OPINION

Approach to diagnosing and treating central sleep apnea in heart failure

Emma Gao

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ABSTRACT

Central Sleep Apnoea (CSA) with Cheyne-Stokes respiration is reported to be more common in people with Heart Failure (HF). The creation of servo-ventilation was intended to alleviate CSA and enhance these patients' Quality Of Life (QoL). In order to test this notion in patients with HF and decreased ejection fraction, a sizable randomised clinical investigation known as SERVE-HF was carried out (HFrEF). According to the trial's findings, assisted breathing in the CSA treatment did not appear to have any positive effects on these patients. More unexpectedly, there was a rise in cardiovascular or all-cause mortality. Due to modifications in the guidelines, this has caused significant changes in clinical practise, with a fall in the frequency of servo-ventilation prescriptions across Europe, including Portugal.

Key Words: *Central sleep apneay; Pleural disease; Interventional pulmonology; Prostate cancer*

INTRODUCTION

Chronic Heart Failure and Central Sleep Apnoea (CSA) are co-morbid conditions (CHF). A ventilatory support technique for Cheyne-Stokes Respiration (CSR) in heart failure is called Servo-Ventilation (SV) (HF). In a sizable randomised experiment called SERVE-HF, the effects of servo-ventilation were examined in patients with HF with decreased Ejection Fraction (HFrEF) and CSA. The results showed higher all cause and cardiovascular mortality, despite analysis of the pre-determined primary endpoints time to first occurrence of death from any cause, life-saving cardiovascular intervention, or unexpected hospital admission due to exacerbation of HF being neutral. 3 These findings cannot be applied to HFrEF in patients with other types of sleep breathing disorders, such as Obstructive Sleep Apnea (OSA). In order to better understand its criteria, screening procedures, and if and how to treat Sleep Disordered Breathing (SDB) in patients with Heart Failure (HF), additional study is required. The SERVE-HF trial revealed poor adherence, methodological flaws, and statistical evidence gaps. The SERVE-HF trial's methodological flaws, including study design, patient selection, data collecting and analysis, treatment adherence, and group crossovers—which haven't been covered in the trial—were all examined in an engaging commentary, which presented a number of serious concerns. In patients with HF with a Left Ventricular Ejection Fraction (LVEF) of 45% who were being treated for predominant CSA, the results of a multistate modelling investigation revealed that SV was linked to an elevated risk of cardiovascular death. The risk of cardiovascular death was discovered to be significantly higher in patients with LVEF below 30% and in individuals who had never been admitted to the hospital before, suggesting occurrences of sudden death. Results from two real-world investigations, however, revealed that the majority of patients receiving SV do not belong to the patient population at risk, in which SV is contraindicated. Additionally, it has recently been demonstrated that the elevated cardiovascular mortality noted in the SERVE-HF trial may not be connected to the progression of HF. The present practise of CSA treatment in HF is described by a Task Force of the European Respiratory Society (ERS) addressing existing diagnostic and therapeutic standards. A prior study that compared the impact of SV with nasal oxygen and CPAP during polysomnography provided support for some of the claims. With SV, but not with oxygen or CPAP, the results demonstrated significant increases in slow-wave and Rapid Eye Movement (REM) sleep. The Apnoea-Hypopnea Index (AHI) was significantly decreased in individuals with cardiac disease and retained left ventricular ejection fraction (pEF) who received ASV for the treatment of CSA. With the publication of the findings from new research, members of the ERS task group discontinued prescribing SV to treat CSA in patients based on the knowledge available at the time. New clinical studies

Editorial Office, Journal of Pulmonology, United Kingdom

Correspondence: Emma Gao, Editorial office, Journal of Pulmonology, United Kingdom, e-mail id: pulmonol@escientificjournals.com

