

# Abstracts: Heart Failure Symposium 2006

**ABBREVIATIONS** angiotensin II receptor inhibitors (ARB's), angiotensin converting enzyme (ACE), B-type natriuretic peptides (BNP), cardiac resynchronisation therapy (CRT), chronic heart failure (CHF), heart failure (HF), implantable cardiac defibrillators (ICD's), left ventricular assist devices (LVADs), left ventricular ejection fraction (LVEF), left ventricular systolic dysfunction (LVSD), peak oxygen consumption ( $MVO_2$ )

## SESSION I WHERE WE ARE NOW AND WHERE WE ARE GOING

Chairman: Dr M Denvir, Consultant Cardiologist, Western General Hospital, Edinburgh, Scotland

### Diagnosis and Investigation

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**Abstract** The definition of HF has progressed a long way from the early physiological descriptions. Currently we use a broad clinical definition based on the presence of symptoms and or signs of HF in the presence of cardiac dysfunction. In the UK most of this cardiac dysfunction is systolic in nature. Modern epidemiological studies using this definition give a population prevalence of chronic heart failure of between 1–2% with an incidence of 1/1000 population per annum. Both prevalence and incidence rise steeply with age. The presence of the syndrome is still associated with considerable mortality and morbidity rates. Of particular concern for healthcare delivery systems is the huge economic cost of HF due mainly to the high hospitalisation rates it incurs.

However the picture isn't all gloom. Hopefully, due to recent improvements in therapeutic options, we are now beginning to see reductions in mortality rates for HF both in Europe and the US.

**Key words** Economic cost, mortality and morbidity rates, prevalence, signs of HF.

**Sponsors** None.

**Declaration** No conflict of interest declared.

### Medical Therapy – Evidence Based Medicine: the Real World Situation and the Pitfalls

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### Abstract

**Background** Clinicians find HF difficult to diagnose. Confirmation of left ventricular dysfunction (systolic or diastolic) is only possible by cardiac imaging. Guidelines suggest echocardiography is the 'gold standard' investigation.<sup>2</sup> However, this is not uniformly available across the UK.<sup>1,3</sup> Recent European Society of Cardiology guidelines<sup>4</sup> and NICE<sup>1</sup> have suggested that BNP and electrocardiography be incorporated in integrated care pathways as a diagnostic tool that supports GPs in their assessment of patients with suspected heart failure. This talk will consider the place for electrocardiography and natriuretic peptides<sup>5</sup> in triaging patients with suspected heart failure, and discuss potential service delivery models to overcome variability in the optimal utilisation of evidence based pharmacotherapy.

Despite inclusion in guidelines<sup>2,4</sup> uptake of assays for BNP or NT proBNP has been slow in the NHS. Clinicians and Primary Care Trusts still harbour concerns about appropriate cut offs, the extra cost of natriuretic peptide assays, which assay to use,<sup>6</sup> lack of expedient referral pathways for patients with a raised natriuretic peptide level and absence of cost benefit/effectiveness data from a pragmatic GP study.

All Guidelines and NICE guidance for the diagnosis and management of heart failure due to LVSD suggest that if an ECG is normal then LVSD is very unlikely.<sup>2,4</sup> Such conclusions are dependent on case selection and the prevalence of LVSD in the population studied. Our experience in assessment of patients with suspected LVSD referred from primary care is that this statement is not always accurate.<sup>7</sup> Furthermore there are difficulties in interpretation of ECG data by GPs in particular.

**Conclusions** Diagnostic and treatment difficulties identified by GPs<sup>1</sup> and hospital specialists<sup>8</sup> are dependent on a complex interplay of patient, clinician and organisational factors. The barriers identified by these qualitative studies need to be overcome in locality specific and multi-faceted implementation strategies across primary-secondary care. Integrated HF diagnosis and management systems<sup>9</sup> that overcome these barriers and in so doing deliver accurate diagnosis, modern evidence based treatment and end of life care that is valued by patients, carers and clinicians are urgently needed in the NHS.

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**Key words** Assays for BNP or NT proBNP, heart failure, left ventricular dysfunction.

**Sponsors** None.

**Declaration** No conflict of interest declared.

## Multidisciplinary Management Programmes

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**Abstract** Chronic heart failure is the cause of increased morbidity and mortality, severely impaired quality of life as well as huge costs to health care providers. Adherence to treatment guidelines can reduce morbidity and mortality and also improve quality of life but recommended treatment is often under prescribed. Numerous studies of various models for the management of CHF have been published over the past decade. In general these models have employed variations of multidisciplinary management programmes. Common components have been the utilisation of a specialised heart failure nurse for education of the patient and family, ensuring adherence to guidelines, up titration of medication, monitoring of safety parameters as well as facilitating long term compliance.

