



# NEWSLETTER

## BSH meetings

- This issue reports on the BSH Satellite Symposium '*Heart Failure in the real world*', held during the BCS Annual Conference in May 2002 and also the BSH Affiliated Group Meeting '*From Cheyne and Stokes to the modern day: disordered breathing in chronic heart failure*', which was part of the main BCS programme.
- The satellite symposium looked at the epidemiology of heart failure, who is at risk of developing it, and how to individualise patient therapy, according to the evidence. This theme of providing practical guidance for healthcare professionals will be continued in the next BSH symposium '*Managing common practical problems in heart failure*', to be held on 29 November 2002 in York. For further details about the meeting, please contact the BSH Secretariat at the address at the end of this newsletter.
- An Extraordinary General Meeting was held following the symposium on 13 May, at which the BSH accounts for the period 2000/2001 were presented. The full accounts can be accessed via the BSH section of the BCS website (<http://www.bcs.com/affiliates/bsh.html>).

## Friends of the BSH

The British Society for Heart Failure gratefully acknowledges the support provided by the valued 'Friends of the Society': AstraZeneca, Medtronic, Merck Pharmaceuticals, Merck Sharp & Dohme, Roche and Servier UK.

## 'Heart failure in the *real world*' – a BSH Satellite Symposium at the BCS Annual Conference, 13 May 2002

### Introduction

Heart failure (HF) is a difficult syndrome to diagnose and manage and results from clinical trials cannot be easily translated to the HF population, who are often old and suffer from much co-morbidity. This meeting brought together healthcare professionals involved in all aspects of HF management, and aimed to provide practical solutions to the problems that affect them, as well as making suggestions for the future direction of HF management.

Dr Jackie Taylor, a geriatrician from Glasgow, asked Professor Michael Lye to set the scene by describing the UK HF population, the disease burden on the NHS and management options.

### Prevalence and prognosis – Professor Michael Lye

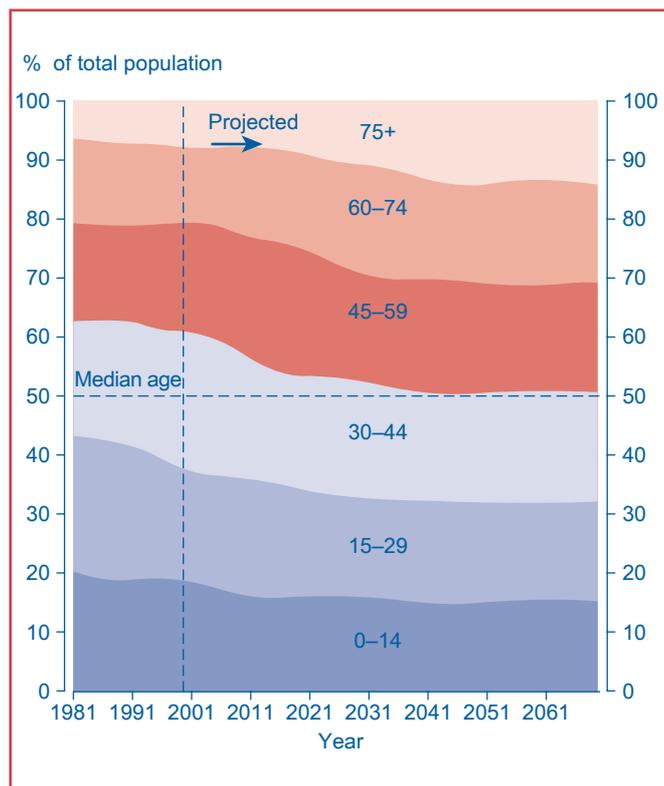
Professor Michael Lye (Department of Geriatric Medicine, University of Liverpool) reminded delegates

of the huge expansion in the number of people over the age of 65 in the UK (Figure 1) and the impact on NHS expenditure. HF prevalence is set to increase as it predominantly affects the elderly and this may mean some overlap in the roles of cardiologists and geriatricians.

