News from the BSH 15th Annual Autumn Meeting

The 15th Annual Autumn Meeting of the British Society for Heart Failure (BSH) entitled 'Heart failure, a multidisciplinary approach,' was held on 29th–30th November 2012 at the Queen Elizabeth II Conference Centre in London. Over 500 delegates attended the meeting, which was introduced by BSH Chair Dr Suzanna Hardman. Colin Cunnington reports on some of the highlights.

Mineralocorticoid receptor antagonists

Professor Faiez Zannad (Université de Lorraine, Nancy, France), the first of two guest lecturers, who has been an investigator in three major randomised controlled trials (RCT) of mineralocorticoid receptor antagonists (MRA) in heart failure,[1-3] opened the first session.

There was a particular focus on the recent EMPHASIS-HF trial,[3] which recruited heart failure (HF) patients with left ventricular systolic dysfunction (ejection fraction [EF] ≤30%, or EF 30-35% with QRS duration >130 ms) and mild symptoms (New York Heart Association [NYHA] class II). Eplerenone treatment resulted in a 37% relative risk reduction in the composite primary end point of cardiovascular death or HF hospitalisation compared with placebo.[3] This benefit was observed despite high levels of concomitant treatment with angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs), and beta blockers. Furthermore all-cause mortality was significantly reduced by 24%, and HF hospitalisation by 48%. Subsequent analyses have shown that eplerenone reduces repeat HF hospitalisations[4] and the incidence of new atrial fibrillation (AF).[5]

These findings, in combination with data from RALES[1] (NYHA III-IV patients with reduced EF) and EPHESUS[2] (reduced EF following myocardial infarction [MI]) are now reflected in the updated 2012 European Society of Cardiology HF guidelines,[6] with MRAs being given an upgraded 1A recommendation in HF with reduced EF (HF-REF).

Potential mechanisms underlying the clinical benefits of MRAs in HF include antifibrotic mechanisms that slow HF progression and cardiac remodelling, and reduce arrhythmogenesis. Indeed, the benefit of spironolactone was greatest in patients with higher baseline serum markers of cardiac fibrosis,[7] raising the future possibility of selectively treating these HF patients.

Clinical benefit of MRAs is the subject of additional studies including TOPCAT, a trial of spironolactone in patients with HF and preserved ejection fraction (HF-PEF, EF ≥45%). This has finished recruiting and should report soon. Two trials (ALBATROSS and REMINDER) are underway investigating early aldosterone blockade in ST-elevation MI (STEMI) and work continues in the development of novel methods to block the deleterious actions of aldosterone.

Cardiac remodelling

Professor Marc Pfeffer (Harvard Medical School, Boston, USA) opened the session on cardiac remodelling with a fascinating historical review of the biology of ventricular remodelling, beginning with animal models, progressing to observations in humans, and finally to large-scale clinical trials of drugs to prevent or reverse the cardiac maladaptation to stress and injury. This inspiring lecture reflected many years of his research with important influences being his late wife, Janice Pfeffer, and Professor Eugene Braunwald. It was intriguing to learn of the many years of 'bench-to-bedside' research that culminates in a clinical trial that changes the face of medicine, such as the SAVE trial (captopril following MI).[8] Professor Pfeffer (**figure 1**) concluded on a positive note talking about the potential role of stem cell therapy as a viable treatment option in HF patients.[9]

Dr Robin Weir (Hairmyres Hospital, Glasgow) spoke on the current state of non-invasive imaging in systolic dysfunction, highlighting

Figure 1. Professor Marc Pfeffer

the fact that EF measurements by different modalities vary and are not interchangeable. Cardiac magnetic resonance remains the gold standard method for assessing ventricular function, although access is still limited in some areas. Professor Iain Squire (Glenfield Hospital, Leicester) gave an update on the role of biomarkers in HF, particularly the use of B-type natriuretic peptide (BNP) to guide HF therapy.[10] There remains significant doubt about the clinical benefit of this approach and it was emphasised that patients should be treated with maximum-tolerated doses of ACE inhibitors/ARBs, beta blockers and MRAs, irrespective of BNP levels.

