

Sleep-disordered breathing and heart failure: an opportunity missed?

ALI VAZIR, MARY J MORRELL, ANITA K SIMONDS, HUGH F MCINTYRE

Abstract

Sleep-disordered breathing (SDB) is common in patients with congestive heart failure (CHF). SDB appears to be associated with accelerated progression of heart failure. However, it is seldom recognised in cardiology clinics, especially as CHF patients with SDB rarely report symptoms specific to SDB, such as excessive day-time sleepiness. The term SDB incorporates both central sleep apnoea (CSA) and obstructive sleep apnoea (OSA). CSA is thought to be a consequence of heart failure, whereas OSA is thought to be associated with hypertension and excessive sympathetic nerve activation, which may exacerbate failure of the heart through haemodynamic and mechanical mechanisms. The treatment of SDB is likely to be an important complementary step in the management of heart failure, particularly OSA, where treatment with continuous positive airway pressure is well established and significant improvements in left ventricular ejection fraction plus quality of life have been reported. The treatment of CSA remains unclear and requires further research. This review will examine the prevalence, diagnosis, pathophysiology, clinical features and treatment of SDB in patients with CHF.

Key words: congestive heart failure, sleep apnoea, ventilation, carbon dioxide.

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Introduction

Sleep-disordered breathing (SDB) occurs in approximately half of

patients with severe congestive heart failure (CHF) on optimal pharmacological therapy yet it is seldom considered in the evaluation and management of CHF. SDB is associated with an accelerated decline in cardiac function and increased morbidity and mortality. Treating SDB may be an important complementary step to established pharmacotherapy in the management of CHF.

Prevalence

A landmark study has shown that SDB with or without symptoms occurs in approximately 50% of patients with stable severe CHF compared to the usual incidence of 2–4% in the general middle-aged population (age range of 30–60 years),² and approximately 20–30% in the elderly³ age groups (age > 60 years).

SDB is more common in men than women. The reason for this is unknown – it has been suggested that it may be related to the effect of testosterone both centrally on the respiratory centres and peripherally on upper airway dilator muscles.⁴ The occurrence of SDB in the mild CHF population is unknown and is currently being evaluated in a large study at the Royal Brompton Hospital. Preliminary results suggest that SDB may be far more common in milder CHF than initially realised, with a prevalence of approximately 50%.

Classification of SDB

Characteristics of obstructive and central apnoea

Obstructive sleep apnoea/hypopnoea (OSA)

This occurs due to collapse of the pharyngeal airway, primarily because of loss of pharyngeal dilator muscle tone during sleep. During an obstructive apnoea there is an absence of airflow, with paradoxical chest wall and abdominal movement (figure 1), in association with an arterial oxygen desaturation. OSA is an independent risk factor for the development of hypertension,⁵ and is also associated with increased prevalence of ischaemic heart disease.^{6,7} In the presence of CHF, OSA may further accelerate the progression of heart failure.^{6,8}

Central sleep apnoea/hypopnoea (CSA)

This results from reduced efferent activity to the respiratory pump muscles and is terminated by arousal from sleep. Unlike OSA, it is thought to be a consequence of CHF. During a central apnoea episode there is an absence of chest wall movement and airflow (figure 1), associated with arterial oxygen desaturation. CSA may be associated with periodic breathing patterns. It often looks similar to Cheyne-Stokes respiration.

Clinical and Academic Unit of Sleep and Breathing, National Heart and Lung Institute, Imperial College, Royal Brompton and Harefield NHS Trust, Dovehouse Street, London, SW3 6LY.

Ali Vazir, Clinical Research Fellow

Mary J Morrell, Senior Lecturer

Anita K Simonds, Consultant Respiratory Physician

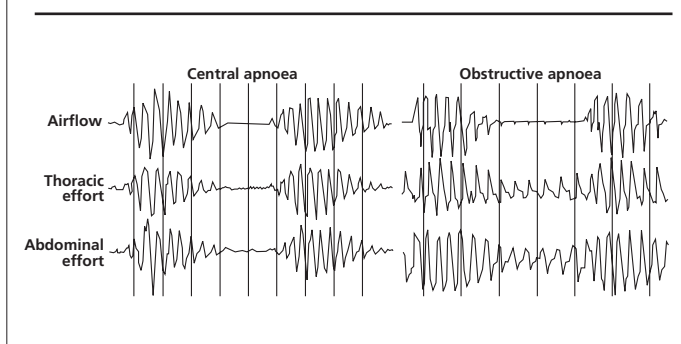
The Conquest Hospital, The Ridge, Hastings, East Sussex, TN37 7RD.