Generally studies of multidisciplinary management programmes have been small, single centre trials that have often studied specific components that could be suitable parts of a multidisciplinary management programme. The overall experience is positive but one has to consider the difficulties involved in designing and performing these studies appropriately as well as the possibility of a bias

towards publishing positive results. However, given the evidence available the most appropriate strategy towards establishing multidisciplinary management programmes is reasonably to combine suitable components based on an analysis of local, regional or national needs. The aim of this being to supply an optimal logistic framework appropriate for implementation of guidelines. Adherence to guidelines needs to be monitored by establishing instruments for quality control. Further research should be focused on identifying the most efficacious components for a multidisciplinary management programme.

**Key words** Chronic heart failure, logistic framework, long term compliance, multidisciplinary management programmes, monitoring of safety parameters, specialised heart failure nurse, treatment guidelines, up titration of medication.

**Sponsors** None.

**Declaration** No conflict of interest declared.

## SESSION 2 DEVICES

Chairman: Dr N Grubb, Consultant Cardiologist, Royal Infirmary of Edinburgh, Scotland

### CRT±D: Evidence and Economics

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**Abstract** Up to 30% of patients with advanced heart failure have conduction disturbances, predominantly left bundle branch block. Atrioventricular, inter and intraventricular conduction delays all contribute to mechanical dyssynchrony and mitral regurgitation, and are associated with a worsening prognosis. By pacing the free wall of the left ventricle as well as the interventricular septum, CRT improves left ventricular ejection fraction, functional class, exercise capacity and quality of life.<sup>1</sup> Systematic review and meta-analysis of nine early small scale or short term trials of CRT<sup>2</sup> demonstrated a relative risk of 0.79 (95% confidence interval 0.66–0.96) for all cause of mortality, and 0.68 (0.41–1.12) for heart failure hospitalisation. Recently, the CARE-HF Study<sup>3</sup> has shown during a mean follow-up of 36 months that CRT reduces the combined end-point of death or unplanned cardiovascular hospitalisation, as well as reducing all cause mortality, progressive heart failure mortality and sudden cardiac death.

Problems with CRT include the technical difficulty of the implant procedure, a risk of up to one third of non-response and issues surrounding electrode displacement.

However, overall CRT offers considerable symptomatic and prognostic benefit to selected patients with advanced heart failure and conduction disturbances.

Since many patients with heart failure die from ventricular arrhythmias, the addition of a defibrillator to CRT offers the potential for further reduction in total mortality compared with CRT alone. However, the magnitude of this benefit will depend on the relative risks of death from progressive heart failure versus ventricular arrhythmias, and remains to be fully established.<sup>3,4</sup>

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**Key words** cardiac resynchronisation therapy, Conduction disturbances, exercise capacity, functional class, implantable defibrillator, left ventricular ejection fraction, mechanical dyssynchrony, mitral regurgitation, quality of life, ventricular arrhythmias.

**Sponsors** None.

**Declaration** No conflict of interest declared.

### THE DAVIDSON LECTURE

Chairman: Professor N Douglas, President, Royal College of Physicians of Edinburgh, Scotland

#### *Regrowing the Heart: Is Stem Cell Therapy a Realistic Hope?*

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#### Abstract

**Background** The use of stem cells for the treatment of myocardial disorders is gathering pace. However, whether the excitement that has been generated to date is justified by the available data is less certain. This relates to the relative paucity of rigorously controlled blinded studies, as well as the multitude of variables that likely influence the outcome of such studies.

Some of the key variables include:

- a) The cell type used.
- b) The route of delivery.
- c) The sensitivity of the outcome measures.
- d) The design of the clinical studies including power calculations.
- e) Whether treatment is aimed at acute, acute-on-chronic or end-stage disease.
- f) The duration of effect of a single application, and hence the need for repeated application of stem cells.
- g) The need, or otherwise, for pre-treatment or pre-conditioning of the cells with growth factor genes or proteins.

The talk will summarise the available evidence on these variables, as well as provide an update on the clinical studies to date. The rationale for a more coordinated, less competitive approach to this field will also be discussed

**Conclusions** The field needs to be cautious in its approach to this potential, but as yet unproven, new treatment. Over enthusiastic positive or negative responses in the absence of strong data, are some of the key roadblocks. The onus is on the field to refute the null hypothesis ie stem cells are not a useful treatment for cardiac disease.