Most people with HF are treated for the majority of time in primary care, with short periods in secondary care. Professor Lye commented that about 18% of people aged over 80 have some degree of HF that limits their lifestyle, but many will not be known to primary care. GPs need to identify these patients in the community at an early stage to help reduce the high costs associated with the treatment of more advanced HF.

Studies from the UK (Liverpool) and Sweden show that nearly half the expenditure in HF is incurred on social and residential care, whilst only about 10% is spent on drugs and 20–30% on in-patient treatment. Most economic studies of HF have not taken this into account. The NHS also currently receives considerable unpaid support from carers, an "informal workforce" mainly comprising women aged between 45–55, who leave their jobs to look after relatives with HF. It should

**Figure 1. Actual and projected UK age distribution, 1981–2070**



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be remembered that this segment of the population is decreasing.

The average duration of a patient's stay in hospital is much longer in the UK than in the USA, and it is getting longer. American clinicians often carry out echocardiography to diagnose HF on the day that a patient comes into the clinic. This remains an extremely rare occurrence in the UK and needs to be addressed.

Although HF is a major killer it is seriously neglected by research. For example, although more females die of HF than breast cancer, three times more money is spent on breast cancer research. Its poor prognosis is reflected in the following statistics:

- In people with HF over the age of 85, approximately 60% will die within one year.
- The five-year mortality rate of patients diagnosed with HF aged below 55 is about 50%.
- The five-year mortality rate of patients diagnosed with HF aged over 85 is 90%.

The incidence of diastolic HF increases with age. Studies have confirmed that patients with diastolic HF live longer than those with systolic HF.<sup>1,2</sup> However, there is a strong negative link between diastolic HF and exercise capacity with the consequence of increased disability in this population. The focus of current clinical trials is on treatments that reduce mortality, not morbidity. Professor Lye commented that therapeutic intervention "puts off death in HF at the cost of increasing disability – the real economic burden to society".

He concluded with the message that morbidity in HF should be taken as seriously as mortality when looking at outcomes of clinical trials and suggested that cardiologists and geriatricians should work together in the management of HF in the very elderly, where their combined skills and experience will optimise outcomes.

### **Risk factors and their management – Dr Hugh McIntyre**

Dr Hugh McIntyre (Department of Medicine, The Conquest Hospital, Hastings) commented that when people present with HF it is often too late to give them any treatment that would arrest a rapid decline in their health. He also said that patients were rarely on optimal treatment when they were admitted. Dr McIntyre focused particularly on the roles of hypertension (HT) and myocardial infarction (MI) in the development or progression of HF and whether treatment would slow progression or improve prognosis.

Unfortunately most of the large cardiovascular trials are carried out at the stage where people have already suffered an MI or when they have developed recognised HF (defined as left ventricular systolic dysfunction [LVSD]). In the 'real world' there is not much data in between to help clinicians understand whether using medical therapies to treat the risk factors prevents the development of HF.

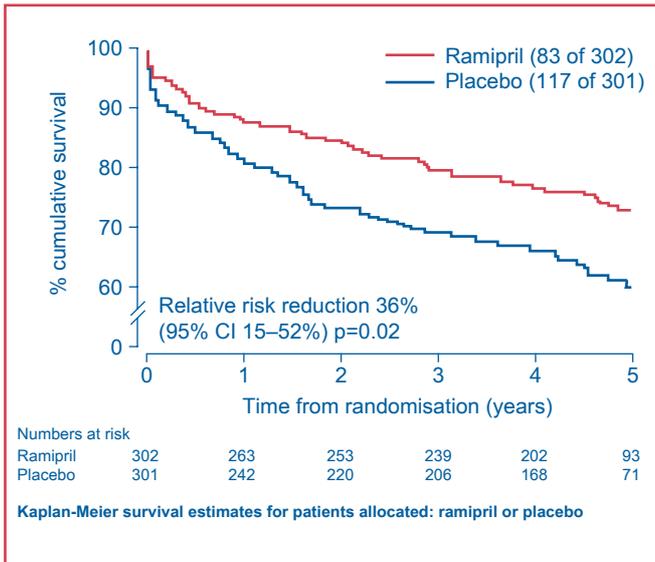
The Framingham study has implicated hypertension in the *development* of HF. However, this is difficult to verify with clinical studies; many do not look at HF as a single endpoint and in others the definition of heart failure is unclear. Only in recent studies of blood pressure lowering in hypertensive diabetics is there clear evidence that this helps to prevent HF.<sup>3</sup> At this stage it is not possible to determine whether hypertension makes existing LVSD worse as hypertension trials often have HF as an endpoint (at which stage the study closes), but HF trials tend not to include hypertensive patients.

