ISSUE 19 SPRING 2006

British Society for Heart Failure

NEWSLETTER

In this issue…

We report highlights from the 8th BSH Annual Autumn Meeting – Managing heart failure: picking up the pieces – held at the Queen Elizabeth II Conference Centre, London, on 25 November 2005. The meeting included sessions on:

The meeting was held in association with the British Heart Foundation (BHF).

The 9th BSH Annual Autumn Meeting and Charity Ball will be held in London on 24–25 November 2006.

8th BSH Annual Autumn Meeting – Managing heart failure: picking up the pieces

Acute heart failure: an ever-widening chasm

The critical components of an ideal integrated heart failure service were presented by Suzanna Hardman (London), emphasising the need for early, accurate diagnosis, alongside optimal, timely treatment delivered by multidisciplinary teams, structured so that the intensity of care can be rapidly responsive. An ideal heart failure service would recognise that the 'community' has diverse influences and components, and that the guiding philosophy should be inclusive of these rather than exclusive of them.

In recent years there has been considerable investment in increasing heart failure services across primary care, led by the BHF. Paradoxically, care for those patients who present to hospital with acute decompensated heart failure and have the worst prognosis has been relatively neglected. Emphasis on early intervention for these inpatients, optimisation of therapy prior to discharge, effective discharge planning and continuity of care within primary care may exert a substantial benefit on outcome as data emerging from the Whittington Heart Failure study suggest.

There are few data on the epidemiology of acute decompensated heart failure, possibly due to lack of a robust definition. The European Society for Cardiology has recently published guidelines for the diagnosis and treatment of acute heart failure.[1] Martin Cowie (London) presented data from four surveys: the London Heart Failure Studies, the EuroHeart Failure Survey, the EFFECT study and the Acute Decompensated Heart Failure National Registry (ADHERE), which although not all strictly epidemiological were conducted in relevant, relatively unselected populations. On the basis of these data, it was concluded that the typical acute heart failure patient admitted to hospital will be aged >70 years, equally likely to be male or female, will have many other co-morbidities and, for those undergoing echocardiography, less than half will have a left ventricular ejection fraction (LVEF) <40%. Hospital mortality rates are between 4% and 9%, increasing to 30% or more by 12 months. There is a high risk of rehospitalisation within 3 months. A minority of patients are under the care of a cardiologist. Length of hospital stay is longer in Europe, which may account for the lower rate of early readmission, compared with North America.

In a presentation on the inpatient management of acute heart failure, Kenneth McDonald (Dublin) stated that optimisation of in-patient care improves outcomes, but requires significant changes in management strategies. All patients hospitalised with heart failure should be placed in the care of a cardiologist leading a multidisciplinary care team, as this results in more complete investigation, better use of proven therapies and better outcomes. Screening of admissions is required to identify relevant cases. Patient and family education (to optimise self care), structured care and discharge planning (**Table 1**) and risk stratification for readmission are essential to optimise outcomes.

Table 1. The 2-day rule for discharge planning

Clinically improved
Off intravenous therapy for 2 days
On stable oral therapy for 2 days
Body weight stable for 2 days
Creatinine not >50% baseline value

Acute heart failure: recognition of the problem, contemporary audit data and how we move forward

An audit of the provision of heart failure care in the UK by the Health Care Commission is due to start in 2006. Results of a pilot audit in a secondary care population of 600,000 (tertiary care ~1.2 million) were presented by Andrew Clark (Kingston-upon-Hull). Between March 2003 and June 2005, 3013 patients had 4336 admissions for heart failure. Of these, 19% died during the index admission and 43% died subsequently. The mean length of stay for patients who were discharged alive was 12 days, compared with 15 days for patients who died in hospital. The survival rate for patients treated in a cardiology department (n=600) was 81% at

1 year compared with 53% for non-cardiology patients (n=2413). Overall, non-cardiology patients without an echocardiogram had the worst outcome and cardiology patients with an echocardiogram had the best outcome. The audit identified a number of problems associated with data collection, including an incompatibility in recording methods which meant that no data were available on drug therapy and diagnostic coding errors.