Atrial fibrillation

A further session addressed the complex issue of AF in HF. First, Dr Christopher George (Cardiff University) gave an illuminating lecture on the mechanisms underlying arrhythmogenesis in HF, focusing on a shift in thinking away from traditional therapies that target cell-surface ion channels, towards modulation of intracellular drivers

of arrhythmogenesis, including ryanodine receptor-dependent calcium signalling.[11]

Professor John Cleland (University of Hull) emphasised the clinical importance of AF, particularly when it occurs after the onset of HF, when it is associated with worse outcomes.[12] A number of drugs including ivabradine appear to be associated with an increased risk of AF. RCT data has not indicated any benefit of rhythm control over rate control in HF, with a tendency towards worse outcomes.[13,14] This is also true where dronedarone is used.[15] Ranolazine has been noted to reduce arrhythmias (including AF) following MI[16] and, interestingly, is currently being tested in combination with low-dose dronedarone in paroxysmal AF in the HARMONY trial. Vanoxerine has shown promise in animal models of AF.[17] Professor Cleland also discussed the importance of anticoagulation of HF patients with AF, even if sinus rhythm is restored, with warfarin or possibly one of the new oral anticoagulant drugs (dabigatran, rivaroxaban and apixaban).

Dr Stephen Furniss (East Sussex Healthcare NHS Trust, Hastings) summarised the evidence for catheter ablation for AF in HF. Registry data[18,19] and small non-randomised studies[20] have suggested a possible benefit of ablation over medical therapy, while a recent small RCT indicated an improvement in certain measures of cardiac function with ablation,[19] although EF is especially subject to error during AF. Larger RCTs of ablation are needed to establish the efficacy of AF ablation in HF. Dr Rakesh Sharma (Royal Brompton Hospital, London) discussed the controversial topic of cardiac resynchronisation therapy (CRT) in patients with AF. Again, non-randomised studies have indicated a significant benefit of CRT in AF.[21] However, RCT data remain sparse. The two trials (MUSTIC-AF[22] and RAFT[23]), which included limited patients with AF did support CRT use in AF. Notwithstanding the lack of trial data, CRT devices are frequently implanted in AF patients in Europe.[24] As with AF ablation, larger RCTs are warranted.

Acute heart failure

Acute HF has seen relatively few advances in recent years compared with chronic HF. Dr Simon Williams (University Hospital of South Manchester) reviewed a selection of recent studies in acute HF from a medical perspective. Serelaxin infusion reduced dyspnoea but there was no effect on early prognosis compared to placebo (RELAX-AHF[25]); there was, however, a reduction in death at six months. Nesiritide, which has been used clinically in acute HF in the USA, failed to show any benefit in ASCEND-HF, a large RCT.[26] Furthermore, there was no difference in continuous or bolus intravenous diuretic regimes in the DOSE trial.[27] Dr Robyn Smith (Golden Jubilee National Hospital, Glasgow) gave a practical lecture on management of acute HF from an intensive care perspective, and Mr Steve Tsui (Papworth Hospital, Cambridge) discussed surgical interventions in acute HF, with a particular reference to his algorithm for mechanical circulatory support in those awaiting urgent transplantation.

Young Investigators' Award

Three abstracts of outstanding quality were presented at this year's Young Investigators' Award session.

Dr Syed Ahsan (The Heart Hospital, London) studied the effects of multiple biventricular pacing configurations using a novel octapolar LV pacing electrode in an acute physiological study of patients referred for CRT. He showed that selection of pacing configuration on an individualised basis could improve LV haemodynamics, as measured invasively by LV dP/dt_{max}.