Dr McIntyre said that untreated hypertension (systolic blood pressure >160 mmHg) may be associated with the development of HF, but this cannot currently be proved. Physiologically, he said that it was "highly plausible" that hypertension would exacerbate pre-existing LV dysfunction post-MI.

Dr McIntyre then discussed the role of MI in HF. Myocardial infarction clearly predicts the subsequent development of heart failure. In 1987, studies in America linked reduced end systolic volume post-MI to outcome.<sup>4</sup> These researchers said that the goal of treating MI was to limit infarct size (reducing LV damage) and prevent ventricular dilatation. Later Braunwald *et al.*<sup>5</sup> published a review that concluded that the bigger the heart attack, the greater the degree of LV dilatation, and said that LV enlargement post-MI can be influenced by infarct size, healing and wall stress.

A number of trials have now shown the benefits of treatment with ACE inhibitors (ACEIs) and beta-blockers

**Figure 2. Does delay in ACEI initiation post-MI influence outcome? Results from the AIREX study**



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in preventing HF and mortality in post-MI patients.<sup>6,7</sup> Timing of ACEI initiation is important. The AIRE<sup>8</sup> study showed that giving ACEIs post-MI delays the progression of HF and improves survival. Comparison of the AIRE and AIREX<sup>9</sup> studies confirms that delay in ACEI initiation post-MI influences prognosis (Figure 2). Inadequate dosing also seems to influence outcome in terms of hospitalisation, but not mortality.

To improve patients' chances of not developing HF, it is clear that limitation of infarct size is important as well as preventing ventricular dilatation. However, in those patients who survive their MI, LV dysfunction is the major cause of morbidity and mortality. Identifying those at risk of ventricular dilatation is therefore important.

Simple clinical indicators based around the AIRE criteria can be used to identify patients at risk. The inclusion of peak enzyme rise as an index of infarct size increases the likelihood of *predicting* subsequent LV dysfunction. It is possible that estimation of natriuretic peptide levels (not just initial peak but subsequent levels) may be particularly useful.

Up to 50% of patients with MI will develop heart failure. Clinicians should be actively identifying those at risk of subsequent LV dysfunction and aggressively up-titrating ACEIs to trial doses, Dr McIntyre said. Progress of those at risk should be actively monitored. More aggressive use of beta-blockers for LV dilatation at an early stage is mandatory if there is significant LV dysfunction, and should be considered where significant LV damage has been identified.

Dr McIntyre suggested that clinicians should be careful not to under-treat patients in order to prevent HF worsening, and encouraged increased nurse-led intervention. He also highlighted the need for a team approach by all healthcare professionals involved.

**Diagnosis of heart failure in older patients; complexity and importance argue against ageism – Dr Mark Cheesman**

Dr Mark Cheesman (Department of Medicine for the Elderly, Southmead Hospital, Bristol) highlighted the need to focus efforts on the real sufferers of HF. He pointed out that the MONICA study did not include patients over 74 years of age, thus excluding the very people who actually suffer from HF in 'the real world'.<sup>10</sup> He considered it important for clinicians and clinical trials to discover what patients actually want from their HF treatments – would they prefer a longer lifespan or better quality of life (QoL)? Morbidity, he commented, is very important to these people. Hospitalised HF patients show significantly lower QoL scores (SF-36) versus age-matched people without HF<sup>11</sup> and the greatest benefits of treatment were recorded as being in social function, vitality and mental health. Hospitalisation and side-effects are other clinical endpoints important to the elderly patient. Therapies should be chosen carefully to take these issues into consideration. Geriatricians and cardiologists should work together in designing drug therapy, exercise programmes and support networks to ensure optimal management.