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have been completed or are being conducted to further comprehend the SERVE-HF trial's true significance. In hospitalized HF patients with moderate-to-severe sleep apnea, the CAT-HF trial sought to determine whether Minute Ventilation (MV) ASV improved cardiovascular outcomes. Adding SV to Optimum Medical Therapy (OMT) in these patients did not enhance cardiovascular outcomes at 6 months. Despite its limitations, this study was able to draw the conclusion that significant reverse Left Ventricular (LV) remodeling was seen among HFrEF patients with SDB, regardless of treatment allocation. These limitations included the inability to detect safety signals and identify differential SV effects in HF patients with AF. Significant decreases in left atrial volume among HFrEF and HFpEF patients receiving SV point to a potential benefit for improving diastolic function and call for more research. A proof-of-concept study showed that using SV in the treatment of sleep apnea reduces the burden of atrial fibrillation compared to using OMT alone, without increasing the number of Ventricular Tachycardia/Ventricular Fibrillation (VT/VF) events. But more studies should be done to test this theory. The ADVENT-HF (NCT01128816) is an open-label, multicenter, randomized research that compares routine medical therapy for HFrEF with and without the addition of SV in patients with HFrEF and SDB in both non-sleepy OSA and CSA. To discuss the role of adaptive servo-ventilation as a therapeutic strategy for treating central sleep apnea in heart failure, a Portuguese Task Force of nine pulmonologists and cardiologists with expertise in servo-ventilation in patients with heart failure met twice. The Task Force's conclusions were accepted based on current clinical recommendations and relevant academic articles. As a result of the SERVE-HF trial results, there are currently two main issues with the prescription of ASV. First, doctors are reluctant to prescribe it because of safety concerns. Second, the Portuguese National Health Authority immediately released a document advising the withdrawal of SV from patients who share the SERVE-HF population's characteristics and not prescribing it to new patients. These two explanations help to explain why prescription levels of SV are still considerably below the prescribed levels even if they have been slowly rising in recent years. Since there are various types of SV, it is essential to be able to analyze the Cheyne-Stokes curve and determine in advance which form of SV is best for each patient. One of the challenges in making this determination is the value of the minimum support pressure of the devices. Patients who hyperventilate experience a drop in CO_2 levels, which causes a corresponding drop in HCO_3 to keep the pH stable. Hypokalaemia, which is linked to this alkalosis and may cause arrhythmia and even cardiac arrest, is also present. Because any pressure above zero may worsen the already present hypocapnia and lead to cardiac changes, the support pressure should be zero when the patient is in a phase of hyperventilation. On the other hand, the maximum scheduled pressure ought to be applied when the patient is apneic. In fact, it has been proposed that one of the factors that may have contributed to the higher mortality seen is the fact that the ASV device employed in SERVE-HF was unable to drop the minimum support pressure below H_2O. This issue has subsequently been resolved, and this model of ASV is no longer in use. Although there has been an improvement in prescriptions overall, some people who may benefit from SV still go untreated. The definition of the treatment algorithm being unclear is one of the key causes. This may be due to the inadequate level of resources available, which impedes SV treatment and, as a result, diagnosis. In an effort to develop a diagnostic and therapeutic strategy for the management of CSA in patients with HF, the authors initially concurred that every patient is a unique case that requires constant individual assessment. In fact, the most recent SV guidelines specify that the doctor must make the final decision for any given course of treatment. After taking these factors into account, a diagnosis and treatment algorithm was created and the various therapy choices were presented. Referrals of patients with stabilised and under control HF serve as the beginning point. If a level III sleep study was used to make the diagnosis of central sleep apnea, it is essential to confirm it as quickly as feasible with a level I or II PSG. Although PSG is regarded as the gold standard, it is crucial to note that it is not always simple to accomplish due to practical limitations, and results can take a very long time to obtain. If this is the situation, CPAP may be utilized while waiting for PSG. An arterial blood gas analysis, Brain Natriuretic Peptide (BNP), ECG, and echocardiogram with LVEF assessment are required as additional diagnostic tests. A patient review by the Cardiology Department is required if the results show an LVEF of less than 45%. In this situation, fresh echocardiography under stable circumstances, myocardial scintigraphy, or cardiac magnetic resonance should be done in some cases, and the kind of heart failure should be identified as ischemic or non-ischemic. ASV is not advised if NYHA classes are found; instead, medical care should be optimized, with CPAP as a potential option. The guidelines are listed below in the event that the patient is enrolled in NYHA classes. A full-night PSG titration or a daytime ventilatory adaption should be used for the titration. We advise using a modified CANPAP study protocol when positive pressure titration is not attainable within a few weeks and if the patient may suffer injury as a result of the continued sleep apneas. In this instance, a low-pressure fixed CPAP is used, and the pressure is gradually increased up to a maximum of H_2O. However, due to hemodynamic changes, pressures more than 3 cm H_2O should only be taken into consideration individually. According to LVEF, alternative measures must be taken into account if CPAP is ineffective. A split-night study is not advised due to the short titration period. It is advised to use ASV with an auto-EPAP pressure set to the value that resolved the obstructive events. The respiration rate needs to be automatic or less than that of rest. Zero should be the minimum and water should be the greatest support pressure. It is significant to note that, depending on the patient's respiratory cycle period, one must wait 10 minutes–20 minutes before increasing the EPAP pressure while titrating EPAP manually. CPAP is advised, whether with or without oxygen. In patients without CSR who sign informed permission and with physician agreement, as done in multiple studies, ASV can be a possibility, examined on a case-by-case basis. Some Task Force participants advise having the neighborhood ethical committee accept these situations as well. If no consent is given, CPAP must be kept up and pressures must be adjusted to a maximum H_2O. Depending on the circumstance, higher pressures may be taken into account. If appropriate trials of the advised therapy are unsuccessful, the Bilevel Positive Airway Pressure, Spontaneous/Timed may be an alternative only in normo/hypercapnic CSA associated to HFrEF. The same treatment strategy as for LVEF between 30%-45% should be employed for oxygen therapy, CPAP, Bilevel Positive Airway Pressure, Spontaneous/Timed, and these other therapies. In these

circumstances, ASV is not advised and should not be prescribed. Some Task Force participants advise having the neighbourhood ethical committee accept these situations as well. If no consent is given, CPAP must be kept up and pressures must be adjusted to a maximum H_2O. Depending on the circumstance, higher pressures may be taken into account. If appropriate trials of the advised therapy are unsuccessful, the Bilevel Positive Airway Pressure, Spontaneous/Timed may be an alternative only in normo/hypercapnic CSA associated to HFrEF. The same treatment strategy as for LVEF between 30%-45% should be employed for oxygen therapy, CPAP, Bilevel Positive Airway Pressure, Spontaneous/Timed, and these other therapies. In these circumstances, ASV is not advised and should not be prescribed. Low-flow oxygen treatment is an additional possibility. For many years, central sleep apnea and CSR have been treated with low flow oxygen therapy. The American Academy of Sleep Medicine advises using it because studies have indicated that it reduces Cheyne-Stokes respiration and central sleep apnea. However, only one prospective randomised controlled trial is now looking into the long-term impact of low-flow oxygen therapy on morbidity and mortality of HF patients with CSA/CSR. As a result, it is now unable to make a firm recommendation for this therapy. Although novel therapeutic approaches, including unilateral phrenic nerve stimulation, have demonstrated encouraging outcomes in recent publications, the task force is unable to endorse its application at this time.