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**Key words** Cardiovascular, stem cells.

**Sponsors** British Heart Foundation, Medicor Foundation.

**Declaration** No conflict of interest declared.

### SESSION 3 EMERGING THERAPIES

Chairman: Ms K Russell, Heart Failure Nurse, Royal Infirmary, Glasgow, Scotland

#### Anaemia

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**Abstract** Although CHF therapy has been revolutionised over the last two decades with angiotensin converting enzyme inhibitors, beta-blockers, aldosterone antagonists,

and devices, studies are now focusing on the treatment of co-morbidities and their subsequent effects on morbidity and mortality rates.

Anaemia is prevalent in patients with chronic heart failure, the proportion of which increases with deteriorating New York Heart Association functional class. Anaemia is associated with increased symptoms, more frequent hospitalisations and, in most studies, with an increased mortality rate. The causes of anaemia in CHF, however, remain unclear, although impairment of renal function and inflammatory cytokines are proposed mechanisms. Both may act through impairment of the synthesis or action of erythropoietin.

Preliminary studies have demonstrated improvement in symptoms, exercise tolerance, quality of life and reductions in hospitalisations when patients with severe CHF were treated with erythropoietin. The benefits and the potential risks of such therapies will be further addressed in upcoming larger randomised trials. The recent interest in anaemia reflects a new perspective in heart failure therapy, focusing on non-cardiovascular co-morbidities.

**Key words** Anaemia, CHF therapy, erythropoietin.

**Sponsors** None.

**Declaration** No conflict of interest declared.

#### **LVADs, Surgical Thoughts**

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**Abstract** Heart failure is a major public health concern because it is common, associated with disabling symptoms, detectable, treatable and carries a poor prognosis.<sup>1</sup> The prevalence is between 1% and 3% of the entire population increasing sharply with age. The incidence is between 1 and 4 per 1,000 per annum, also showing a steep rise with age. In the UK the total cost of HF to the health service is estimated to be at least 2% of the total health budget. The major component of the cost (70%) is hospital admissions.

Medical treatment for patients in NYHA Class IV is a combination of diuretics (including aldosterone inhibitors), ACE inhibitors and beta-blockers with or without digoxin. These treatments have been shown to reduce mortality and improve quality of life. Additional drugs, invasive catheter interventions, biventricular pacing (CRT) and ICD's are used in selected patients but there is less evidence for efficacy. New classes of drugs being introduced into clinical practice include ARB's, statins and new inodilator agents such as levosimendan.

Surgical interventions such as revascularisation of hibernating myocardium, mitral valve repair and remodelling of the left ventricle (Dor procedure) are not common operations. The only surgical treatment generally accepted as providing survival benefit together with an improved quality of life is heart transplantation, but transplantation will never be widely available because of the limited supply of good donor hearts. Many patients with severe heart failure are not considered for transplantation because of limited availability of donor organs, elevated pulmonary vascular resistance or concomitant disease. In the last few years less than 200 donor hearts per annum have been used in the UK in contrast to an annual burden of around 100,000 new patients with advanced heart failure. The adverse effects of chronic immunosuppression, allograft coronary artery disease, impaired exercise tolerance of the denervated heart have constrained improvement in outcomes after transplantation.

Despite these treatments severe heart failure still carries a poor prognosis. In the CONSENSUS trial half the patients in the control arm had died within six months. In the REMATCH trial<sup>2</sup> only 8% of patients in the medically treated group were alive at two years.

Left ventricular assist devices were developed to maintain the circulation in patients who are awaiting transplantation ('bridge to transplant'). Uncommonly the use of a LVAD is associated with substantial recovery of ventricular function and the device can be removed ('bridge to recovery'). Such devices are now being used as a lifetime treatment where transplantation is not an option (life-time or 'destination' therapy). These three strategies are not exclusive at the point of intention to treat.<sup>3</sup> Nonetheless, patients tend to be classified into one of these groups at the moment when a decision is made to insert a LVAD.