Dr Cheesman pointed out that many high-risk groups are not screened for HF. Clinicians should pay particular attention to post-MI, hypertensive or diabetic patients. In addition, those suffering from depression have a 4-fold greater risk of developing left ventricular hypertrophy (LVH) than normal subjects.<sup>12</sup> Clinicians should also be screening older patients, those who are on NSAIDs, or have peripheral vascular disease or atrial fibrillation.

Dr Cheesman emphasised the need to take the diagnosis of HF more seriously. Clinical diagnostic methods for HF are often antiquated or open to misinterpretation. He suggested that echocardiography is the best tool available as it can diagnose systolic dysfunction, and also pick up many other abnormalities, such as lesions, LVH and wall motion abnormalities. Brain natriuretic peptide (BNP) testing is also useful, but limited in terms of specificity and sensitivity, and is perhaps more useful for prognosis.<sup>13</sup>

He suggested that the many objections for not using echocardiography can all be overturned. In the future it is likely that there will be merging of MRI and complex echocardiography technology, handheld machines will become prevalent for diagnosing systolic dysfunction, and remote reporting, consultation and archiving will become available. He concluded by saying that, "If clinicians want to serve the elderly patients with HF as they deserve, they and their managers must embrace echocardiography".

**Clinical outcome trials in the older patient – Dr Simon Gibbs**

Dr Simon Gibbs (Department of Cardiology, Hammersmith Hospital, London) suggested that the following factors are important in the care of older HF patients:

- A fast, accurate diagnosis
- Treatment with humanity, dignity and respect
- Good information and communication
- Psychological, spiritual and social support, possibly rehabilitation
- Optimal symptom control
- Well co-ordinated care
- End of life care and support for carers throughout the illness.

Dr Gibbs said that hospital re-admission is one of the most common endpoints in HF trials and can be considered a surrogate measure of symptom control. Elderly patients are frequently admitted to hospital as they have short stays and have many co-morbidities. However older HF patients should not be considered as one homogenous group – different age groups are likely to have different co-morbidities.

A study at Duke University in America showed that depression affects more than 50% of HF patients. Episodes are prolonged and there is a definite link between severe depression in HF, hospital admissions and mortality.<sup>14</sup> Dr Gibbs said the reason for the link between HF and depression is unknown, but may be associated with the same neuroendocrine activation.

Often older patients are re-admitted as they do not know when to seek medical help. Dr Gibbs described how those who received home-based intervention including optimisation of drug therapy, identification of clinical deterioration and education of the patient and carer, had a lower mortality risk and risk of unplanned admission.<sup>15</sup> Dr Gibbs said that in the community, effective management of HF includes better patient education, the use of multidisciplinary teams and specialised follow-up, resulting in better prescribing, cost-saving and reduced re-admission rates, but not, sadly, in measurable improvements in QoL.

It is particularly difficult to treat older HF patients as many have renal problems. Clinicians may be hesitant to up-titrate ACEI doses and are concerned about the toxicity of digoxin in these patients. The National HF Programme shows the number of patients on ACEIs or beta-blockers falls significantly with increasing age.<sup>16</sup>

Clinical trials are needed in elderly HF patients to guide a clinician's therapeutic choice. Results from the CONSENSUS study showed that patients over the age of 70 benefited from enalapril, so there is a case in favour of ACEI prescription, but the optimal dose remains unclear.<sup>17,18</sup> The prescription of ACEIs for elderly HF patients with preserved systolic function will soon be addressed in the PEP-CHF study.<sup>19</sup> Beta-blocker trials in HF have been in relatively young patients, and so no real conclusions can be drawn about the recommended dose in the elderly.

Dr Gibbs suggested that care of HF patients should take a more multidisciplinary approach, with models of care encompassing the broader needs of patients, beyond pharmacological therapy alone. Trialists also should take the opportunity to involve older patients in

designing HF research, so that questions about the benefits of HF treatments can be answered.