Data on 80 patients from a Heart Failure Nurse Specialist service, which provides community support for patients with a primary diagnosis of heart failure in a predominantly Asian community in Bradford, were presented by Mary Crawshaw-Ralli (Bradford). The majority of patients were referred from general medicine and care of the elderly. Most patients were aged >70 years, 70% were male, 80% had ischaemic heart disease, most were in New York Heart Association (NYHA) functional class III at referral, and 38% of patients had a history of renal disease and 29% of respiratory disease. Patients referred from cardiology departments were generally receiving more appropriate drugs and dosages; however, many patients were confused about their medication. On referral, 89% of patients were receiving an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker, but only 38% were receiving a beta-blocker. A key finding was that outpatient titration of drugs to their optimal dose was a time-consuming process for nurses and patients, and that this should be taken into consideration by physicians treating patients in hospital prior to discharge.

Three audits of heart failure in general practice were presented by Nigel Rowell (Middlesborough). Data on the use of B-type natriuretic peptide (BNP) testing showed that there was considerable variation between different practices. Approximately one-third of patients tested had normal BNP values (0–150 pg/ml), one-third had mid-range values (151–500 pg/ml) and one-third had high BNP levels (>500 pg/ml). Only patients with high BNP levels were referred to the local heart failure clinic for investigation, which helped reduce waiting times for heart failure clinics. Other datasets suggest that few patients are missed by this process. Of 60 patients (average BNP level 2025 pg/ml) referred to the heart failure clinic, only eight had left ventricular systolic dysfunction (LVSD) (average BNP 4829 pg/ml). Referrals might be further reduced by using screening with electrocardiography; an audit is currently underway and findings will be reported next year. Finally, a survey of the prescribing practice of 37 GPs reported that 70% were confident to prescribe beta-blockers and 80% ACE inhibitors provided there was nurse support for monitoring patients' clinical status and renal function.

John Baxter (Consultant Geriatrician, Sunderland) presented data on the development of a heart failure service to improve outcomes in older patients with heart failure. Prior to implementation of the new service >30% of heart failure patients were readmitted to hospital within 3 months of discharge, and inpatient mortality was 15%. The new heart failure service included rapid-access echocardiography, supported discharge from hospital, with a visit from a heart failure nurse within 10 days post-discharge, and a heart failure clinic dedicated to elderly patients with follow-up within 4 weeks of discharge. Following implementation of this service, 3-month readmission rates fell by 50%, and prescribing rates for ACE inhibitors and beta-blockers improved dramatically. However, beta-blockers were poorly tolerated in some elderly patients. It was concluded that implementation of current evidence-based guidelines for the treatment of elderly patients with heart failure can improve outcomes.

A 5-year audit of data from patients using the Glasgow Heart Failure Liaison Service, a specialist nurse service, was presented by Kirstin Russell (Glasgow). Following initiation of the service in 2000, beta-blocker prescribing had increased from 49% to 63%. The number of patients using the service had increased from 900 to 1189 and was growing. Average readmissions per patient had decreased from 2.2 to 1.8, and multiple readmissions were also reduced. By December 2004, 35% of patients using the service had died; the primary cause was chronic heart failure in 35%. Further involvement of palliative care teams and community pharmacists was thought desirable.

An overview of the treatment of acute heart failure in the UK compared with the rest of Europe was given by John Cleland (Kingston-upon-Hull), based on data from the EuroHeart Failure survey. Fewer heart failure patients in the UK are treated by a cardiologist, the UK has the lowest utilisation of basic diagnostic tests and higher than average death and readmission rates. Once LVSD has been demonstrated, the use of ACE inhibitors and beta-blockers is similar to the rest of Europe, but spironolactone is used less. The major weakness in the management of heart failure in the UK appears to be inadequate investigation of suspected heart failure.