#### **Bridge to transplant or recovery**

The treatment of end-organ failure should be seen in perspective. Current figures for survival on haemodialysis for renal failure are 60% at two years, the use of the MARS charcoal filter in liver failure as a bridge to transplantation is associated with a five year survival of 66%, while LVAD bridge to heart transplantation is associated with a five year survival of 73%. The use of a LVAD can on occasion result in so great an improvement in the function of the native heart that the device can be removed and transplantation is no longer necessary. Recovery of haemodynamic and nutritional status with reversal of the metabolic and cellular abnormalities of heart failure improves survival after heart transplantation. This improvement results from reversal of cell deficiencies in the myocyte limiting contractile function. Abnormalities have been shown in the contractile proteins, the control of contraction, the provision of energy for contraction and expression of genes.

Hypertrophied myocytes revert toward normal size, cell apoptosis and oncosis are reduced and calcium control by the sarcoplasmic reticulum is largely restored. Even the transcription of inhibitors of apoptosis is upregulated.

Overall, mechanical unloading by use of a LVAD leads to reversal of the adverse remodelling process, normalisation of passive pressure-volume relationships and improved contractile response to increased heart rate and beta-agonists.

### Destination therapy

The REMATCH study evaluated the HeartMate LVAD in patients with severe heart failure despite maximal medical treatment. Entry criteria were a need for intravenous inotropic therapy for symptomatic hypotension, decreasing renal function or worsening pulmonary oedema together with LVEF less than 25% and MVO<sub>2</sub> less than 12 ml/kg/min. The investigating transplant centres had to overcome major ethical, logistic and economic hurdles in order to recruit 129 patients who were deemed unsuitable for transplantation and who were willing to be randomised. All cause mortality (the primary end-point) was 48% lower in the LVAD group ( $p=0.09$  at two years,  $p=0.001$  at one year). Median survival was 408 days in the LVAD group and only 150 days in the medically treated group. Few patients in the LVAD group survived for two years (23% versus 8% in the medically treated group,  $p<0.09$ ). Quality of life was limited by a 28% incidence of device infection at three months, a 42% incidence of bleeding at six months and a 35% probability of device failure at two years. Of the 68 patients who received a LVAD, ten had the device replaced. After REMATCH, 67 centres in the USA have started lifetime treatment programmes. Clinical outcomes are now better than in REMATCH. The Health Care Advisory Board (USA) now predicts that LVADs will provide conventional treatment for advanced heart failure by 2010.

### LVAD development

In 1994, the devices and technology branch of the National Heart Lung and Blood Institute invited submissions for the development of innovative circulatory support systems as a long-term treatment for heart failure. The engineering strategy for these devices was to encompass a number of preferred characteristics. These were:

- 1 Small size and weight allowing the pump to be fully implantable.
- 2 Reduced blood contact surface area to decrease activation of the immune and coagulation systems.
- 3 A simple blood propulsion mechanism without prosthetic valves or the need for heparin.
- 4 A reliable operating system easily learned by the patient and safe in the community.

As a result of this initiative, new minaturised centrifugal and axial flow devices are now available for clinical

evaluation.<sup>4</sup> These newer rotary pumps differ from the old larger pusher-plate pumps, by offering assistance to the ventricle rather than wholesale replacement. Thus with the rotary pump as a LVAD, the native LV continues to make a small but significant contribution to the cardiac output and thus the flow exhibits low pulsatility. These devices are preload and afterload sensitive. The overriding principle of managing these pumps is to reach the desired flow with the lowest possible rotational speed, thus minimising blood trauma and platelet activation. Careful afterload reduction is essential, together with close monitoring of antiplatelet therapy.

It is not yet clear whether the degree of ventricular unloading provided by these rotary pumps is sufficient to allow for recovery of left ventricular and biventricular failure. Further clinical experience is required.<sup>5</sup> The small observational studies available on these second generation rotary pumps suggest that the causes of mortality and morbidity are similar to the large pusher pumps but the frequency of complications is lower. Infection, bleeding and stroke remain the most significant problems, and there is an urgent need to understand the coagulopathy that can be problematic with the axial impeller pump.

When considering the use of an implantable LVAD, we need to counsel our patients regarding their best options and to allow them to come to an informed decision according to their personal preferences.

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**Key words** Antiplatelet therapy, CONSENSUS trial, HF, heart transplantation, left ventricular assist devices, minaturised centrifugal and axial flow devices, REMATCH trial, rotary pumps.

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**Declaration** No conflict of interest declared.

### Nursing Perspective

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#### Abstract

**Background** Once the 'Cinderella' of cardiology, HF is now recognised as a sub-speciality, requiring the skills of multi-agency teams. Managing need, expectation and clinical outcomes in a timely, economical and auditable manner is essential.