## **‘From Cheyne and Stokes to the modern day: disordered breathing in chronic heart failure’ – a BSH Affiliated Group Meeting at the BCS Annual Conference, 16 May 2002**

### **Introduction**

Cheyne-Stokes respiration (CSR) and associated sleep apnoea affect a considerable number of HF patients, yet are often undiagnosed. Daytime somnolence and fatigue are the key symptoms of sleep apnoea and those who suffer from it have greatly impaired motor function, making activities such as driving dangerous. The condition is also associated with nocturnal sympathetic nervous system activation that can exacerbate HF and cause HT.

Dr Alan Cowley (Queen's Medical Centre, Nottingham) commented that interest in sleep-disordered breathing is growing amongst cardiologists. This symposium aimed to help healthcare professionals identify the condition in their HF patients and to provide advice on treatment.

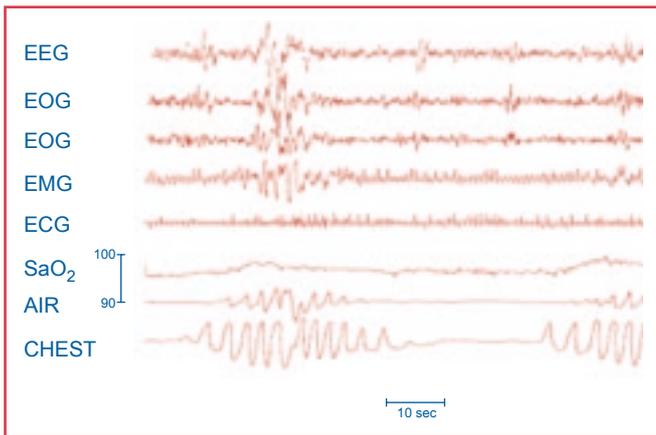
### **Pathophysiology of Cheyne-Stokes respiration and disordered breathing – Dr Andrew Staniforth**

Dr Andrew Staniforth (Department of Cardiology, St Bartholomew's Hospital, London) provided an overview of sleep-disordered breathing in chronic HF. He began by suggesting a number of definitions:

- Periodic breathing – rhythmic waxing and waning pattern of ventilation.
- Sleep apnoea – cessation of airflow during sleep.
- Central sleep apnoea (CSA) – sleep apnoea without respiratory effort (a period of at least 10 seconds without airflow).
- Obstructive sleep apnoea (OSA) – sleep apnoea caused by blocked upper airways. The main cause of OSA in adults is obesity, although there are other causes, such as being born with a small jaw or a large tongue.
- CSR – periodic breathing with a crescendo-decrescendo pattern of hyperpnoea (excessive ventilation) with central apnoea.

The study of sleep-disordered breathing began in the 19<sup>th</sup> century, when John Cheyne identified this pattern of breathing in patients with atrial fibrillation, hypertension, stroke and heart failure. Following Cheyne's initial observations, William Stokes described the breathing pattern in HF patients alone, with later researchers observing its occurrence in normal subjects. The advent of polysomnography in 1950 confirmed these observations (Figure 3). The prevalence of CSR in the general population is unknown, but its most common cause is heart failure, with 20–40% of stable HF patients suffering from it.<sup>20</sup>

**Figure 3. Cheyne-Stokes Respiration: polysomnography**

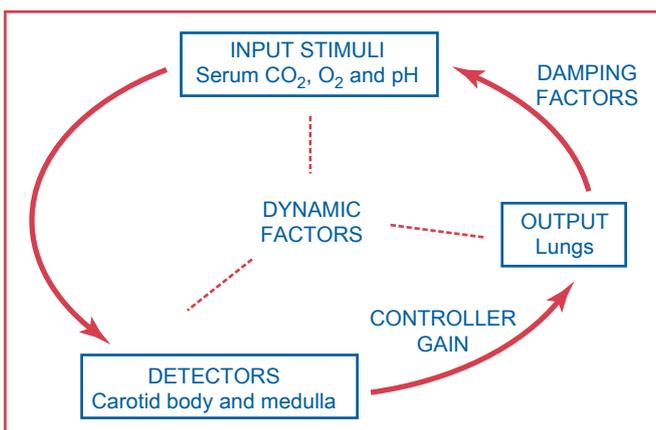


Dr Staniforth explained that breathing in normal subjects is controlled by a respiratory pacemaker in the medulla. The output of the medulla is controlled by a metabolic feedback system – the inputs being  $\text{CO}_2$ , pH and  $\text{O}_2$ . The medulla is also responsive to inputs from the vagus nerve.