Current BSH initiatives to improve the multidisciplinary approach to heart failure therapy were presented by Theresa McDonagh (London). An integrated heart failure service should include a cardiologist with expert knowledge of heart failure, specialised heart failure nurses, and additional specialists including geriatricians, pharmacists and GPs. Accordingly, revision of the Specialist Registrar curriculum to train cardiologists with expertise in heart failure is currently ongoing. The BHF nurse training programme now includes 183 nurses in the UK. 'Standards of care', defining minimum heart failure service requirements are now published on the BCS website. In addition, minimum cardiac workforce requirements, have recently been specified by the BCS. It was concluded that the required components of a heart failure programme are: local community guidelines, heart failure clinics, diagnostic services and therapeutic services. Standards will be published on the BSH website shortly. Finally, an audit of HF services is planned to start in 2006.

Heart failure research

Four programmes funded by the BHF were presented.

The MONICA (Multinational Monitoring of Trends and Determinants in Cardiovascular Disease) survey included 2000 randomly selected individuals from North Glasgow.[2] Theresa McDonagh reported new data from the long-term follow-up of these patients conducted over a mean of 12.2 years, showing that LVSD in the community has a poor outcome even in asymptomatic patients, and that BNP and N-terminal atrial natriuretic peptide (NT-ANP) were both independent predictors of mortality. Mean survival rate was 12.4 years in patients with a normal ejection fraction (EF), falling to 8.9 years in patients with an EF 30%. Patients with BNP and/or NT-ANP levels in the highest quartile showed a fivefold increase in mortality compared with those with values in the lowest quartile ($p<0.0001$).

Beta-blockers have effects at both $beta_1$- and $beta_2$-adrenoceptors, with some beta-blockers being more selective than others. Most of the benefits of beta-blockers in heart failure are thought to be mediated by inhibition of the $beta_1$-adrenoceptor. The role of the $beta_2$-adrenoceptor, which has complex signalling pathways, is less clear. Sian Harding (London) presented evidence that activation of, or over-expression of, the $beta_2$-adrenoceptor has a negative inotropic effect mediated through the Gi protein pathway rather than through cyclic AMP, which could be reversed by chronic carvedilol exposure. Also, beta-blockers (other than carvedilol) stimulate p38-MAP-kinase production leading to negative inotropic effects. Carvedilol appears to have many properties that set it aside from other beta-blockers. These new data may help design even more effective agents.

There are three key aspects to energy metabolism: substrate utilisation, mitochondrial function and ATP transport and utilisation, all of which can be limiting steps in patients with heart failure. The heart consumes about 6 kg ATP per day. Genetically modified experimental models can be used to determine the role of the different pathways involved in cardiac energetics. Results from creatine kinase and guanodinoacetate methyl transferase knockout models suggest that energy 'starvation' may result in heart failure. Stefan Neubauer (Oxford) reported that cardiac magnetic resonance imaging and spectroscopy are highly suitable non-invasive methods for the assessment of the functional and metabolic consequences of heart failure, both in humans and in transgenic models, and will facilitate further evaluation of the role of cardiac energetics in heart failure. Metabolic therapy for heart failure may be feasible, and large-scale clinical trials are now required.

Medical treatment of heart failure with ACE inhibitors and beta-blockers has been shown to be effective, but response can be variable. Nikolay Nikitin (Kingston-upon-Hull) presented data from a study to establish whether scar extent assessed by cardiac magnetic resonance (CMR) with delayed enhancement (DE) could predict response to therapy. Thirty-eight patients with NYHA class II–III heart failure and EF <45% who had been receiving optimal pharmacological therapy for at least 6 months underwent CMR with delayed gadolinium enhancement to assess total scar mass and scar extent at baseline and after 12 months. Twenty-four patients showed DE, of these, 23 had ischaemic aetiology; in the 14 patients with no DE, aetiology was predominantly non-ischaemic. Mean scar mass was 24±9 g. There were no differences in clinical or CMR-derived parameters at baseline. However, at 12 months, patients with no DE had lower left ventricular end-diastolic and -systolic volumes, and increased EF compared with baseline. A strong negative correlation between scar extent and change in EF was reported. It was concluded in patients with heart failure due to LVSD the presence of scar and scar extent predicts the risk of persistent adverse left ventricular remodelling despite adequate treatment with ACE inhibitors and beta-blockers.