Hugh McIntyre, Consultant Physician, and Honorary Consultant (Royal Brompton Hospital)

Correspondence to: Dr A Vazir

(email: alivazir@doctors.org.uk)

Figure 1. This demonstrates typical central and obstructive apnoea events obtained from a patient with CHF. During the central apnoea there is absence of airflow and absence of both chest wall (thoracic effort) and abdominal movement (abdominal effort). During the obstructive event there is absence of air flow together with continued but paradoxical chest wall and abdominal movement



Cheyne-Stokes respiration (CSR)

Cheyne-Stokes respiration is characterised by crescendo-decrescendo oscillation of tidal volume, with intervals of hypoventilation separated by periods of hypopnoea and apnoea. A key feature of CSR is that the cycle length of the periodic breathing pattern (crescendo-decrescendo) is typically prolonged compared to simple CSA. For simplicity, CSA and CSR will be termed CSA in this review.

Diagnosis

In general the diagnosis of SDB is made in the presence of at least 10–15 apnoea/hypopnoea events per hour of sleep (apnoea-hypopnoea index [AHI]).

Nocturnal polysomnography (NPSG)

The most comprehensive test for the diagnosis of SDB is NPSG, which involves monitoring electroencephalography, electrooculography and electromyography to determine wakefulness and sleep. Electrocardiography (ECG), respiratory parameters (oro-nasal airflow/pressure, abdominal and chest movements) and pulse oximetry are also monitored. The AHI is determined from oro-nasal airflow/pressure, and the abdominal and chest movement component of the NPSG. Although NPSG is considered to be the gold standard for the diagnosis of SDB, it is expensive, time-consuming and not readily available in all hospitals.

Respiratory screening devices

Monitoring oro-nasal airflow/pressure, chest and abdominal movement and pulse oximetry may be sufficient in diagnosing clinically significant SDB. These devices can be used in hospitals and the home, and offer the advantages of being easier and cheaper to use than NPSG. They are an acceptable alternative to standard NPSG in patients with a high pre-test probability for SDB.⁹

Single parameter screening device

Overnight pulse oximetry used alone may not detect CSA as these apnoeas are not always associated with significant desaturation but it may be sufficient to exclude significant OSA.¹⁰

Apnoeas can result in repeated autonomic arousals (i.e. increases in heart rate following an apnoea) associated with a cyclical variation in heart rate. On this basis, 'Holter-style' ECG monitoring devices have been developed, which incorporate the detection of SDB from the ECG. These devices are as yet unproven in the heart failure population but one study has demonstrated that the ECG monitor was able to detect 33/35 patients with a diagnosis of sleep apnoea, of which half the patients had a history of a cardiac disorder.¹¹ The presence of frequent arrhythmias, however, could cause a high number of false-positive results. A prospective trial which would include all patients referred for evaluation of suspected sleep apnoea is required to determine the true value of Holter ECG recording as a screening tool for sleep apnoea.

Pathophysiology

Obstructive sleep apnoea (OSA)

The pathophysiology of OSA involves the loss of pharyngeal muscle dilator tone during sleep¹² and pharyngeal collapse, which mechanically obstructs ventilation and prevents airflow into the lungs, causing a rise in partial pressure of carbon dioxide (PaCO₂) and hypoxaemia, with resultant arousal.