During the day other inputs such as waking inputs from the cortex and reticular formation and behavioural inputs (such as speaking) suppress pure negative feedback and help maintain ventilatory stability. At night though, these inputs are lost and breathing is entirely controlled by the negative feedback system, which can generate instability in prone individuals (Figure 4).

In HF it is suggested that prolonged circulatory delay between the lungs and the chemoreceptors, reduced damping of the chemical negative feedback loop and increased chemosensitivity encourages the development of CSR. Heightened chemosensitivity is thought to be the main cause of CSR in HF patients. Abnormal sensitivity to  $\text{CO}_2$  results in increased ventilation to allow the sufferer to remove their perceived 'excess'  $\text{CO}_2$ . Hyperventilation drives their  $\text{CO}_2$  threshold down below the apnoeic threshold. Many HF sufferers with increased ventilatory responsiveness have lower blood levels of  $\text{CO}_2$  than normal subjects.<sup>21,22</sup>

**Figure 4. Sleep: pure chemical negative feedback**



A recent study has shown that chemosensitivity in HF is associated with changes in pulmonary capillary wedge pressure (PCWP). Patients with CSR had the highest ventilatory drives and the highest filling pressures.<sup>23</sup> The authors suggested that the presence of water in the lung (caused by pulmonary oedema) stimulates J receptors resulting in increased traffic down pulmonary vagal C fibres and consequently increased chemoreceptor drive and hyperventilation.

Dr Staniforth suggested that hypoxia plays a role in the genesis of CSR, but because supplemental oxygen only attenuates and does not abolish CSR, it is not the prime driving factor.<sup>24</sup>

### **Disorders of breathing during sleep – Dr William Kinnear**

Dr William Kinnear (Department of Respiratory Medicine, Queen's Medical Centre, Nottingham) gave some reasons why cardiologists should be interested in disorders of breathing during sleep:

- Some people with cardiac problems also have respiratory problems.
- Many patients seen by cardiologists fight for breath at night and LV failure is not the only cause of this.
- Patients are demanding to know more about sleep apnoea – they are concerned about whether it causes an increase in blood pressure or heart attacks.

Dr Kinnear emphasised that cardiologists should be aware of other causes of breathing disorders such as OSA and CSA. He explained that in REM sleep a person under-ventilates and breathing is irregular. The diaphragm is the main respiratory muscle during sleep and if it is weak (as occurs in HF) there will be no airflow and apnoea will occur.

In CSA there is increased ventilation followed by apnoea (but no respiratory effort). This is due to:

- Muscle weakness: the brain is producing signals to breathe but the effector muscle (the diaphragm) is not working properly.
- CNS disorder: no signal is being sent down the phrenic nerves to the diaphragm.

The net result of both CSA and OSA is no airflow with sufferers needing to wake up in order to breathe. Waking is associated with a burst of sympathetic activity and tachycardia ensues. OSA sufferers do not have diurnal variation in systolic and diastolic blood pressures (unlike normal people) and this may be the key to explaining their cardiovascular morbidity.

Dr Kinnear emphasised that OSA causes hypertension and is probably associated with an increase in cardiovascular morbidity, although this remains unproven. Treatment with continuous positive airway pressure (CPAP) reduces blood pressure but it is not known whether it decreases cardiovascular events.<sup>25</sup>

### **Sleep-disordered breathing – does it matter to the clinician? – Professor Andrew Coats**

Professor Andrew Coats (Department of Cardiology, Royal Brompton Hospital, London) commented on the importance of night-time breathlessness as shown in a 18-month qualitative study of the symptomatic burden of HF.<sup>26</sup> Night-time breathlessness was one of the most important and severe symptoms and was extremely distressing for patients and their partners.