**Methods or Theme** Integrated healthcare systems and models provide structure to service delivery, and should reflect the current evidence-base, meet the needs of the patient and society, be auditable and facilitate future research, and flexible to meet changing and regional differences.

The boundaries between other clinical conditions and disciplines, with an ageing, complex and co-morbidity client group, coupled with the change in clinical service commissioning and delivery, and the debate around nurse specialists, is requiring nurses to structure and formalise their education and skills, share and blend with other professions, whilst trying to explain and validate their role for auditable and financial reasons.

Treatment and management options for HF patients are diverse, encompassing diagnoses, rehabilitation, life-style modification, motivational training, drug therapy, counselling, device therapy, surgery and palliation. This raises expectations in both patients, relatives and healthcare professionals, at a time when death and reduced capacity are societal new taboos, and healthcare providers are financially accountable.

**Conclusions** Nurses need to consider the wider social, epidemiological, financial and political implications, evolving clinical treatments, and research and audit requirements, whilst delivering a client centred service, which embraces their views and expectations as individuals and as a consultative party in service design and review.

**Key words** Client centred service, HF, integrated health care systems, nurse specialists, service design.

**Sponsors** None.

**Declaration** No conflict of interest declared.

### Percutaneous Coronary Intervention

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Trust, Leicester, England

**Abstract** Not available at the time of going to press.

## SESSION 4 EMERGING THERAPIES FOR QUALITY OF LIFE

Chairman: Dr K Boyd, Consultant in Palliative Medicine, Royal Infirmary of Edinburgh, Edinburgh, Scotland

### Exercise

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**Abstract** Until the mid-1980's, the traditional advice given to patients with CHF was to 'rest'; small uncontrolled studies from the 1960s suggested that long term bed rest might improve cardiac function. However, many of the pathophysiological changes seen in patients with CHF are similar to those seen in normal subjects undergoing a period of detraining. For example, neurohormonal activation, muscle wasting and decreased exercise performance are typical features of both syndromes. Additional information has accumulated suggesting that the principal determinant of symptoms in HF is not cardiac function, but rather, the state of the skeletal muscle. Physical training to try to reverse skeletal muscle changes thus seems a sensible therapeutic target.

Many randomised controlled studies have subsequently shown that formal exercise training can reverse many of the muscle abnormalities associated with CHF and improve exercise capacity by around 20%. In addition, it can reverse many of the pathological changes associated with a poor prognosis. Meta-analysis of the available data suggests that training may even be associated with a survival benefit.

The reality of trying to implement training programmes is difficult. Most patients with CHF are elderly and many have co-morbidities. The degree of supervision required isn't clear; there is no support from pharmaceutical industries and cost-cutting tends to target the less glamorous fields. We have shown that electrical muscle stimulation is an effective form of training, and this technique might be appropriate for patients with HF. Delivering effective training as a therapy remains the greatest challenge.

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**Key words** Cardiac function, CHF, electrical muscle stimulation, formal exercise training, long term bed rest, survival benefit.

**Sponsors** None.

**Declaration** No conflict of interest declared.

### Palliative Care

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### Abstract

**Background** Palliative care in the UK has traditionally focussed on the care of patients with cancer. Studies have highlighted the inequity for advanced HF patients who also suffer in all domains of life. There are accepted difficulties with prognosis leading to reluctance to address end-of-life issues. Thus it is less likely for a patient with HF to be able to die at home or in hospice, or access symptom control. Both cardiology and palliative care are responding to this issue and collaborative services are growing.

**Methods or Theme** Review of key recent publications, particularly the Regional Study of Care for the Dying;<sup>1</sup> the US SUPPORT study;<sup>2</sup> studies comparing experiences with palliative care or lung cancer patients;<sup>3, 4</sup> studies of symptom control measures.<sup>5, 6</sup>

Physical symptoms, psychosocial problems and spiritual concerns are comparable with cancer patients'. The inequitable provision of services, open communication and information is confirmed. There is, as yet, little

evidence base for symptom control in HF although experience in units extending care to HF patients report that knowledge of symptom management of cancer patients is largely transferable.<sup>7</sup>

**Conclusions** Despite advances in the treatment of HF, it is clear that cancer patients receive better care. Barriers for HF patients include concerns from the palliative care community regarding skills and service capacity. Conversely it can be very difficult for cardiologists to recognise when involvement of palliative care services, would improve the overall management of their patients.

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**Key words** Heart failure, palliative care, supportive care.

**Sponsors** None.

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