In a large prospective study of more than 1,000 patients, Dr Colette Jackson (University of Glasgow) investigated the prognostic significance of microvolt T-wave alternans (MTWA) testing in HF. This showed no difference in mortality if patients were stratified according to MTWA (either positive, negative or indeterminate), and concluded that MTWA testing is not a useful strategy to identify HF patients who may benefit from an implantable cardioverter-defibrillator (ICD).

Finally, Dr Donah Zachariah (Portsmouth Hospitals NHS Trust) investigated the impact of chronic kidney disease (CKD) on secondary prevention therapy following primary percutaneous coronary intervention. In a retrospective, multicentre UK study, she demonstrated that current prescribing rates of secondary prevention medication are high compared to historical data, however ACE inhibitor usage was significantly lower in patients with CKD.

All presentations were of a very high standard with Dr Colette Jackson gaining the Young Investigators' award. Abstracts from these three winning entries can be found on www.bjcardio.co.uk

Other sessions in brief

Professor Theresa McDonagh (King's College Hospital, London) summarised the 2012 ESC guidelines on the management of acute and chronic HF.[6] These guidelines incorporate 19 new RCTs (mainly HF-REF). The main changes since 2008 relate to:

- an expansion in the role of MRAs (as described above)
- a new indication to consider ivabradine treatment (based on the SHIFT trial[28])
- expanded indications for CRT
- the role of coronary revascularisation in HF (based on the STICH trial[29])
- recognition of the growing use of ventricular assist devices, and
- the emergence of transcatheter valve interventions, including transcatheter aortic valve implantation and percutaneous mitral valve repair, in patients with unacceptably high surgical risk.

Professor Henry Dargie (University of Glasgow) gave important insights from the 2012 National Heart Failure Audit (available to download from www.bsh.org.uk). Disappointingly, mortality remains high following admission with decompensated HF (11.1% in-patient mortality; 37.3% at 12 months) with limited numbers gaining earlier access to the specialist cardiology services associated with improved outcomes. Following this, Sir Mike Richards (Department of Health) detailed forthcoming national strategies to reduce the burden of cardiovascular disease in the modern NHS. It is to be hoped that this will include acute hospital HF care.

In a thought-provoking session on palliative care, Dr Karen Hogg (Glasgow Royal Infirmary) Dr Nigel Rowell (Endeavour Practice, Middlesbrough), Mrs Annie

MacCallum (NHS Gloucestershire), Dr John Baxter (Sunderland Royal Hospital) and Mr Michael Connelly (University Hospital of South Manchester) covered the multidisciplinary approach to end-of-life care. Topics included Anticipatory Care Pathways, practical advice on symptom control at end-of-life and in the elderly, ICD deactivation discussions, and holistic support of the HF patient and their carers.

The importance of heart rate was discussed in a dedicated session. Professor Andrew Clark (Castle Hill Hospital, Hull) demonstrated the epidemiological evidence that underpins the association between lower heart rate and longer life. Professor Dargie discussed the robust evidence to support beta-blockade, and Dr Suzanna Hardman (Whittington Hospital, London) explored the mechanisms of action of ivabradine, and possible recommended usage in light of SHIFT,[28] its recent license in HF, and publication of the NICE STA guidance. Dr Roy Gardner (Golden Jubilee National Hospital, Glasgow) finished with optimisation of complex devices, including the recent MADIT-RIT study.[30]

Dr Alison Duncan (Royal Brompton Hospital, London) presented a case of HF secondary to ischaemic cardiomyopathy with concomitant severe mitral regurgitation. An expert panel of Dr Alison Seed (Blackpool Victoria Hospital), Mr Ben Bridgewater (University Hospital of South Manchester) and Dr Jonathan Byrne (King's College Hospital, London) discussed the possible medical, surgical, and interventional therapeutic interventions respectively. Dr Steve Shaw (University Hospital of South Manchester), Dr Jim Moore (Gloucestershire Heart Failure Service) and Mrs Jayne Masters (University Hospital Southampton NHS Trust) presented a series of HF cases provoking animated and informative discussions.

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References

A full reference list for this report is published online at www.bjcardio.co.uk.

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