Stokes breathing (CSB).[3] A study using a prospective, cross-sectional, case-control design revealed that patients with HFpEF have a higher incidence of SDB and that the degree of diastolic dysfunction is correlated with the severity of AHI.[4] The severity and prevalence of OSA are exacerbated by heart failure, and OSA influences the development of chronic HF through a variety of mechanisms. A bidirectional relationship exists between heart failure and sleep apnea and it has been acknowledged that CSA/CSR is more of an effect of HF than a cause of it.[5]

Adaptive servo-ventilation is a noninvasive positive pressure ventilation tool that delivers servo-controlled inspiratory pressure support on top of expiratory PAP. Through a countercyclical compensatory mechanism (counterbalance proportional system), the ASV device facilitates breathing. By raising inspiratory pressure support and/or respiratory rate in response to a decrease in ventilation, the ASV mode may offer higher respiratory support (i.e., minute ventilation or peak flow). This mode reduces support to a minimum when ventilation stabilizes to a more regular breathing pattern. The device automatically reduces the pressure support given when it senses a stronger breath.[6] When used properly for at least four hours at night, ASV can help patients with congestive heart failure breathe easier, suppress sympathetic nervous system activation, and improve pulmonary/systemic congestion by lowering cardiac preload and afterload.[7] The evidence for ASV utility is still scarce.

The Canadian continuous PAP for patients with central sleep apnea and heart failure (CANPAP) trial was an open-label, randomized study that randomly assigned 258 patients who had CSA and HFrEF to receive CPAP (128 patients) or no CPAP (130 patients), with follow-up occurring over an average of two years. This study investigated the idea that patients with CANPAP who receive continuous positive airway pressure (CPAP) would have a higher survival rate without requiring a heart transplant. However, survival was unaffected by CPAP, despite its ability to reduce CSA, enhance nocturnal oxygenation, raise the ejection fraction, decrease norepinephrine levels, and augment walking distance in six minutes. This trial did not support the routine use of CPAP to extend life in patients with central sleep apnea and heart failure.[8]

In the SERVE-HF trial, 1,325 patients with AHI of 15 or more events (occurrences of apnea or hypopnea) per hour, a predominance of central events, and a left ventricular ejection fraction of 45% or less randomly assigned to receive either guideline-based medical treatment plus ASV, or guideline-based medical treatment alone (control). A primary endpoint was defined as the first event of death from any cause, an unplanned hospitalization due to worsening heart failure, or a life-saving cardiovascular intervention such as a cardiac transplant, ventricular assist device implantation, resuscitation following sudden cardiac arrest, or appropriate life-saving shock. This trial concluded that for patients who had HFrEF and predominantly CSA, ASV increased all-cause and cardiovascular mortality but had no discernible effect on the primary endpoint.[9] Many plausible explanations for increased mortality were given, including patients having poor cardiac reserve in the ASV group, increased cardiovascular acute events, low-pressure settings of ASV, and even

[1–5]Department of Pulmonary, Critical Care and Sleep Medicine, Vardhaman Mahavir Medical College & Safdarjung Hospital, New Delhi, India

Corresponding Author: Pranav Ish, Department of Pulmonary, Critical Care and Sleep Medicine, Vardhaman Mahavir Medical College & Safdarjung Hospital, New Delhi, India, Phone: +91 9958356000, e-mail: pranavish2512@gmail.com

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poor adherence. The SERVE-HF trial has several drawbacks, including an excessive number of treatment arm switches, surprisingly low adherence, missing LVEF data, and uneven antiarrhythmic medication use. However, after this trial, it was recommended not to use ASV in patients with predominant CSA and LVEF <45%.

ADVENT HF trial has been a long wait for providing clarity on the utility of ASV. An alternative ASV device was used in this trial, which enables automatic expiratory pressure adaptation to the patient's current needs. It also made it possible to apply zero-pressure support. By doing this, needless mechanical ventilation was avoided. However, due to poor recruitment and the COVID-19 pandemic, the results were finally published in 2024. Patients with HFrEF (left ventricular ejection fraction ≤45%) who were stabilized on optimal medical therapy and co-occurring SDB [predominantly OSA with an Epworth Sleepiness Scale score of 10 or lower or predominantly CSA, apnea-hypopnea index (AHI) ≥15 events/h of sleep] were recruited for this multicenter, multinational, parallel-group, open-label, phase 3 randomized controlled trial random assignments were used to place participants in either the standard optimal treatment without ASV or the standard optimal treatment plus ASV (1:1). The cumulative incidence of the composite of all-cause death, first hospital admission for a cardiovascular reason, new-onset atrial fibrillation or flutter, and administration of an appropriate cardioverter-defibrillator shock served as the primary endpoint. The secondary endpoint was mortality from all causes. This study interpreted that while safely eliminating sleep-disordered breathing, ASV did not affect mortality or the primary composite outcome in patients with heart failure, reduced ejection fraction, or SDB. This trial demonstrated several distinct advantages such as having patients from nine different nations across four continents, covering the whole range of SDB, and analyzing the results independently in each unique subgroup by adding patients who had either mostly OSA or predominantly CSA, using a more recent ASV device, high data quality by centrally scored polysomnograms, core laboratory analysis, and interpretation. The study found no evidence of ASV harm, in contrast to SERVE-HF, however, failed to achieve the predetermined level of power to identify meaningful variations in the main endpoint and overall mortality.[10]

To conclude, the evidence to date is poor regarding the role of ASV in sleep-breathing disorders despite its physiological and theoretical benefits.

Orcid

Pranav Ish https://orcid.org/0000-0003-1701-4970
Rohit Kumar https://orcid.org/0000-0001-6398-7840
Nitesh Gupta https://orcid.org/0000-0002-5842-5584
Manu Madan https://orcid.org/0000-0001-9245-4568

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