# The SERVE-HF study: investigating the impact of central sleep apnoea on heart failure

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When reference is made to sleep-disordered breathing (SDB), obstructive sleep apnoea (OSA) often springs to mind. Indeed, much research has been centred on identifying individuals at risk of OSA, determining the most effective form of therapy and unearthing the manner by which OSA increases cardiovascular disease (CVD) risk. As a result, factors such as central adiposity, neck circumference and age have been identified as OSA risk factors, and continuous positive airway pressure (CPAP) has become a well-recognised treatment for OSA. Studies also indicate that OSA may increase CVD risk via mechanisms involving tissue hypoxia and increased sympathetic nervous system activity, and that CPAP therapy counteracts these mechanisms.[1] The case for the OSA–CVD link has been further strengthened by additional research showing that CPAP can reduce elevated blood pressure and reduce the risk of cardiovascular events, such as heart attack and stroke.[2,3]

## An overlooked form of SDB

Another form of sleep apnoea – central sleep apnoea with Cheyne Stokes respiration (CSA-CSR) – has received less in-depth investigation than OSA. Nonetheless, it carries significant importance, particularly in heart failure patients. Moderate-to-severe forms have been reported to occur in up to 50% of chronic heart failure patients.[4-7] Unlike OSA patients, whose loud night-time snores are punctuated with dramatic apnoeic episodes, CSA-CSR patients exhibit a different style of breathing. In this patient group, night-time breathing follows a waxing and waning pattern in which successive breaths grow larger and then diminish in size until breathing stops. The cycle is then repeated again and again. A 2007 study by Javaheri *et al.* demonstrated that CSR increases the risk of death among heart failure patients.[8]

It has also been hypothesised that CSA-CSR can be treated with CPAP ventilation, thus improving survival and morbidity outcomes for heart failure patients.[9] However, only one large-scale study – the Canadian Continuous Positive Airway Pressure for Patients with Central Sleep Apnoea and Heart Failure (CANPAP) – has attempted to evaluate this to date. Unfortunately, the CANPAP study had to be terminated early – after only six months' follow-up among 200 patients – and the results obtained indicated no survival benefit associated with the use of CPAP therapy in this patient group.[10]

## Positive steps forward

A group of physicians, including myself, have since come together to conduct a large international, randomised study designed to assess the effect of adaptive servo ventilation (ASV) on all-cause mortality and hospitalisation rates among patients with chronic heart failure and CSA-CSR. The ventilatory device used in this study – Resmed's AutoSet CS™2 – not only delivers additional ventilation but also adjusts the amount of ventilatory support provided depending on a patient's breathing pattern and depth. In short, it stabilises the breathing of heart failure patients exhibiting CSA-CSR.

The study, known as the SERVE-HF (Treatment of Predominant Central Sleep Apnoea by Adaptive Servo Ventilation in Patients with Heart Failure) study, began recruitment in late 2007 and has just recruited its 1,100th patient. The aim is to enrol around 1,300 patients who will be followed-up for at least two years. It is being conducted in over 70 centres in Europe and Australia.

SERVE-HF really is a landmark study. It is the world's largest study for any aspect of SDB in CVD to date. SERVE-HF has been designed as a cardiac outcome study, with the primary end points of morbidity and mortality. The SERVE-HF study also includes a substudy in which echocardiogram, magnetic resonance imaging (MRI) scanning, biomarker analysis and the assessment of different patient-centred outcomes are being performed. The aim is not only to identify if ASV helps heart failure patients live longer, but also to examine its effects

on quality of life, sleep quality and heart function – factors that often deviate from the norm in heart failure patients.

## Potential for great change in clinical practice

This study has led to an exciting collaboration between a huge number of cardiologists and sleep physicians in many countries across Europe and in Australia, and it is likely to be a landmark study in terms of its design and results. If its findings show that ASV improves heart failure outcomes, heart failure management will inevitably undergo a huge change. At present, few cardiologists actively seek to get involved in diagnosing and managing SDB. This may be because SDB is an area traditionally believed to fall under the remit of sleep or respiratory physicians. A large randomised study like SERVE-HF is, therefore, needed to provide conclusive data about the importance and impact of treating SDB on heart failure outcomes.

Simply being involved in this study has increased my awareness of SDB and its prevalence among heart failure patients. All patients in my clinics are now actively screened for SDB using Resmed's ApneaLink ™ – a SDB detection tool that monitors air flow and oximetry. My colleagues and I have found that a sizeable percentage of these patients do have SDB – either obstructive or central.

The greatest challenge to SDB management today is under-diagnosis and under-treatment. The SERVE-HF study hopes to address this issue. By identifying if SDB offers a new strategy for improving the burden of heart failure for patients and physicians alike, this study is set to potentially revolutionise the specialties of cardiology, respiratory, and sleep medicine. With a study completion date set for 2015, SERVE-HF is a study to watch closely

### Conflict of interest

MC is co-principal investigator of the SERVE-HF study referred to in this article.

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