HOT topics – looking to the future

Data from several key clinical trials in heart failure were reported.

MAGIC

Implantation of skeletal myoblasts into the damaged myocardium has shown promising results in early phase trials.[3] Details of the ongoing MAGIC* study were presented by William McKenna (London). This study aims to assess the safety and efficacy of autologous skeletal myoblasts administered at two dose levels (400 or $800x10^6$ cells) versus placebo in patients with ischaemic heart failure undergoing coronary bypass and defibrillator implantation. Defibrillators are required due to the possible increased risk of sudden arrhythmic death associated with this therapy. All patients must have had a previous myocardial infarction with akinesia affecting at least three accessible contiguous segments, an EF of 15–35% and NYHA class I–III heart failure. The primary endpoints are recovery of contractility at 6 months and change in LVEF. The study is currently ongoing in 50 centres (5 in the UK) and aims to recruit 300 patients with a follow-up of 2 years. To date, 250 patients have been screened, 89 have been treated and 10 have completed the 2-year follow-up. A recent verbal report suggested that enrolment into the study had been terminated due to poor recruitment and disappointing initial results.

CARE-HF

The CARE-HF study was a randomised trial of cardiac resynchronisation therapy (CRT) in patients with advanced heart failure due to LVSD and dyssynchrony receiving standard medications. The results showing a clear benefit of CRT on morbidity and mortality were published earlier this year.[4] Data from an extension study, in which the duration of follow-up increased from 29.4 to 36.4 months, were presented by John Cleland. During the extension phase, despite 25% of patients crossing over to CRT, there were an additional 19 deaths in the CRT group and 34 in the control group. It was concluded that CRT reduces mortality due to reductions in sudden death and death due to worsening heart failure, and improves symptoms. In about 15% of patients the changes are sufficiently striking to consider that CRT may have caused remission of heart failure.[5]

REVIVE and SURVIVE

Levosimendan is a novel calcium sensitiser with inotropic and vasodilatory properties; previous studies in heart failure have shown encouraging results. Results from two studies of levosimendan, REVIVE and SURVIVE, which were reported at the American Heart Association,[3] were presented by John Cleland. REVIVE was a double-blind comparison of a 24-hour intravenous infusion of levosimendan versus placebo in 600 patients hospitalised with heart failure

Definitions of acronyms

Trial acronym	Definition
BEAUTIFUL	Morbidity–mortality evaluation of the I_f inhibitor ivabradine in patients with CAD and left ventricular dysfunction
CARE-HF	Cardiac resynchronisation in heart failure
ESSENTIAL	The studies of oral enoximone therapy in advanced heart failure
ETNA	European trial of nesiritide in acute heart failure
MAGIC	Myoblast autologous grafting in ischaemic cardiomyopathy
REVIVE	Randomised multicentre evaluation of intravenous levosimendan efficacy versus placebo in the short term treatment of decompensated heart failure
SURVIVE	Survival of patients with acute heart failure in need of intravenous inotropic support trial

(EF <35%) and breathlessness at rest that failed to respond to conventional treatment. Clinical outcome (improved/unchanged/worse) over 5 days following randomisation showed that more patients were improved on levosimendan than on placebo (p=0.015); patient global assessment also showed a significant improvement (p<0.001). There was a significant reduction in BNP levels and duration of hospitalisation with levosimendan but not in mortality.