During an obstructive apnoea episode, inspiratory effort continues against an occluded pharynx, with subsequent abrupt swings in intrathoracic pressure which lead to increased left ventricular transmural pressure (transmural pressure is the difference between intra-cardiac and intra-thoracic pressure) and hence afterload.¹³ Venous return is also enhanced, resulting in right ventricular distension and leftward shift of the interventricular septum. This impedes left ventricular filling.¹⁴ Cardiac function is therefore compromised by a combination of diminished left ventricular preload and augmented left ventricular afterload, which together reduce stroke volume.^{8,15}

Large epidemiological studies,¹⁶ and animal¹⁷ and human intervention studies,¹⁸ indicate that OSA contributes to the development of systemic hypertension, a precursor of CHF as demonstrated by longitudinal studies.¹⁹

Recurrent hypoxaemia, hypercapnia²⁰ and baroreflex inhibition (resulting from repetitive surges in nocturnal blood pressure)²¹ contribute to elevated sympathetic nerve activity, which is known to be cardiotoxic in CHF.²² Hypoxaemia may also independently lead to oxidative vascular wall injury.^{23,24} These mechanisms, together with adverse mechanical and haemodynamic effects, may contribute to progression of heart failure in CHF patients with OSA.

Central sleep apnoea

In normal individuals the arterial PaCO₂ is detected by central chemoreceptors, so that a rise in PaCO₂ leads to increased respiratory effort. By contrast, a fall in PaCO₂ will lead to reduced respiratory effort.

Patients with CHF are frequently hypocapnic (or have a PaCO_2 close to the lower limit of normal) and have an increased hypercapnic ventilatory response.²⁵ This hypocapnia is believed to result from hyperventilation in response to stimulation of the pulmonary stretch receptors (J-receptors), which are sensitive to pulmonary congestion.²⁶ Central apnoea will result when PaCO_2 falls below the apnoeic threshold – the point at which respiratory effort is no longer initiated.

During apnoea, PaCO_2 rises and partial pressure of oxygen falls, leading to partial awakening from sleep.^{27,28} Importantly, arousals are accompanied by sudden increases in heart rate and blood pressure. Arousal results in hyperventilation with a subsequent fall in PaCO_2 ; in the subsequent sleep onset, PaCO_2 is close to the apnoeic threshold. Enhanced chemosensitivity and frequent arousals from sleep lead to destabilisation of the respiratory control system, resulting in CSA and periodic breathing with cycles of apnoea.^{25,29,30} Furthermore, circulatory delay, which leads to a time lag between changes in blood gas tensions in the lung and their detection in the brainstem, may lengthen the apnoea/hypopnoea cycle.³¹

CSA is an independent risk factor for death or cardiac transplantation. Hanly *et al.*³² demonstrated that severe CHF patients with CSA have a worse prognosis and a higher mortality rate than patients with severe CHF alone. This has been associated with marked sympathetic activation, supported by significantly higher levels of catecholamines in the urine of CHF patients with CSA compared to those without.³³ Patients with CSA and CHF also have surges in blood pressure and heart rate^{34,35} and are at increased risk of lethal arrhythmias.^{34,36} Risk factors for the development of CSA in CHF patients have been identified: they include male sex, age above 60, hypocapnia and the presence of atrial fibrillation.³⁷

Identification of at-risk patients

In the general population, OSA is typically associated with obesity and snoring. Most patients present with fatigue and daytime hypersomnolence due to sleep fragmentation. Most CHF patients with OSA or CSA are not overweight, and they may not suffer from hypersomnolence. Therefore these symptoms are not always a reliable guide to the diagnosis of SDB in patients with CHF and it may be difficult to identify patients with SDB on clinical grounds alone. For example, fatigue occurs with SDB but may also be a symptom of CHF or a side effect of medication. The clinical features for SDB are summarised in table 1.

Does treatment of SDB in CHF offer any benefit?

Treatment of OSA with continuous positive airway pressure therapy (CPAP) is well established. It reduces episodes of obstructive apnoea, hypopnoeas and associated arousals. It also reduces daytime somnolence and daytime blood pressure.^{38,39} In a recent randomised study of 24 CHF patients with OSA, 12 patients randomised to one month of CPAP therapy (average use of therapy 6.2 hours per night) had a significant improvement in left ventricular ejection fraction (LVEF) of 9% (from 25.8 \pm 2.8 to 33.8

Table 1. Clinical features of sleep-disordered breathing

- Obesity
- Snoring
- Hypersomnolence (excessive daytime sleepiness)
- Fatigue/ lethargy
- Witnessed apnoea
- Paroxysmal nocturnal dyspnoea
- Morning headaches