Professor Coats became interested in sleep-disordered breathing because he believed that factors other than impaired cardiac pumping limited exercise performance in HF. He said that many clinicians have not listened to their patients who linked their nocturnal breathlessness with daytime fatigue.

During exercise patients with very severe HF appear to breathe more. However, Professor Coats commented, “The arterial blood gases of these patients aren’t abnormal but rather ‘super normal’ with lower CO<sub>2</sub> levels than you’d expect and higher pO<sub>2</sub> levels than in an age-matched normal population”. The increased ventilation (VE/VCO<sub>2</sub> production slope) had a better correlation with exercise limitation than ejection fraction.

There are a number of potential underlying abnormalities causing increased ventilation in the HF population:

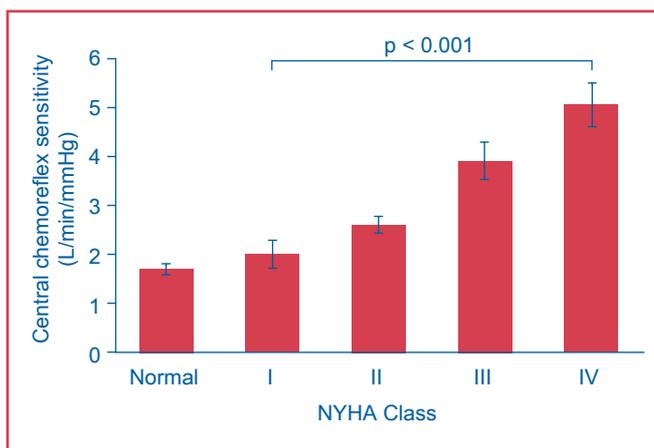
- A mismatch between ventilation and perfusion in the lung
- Non-asthmatic bronchoconstriction
- Stimulation of lung afferent nerves
- Central command spillover (whereby the effort of exercising causes an increase in breathing)
- Abnormalities of respiratory and skeletal muscle.

A study in 300 patients confirmed that there was a link between the VE/VCO<sub>2</sub> slope and NYHA class (p<0.001).<sup>27</sup> Professor Coats and colleagues found both increased central CO<sub>2</sub> sensitivity and peripheral hypoxic sensitivity in HF patients compared with normal controls. This suggested that one of the causes of shortness of breath and the exaggerated ventilation seen in HF might be an increased chemosensitivity to changes in arterial blood gases (Figure 5).

An inverse-baroreflex relationship has been found between blood pressure and heart rate variability in CSR patients.<sup>28</sup> It appeared that the baroreflex was being suppressed and overridden by an exaggerated chemoreceptor reflex. This results in prolonged overactive sympathetic nervous system activity, which is a hallmark of HF and an adverse prognostic marker. Oxygen was shown to normalise this response.

There is evidence to suggest that those HF patients with exaggerated chemosensitivity, leading to increased ventilatory responses and a susceptibility to periodic breathing, have an increased mortality risk. Professor Coats’ group found that the ventilatory response slope was a powerful prognostic indicator, in addition to peak

**Figure 5. Increasing chemosensitivity with symptomatic class<sup>29</sup>**



oxygen consumption (which is a powerful univariate predictor of mortality).<sup>29</sup> Results also showed that in matched patients with HF (for age, NYHA class, aetiology and HF), those with normal chemosensitivity had dramatically increased survival compared with those with chemoreceptor hypersensitivity.

Interventions used to treat CSR and sleep apnoea include CPAP, supplementary CO<sub>2</sub>, O<sub>2</sub> and drugs. A study of 12 HF patients treated with dihydrocodeine showed significant improvements in exercise capacity vs placebo (p<0.002) and dyspnoea (p=0.003) with a significant reduction in chemosensitivity.<sup>30</sup> In preliminary work the drug has also been shown to reduce susceptibility to periodic breathing or CSR. CPAP has also shown some positive results in reducing cardiac noradrenaline.<sup>31</sup>

Professor Coats concluded that sleep-disordered breathing should be taken seriously by clinicians, as it appears to influence daytime HF symptoms. An increased ventilatory response should be considered an important prognostic indicator that should not be ignored. Cardiologists should start using the therapies available to prevent occurrence of this syndrome in their patients.