The SURVIVE study randomised 1327 patients, hospitalised with acute heart failure (EF 30%) and breathlessness or oliguria despite appropriate treatment, to a 24-hour intravenous infusion of levosimendan or dobutamine. This was a very high risk population. Although there was an early trend to benefit with levosimendan, this was not maintained beyond its period of haemodynamic activity. Further trials of levosimendan in heart failure are now required. A meta-analysis of results is consistent with a mortality benefit of levosimendan compared with dobutamine.[3]

ESSENTIAL

Enoximone is a phosphodiesterase III (PDE III) inhibitor with positive inotropic properties. Previous studies of PDE III inhibitors, conducted before the widespread use of beta-blockers in heart failure, showed increased mortality, and development of these agents for heart failure was therefore stopped. However, following the introduction of beta-blockers, which would be expected to attenuate the adverse cardiac effects of PDE III inhibitors, research in heart failure has recommenced. The ESSENTIAL study, presented by Henry Dargie (Glasgow), was designed to evaluate the effect of oral enoximone plus beta-blocker therapy in patients with severe heart failure (NYHA III–IV). Overall, 87% of patients were receiving beta-blockers. The evaluation of time to all-cause mortality showed no difference between enoximone and placebo; however, there was no evidence of excess mortality with enoximone. Similarly, no benefit was reported in patient global assessment or in the 6-minute walk test. There may have been some benefit in patients with more severe symptoms.

ETNA

BNP is produced by the body in response to heart failure; it improves cardiac performance by inducing balanced vasodilation, neurohormonal antagonism, diuresis and natriuresis. Nesiritide (human BNP) has been shown to have beneficial haemodynamic effects in acute decompensated heart failure.[6] However, recent studies have suggested an association with worsening renal function and increased mortality.[7,8] Details of a new study to evaluate the use of nesiritide in acute decompensated heart failure were presented by Henry Dargie. ETNA is a randomised controlled trial of intravenous nesiritide versus placebo administered in addition to standard care. The infusion can be administered for up to 96 hours in addition to standard medical therapy and patients will be followed-up for 180 days. ETNA aims to recruit 2000 patients with acute decompensated heart failure and dyspnoea at rest or on minimal exertion. The primary endpoints are dyspnoea and well-being at 3 and 6 hours. The secondary endpoints assess morbidity and safety.

BEAUTIFUL

Ivabradine is an I_f inhibitor, which delays diastolic depolarisation in the sinus node causing a reduction in heart rate, thereby reducing myocardial oxygen demand, but with no effect on cardiac contractility. Ivabradine has recently been licensed for the treatment of chronic stable angina resistant to beta-blocker therapy. The design of the BEAUTIFUL study, to evaluate ivabradine (7.5 mg twice daily) in patients with CHD and left ventricular dysfunction (LVEF 39%) was presented by Henry Dargie. The study, which aims to recruit 10,000 patients, is placebo controlled, and both treatments will be administered in addition to optimal therapy plus beta-blockers. The primary endpoint is a composite of cardiovascular death, myocardial infarction and hospitalisation for acute heart failure. Another study (SHIFT) to evaluate ivabradine in the treatment of chronic heart failure is planned.

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A report of the BSH 2005 AGM can be found on the BSH website.

Acknowledgements

The BSH is grateful to: Takeda UK Ltd (Gold sponsor), ExtraLife and Pfizer Ltd (Silver sponsors), A. Menarini Pharma UK, Bayer HealthCare, British Heart Foundation, Guidant Ltd, Kimal plc, Medtronic Ltd, Myogen, Response Medical and Servier Laboratories for their contributions towards this meeting, and to the '**Friends of BSH**': A. Menarini Pharma, Bayer Healthcare, ExtraLife, Guidant, Medtronic, Pfizer, Servier and Takeda for their continuous support throughout the year.

Becoming a Member or a Friend of the BSH

Membership is open to anyone involved in the diagnosis, management or science of HF. If you are interested in becoming a Member or Friend of the BSH, please contact:

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