\pm 2.4%). Daytime heart rate and blood pressure were also decreased after use of CPAP for one month.⁴⁰ The improvement was attributed to the reversal of the mechanical and haemodynamic effects of OSA. In contrast, the control group did not experience any improvement in any of these variables. Mansfield *et al.* have also recently shown in a randomised, controlled trial involving 55 CHF patients with OSA, that three months of CPAP therapy can significantly improve LVEF by 5%, reduce sympathetic activity and improve quality of life measures.⁴¹

Optimal treatment of CSA in CHF remains unclear. Several different modes of treatment have been studied, but data from large, randomised, controlled trials are lacking. Continuous nasal oxygen has been found to reduce the AHI, increase oxygen saturation during sleep and improve symptoms and exercise tolerance.⁴² Inhaled carbon dioxide has been shown to reduce apnoeas and hypopnoeas but may increase arousals, and is poorly tolerated.^{43,44} In small studies, CPAP,⁴⁵⁻⁴⁸ non-invasive respiratory support using bi-level non-invasive ventilation⁴⁹ and adaptive pressure servo-ventilation⁵⁰ have been shown to reduce AHI and arousals.

Small numbered, single centred studies have demonstrated that CPAP augments cardiac function in CHF patients with CSA, reduces sympathetic activity and improves quality of life. However, a recent Canadian multi-centre trial of CPAP therapy in over 300 CHF patients with CSA (CANPAP)⁵¹ was prematurely terminated as it demonstrated that CPAP did not reduce mortality, despite improvements in exercise capacity and ejection fraction. The results of this study have not yet been published, and it is unclear whether there is a subgroup of CHF patients that may benefit from CPAP. Therefore, at present, CPAP is not advised for the treatment of CHF patients with pure CSA.

One of the major difficulties with efficacy of assisted respiratory support is patient acceptability and tolerance of the treatment. Experience in treating OSA suggests that 50% of patients may not use CPAP one year after being started on it,⁵² in part because of noise or the need to wear a mask continuously, or the discomfort of the positive airway pressure.

A recent study of cardiac resynchronisation therapy (CRT) with biventricular pacemaker systems, involving 12 severe systolic heart failure patients, with left bundle branch block and CSA, has shown that this treatment with CRT was associated with significant improvement in AHI after an average of 17



Key messages

- Sleep-disordered breathing (SDB) is common, occurring in approximately 50% of patients with both mild and severe symptomatic congestive heart failure (CHF). It mainly consists of central sleep apnoea but a significant proportion of patients have obstructive sleep apnoea
- The presence of sleep-disordered breathing in patients with CHF is associated with an accelerated progression of heart failure, particularly in patients with obstructive sleep apnoea
- SDB should be considered in patients with CHF as part of their routine cardiac assessment
- The treatment of obstructive sleep apnoea in patients with CHF with continuous positive airway pressure support is beneficial and well established. Optimal treatment of central sleep apnoea remains unclear, and requires further investigation

weeks.^{41,53} This was associated with improved New York Heart Association class (from III to II), significantly improved exercise tolerance and an increased ejection fraction (from 25+/-5 to 35+/-9 %). Improvements in underlying cardiac function were associated with improvement in CSA – this is most likely to be related to reduced pulmonary congestion and hyperventilation. It must be noted that trials with pacing are in the early stages and are not proven therapy.

Conclusion

SDB is not widely recognised and thus is not routinely taken into account in the evaluation and management of CHF. There is a growing body of evidence to show that SDB is common in both mild and severe CHF, and its presence may further accelerate the progression of heart failure. Treating SDB in CHF may significantly improve cardiovascular outcome, especially in OSA.

All clinicians who treat CHF should be alert to the possibility of SDB, particularly OSA. SDB should be considered in patients with CHF with the clinical features and risk factors indicated. In these patients a simple sleep study should be conducted.

The treatment of OSA in CHF with CPAP is well established. The optimal treatment of CSA remains unclear. The results of large-scale, randomised, controlled trials should help to formulate diagnostic and treatment strategies. Currently, treating SDB in CHF patients with frequent hypoxaemia secondary to high AHI, severe disruption to sleep architecture, high number of arousals and daytime hypersomnolence seems advisable.

Conflict of interest

AV, MJM and HM have no conflict of interests to declare. AKS is the recipient of a research grant from the ResMed Foundation.

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