### **What treatments are available and how valuable are they? – Dr Douglas Bradley**

Dr Douglas Bradley (University of Toronto, Canada) explained that patients with OSA suffer from surges in sympathetic nervous system activity, hypertension and elevated heart rates during sleep that could precipitate ischaemia in patients with CAD or worsen HF.

Continuous positive airway pressure (CPAP) applied via a nasal mask is the most widely used treatment for OSA (Figure 6). CPAP consists of an air pump that creates positive air pressure, which is transmitted via tubing to a face mask. This in turn pressurises the upper airway and prevents it from collapsing. As a result, CPAP abolishes obstructive apnoeas and normalises breathing, attenuating the degree of negative intrathoracic pressure generation and unloading the respiratory muscles. Hypoxia is also

**Figure 6. CPAP: a widely used treatment for sleep apnoea**



prevented and as a result sympathetic nervous system activity is reduced and blood pressure and heart rate fall. Dr Bradley remarked that benefit can be seen even in patients taking afterload-reducing agents. In addition, because abolition of OSA reduces awakenings, patients sleep more soundly so that they do not feel sleepy during the day.

Describing a small study of eight patients with dilated cardiomyopathy (DCM) and OSA, Dr Bradley said that CPAP has also been shown to improve baroreflex sensitivity.<sup>32</sup> After withdrawal of CPAP, although most parameters returned to pre-treatment levels, patients' heart rates stayed down, suggesting a beneficial carryover effect. In another study, CPAP was applied nightly for one month to eight patients with DCM and OSA. Left ventricular ejection fraction (LVEF) improved, but following a one week withdrawal of CPAP it fell back to the baseline level.<sup>33</sup> This strongly suggested that reversal of OSA by CPAP was responsible for the improvement in cardiac function.

Treatment of HF patients with CSR (i.e. central sleep apnoea) is slightly different to OSA as it is likely that CSR arises from LV failure. Many HF patients have stiff congested lungs, provoking hyperventilation via stimulation of vagal irritant receptors. Increased respiratory chemosensitivity further exacerbates hyperventilation, which drives PaCO<sub>2</sub> below the threshold required to stimulate ventilation, triggering central apnoeas and CSR.<sup>34</sup> Accordingly, the first approach to treating CSR, Dr Bradley explained, is to optimise medical HF therapy to reduce PCWP and pulmonary congestion, thus dampening ventilation and increasing PaCO<sub>2</sub>. Nevertheless, despite optimal medical therapy, 20–40% of HF patients will continue to have CSR.

Turning to the use of oxygen, Dr Bradley said that Andreas *et al.* showed that nocturnal oxygen treatment attenuated CSR in HF patients, but did not improve HF symptoms.<sup>35</sup> There was however, a significant improvement in peak oxygen uptake and the VE/VCO<sub>2</sub>

slope during exercise testing. In addition, Staniforth *et al.* found that oxygen treatment significantly reduced central apnoeas and urinary catecholamines (suggesting attenuation of overnight sympathetic nervous system activity).<sup>36</sup>

Theophylline is a respiratory stimulant that has been used to override central apnoeas in HF.<sup>37</sup> However, it has been associated with increased mortality in HF patients in the past.

CPAP has also been shown to reduce the severity of CSR.<sup>38</sup> It probably does so by increasing intrathoracic pressure and alleviating pulmonary oedema, thus reducing ventilation and increasing PCO<sub>2</sub>.<sup>34</sup> It also improves LVEF and symptoms of HF<sup>38</sup>, and attenuates sympathetic nervous system activity.<sup>39</sup> A small long-term randomised trial of CPAP vs. standard medical therapy in HF patients with CSR has shown that these results seem to translate into survival benefit.<sup>40</sup> Because of these results Dr Bradley has begun a large long-term multi-centre mortality trial (CANPAP) in patients with reduced LVEFs (<40%) and CSA that he anticipates will be completed in two to three years' time.<sup>41</sup>

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