

# News from the BSH 16<sup>th</sup> Annual Autumn Meeting



The 16<sup>th</sup> Annual Autumn Meeting of the British Society for Heart Failure (BSH) entitled '*Making sense of acute heart failure*', was held on 28–29 November 2013 at the Queen Elizabeth II Conference Centre in London. Over 700 delegates attended the meeting, which was introduced by BSH Chair Professor Andrew Clark. Colin Cunningham reports on some of the highlights.

## Counting the cost of acute heart failure

In the first keynote lecture, Professor John McMurray (BHF Cardiovascular Research Centre, Glasgow) began by addressing the definition of acute heart failure (HF). He felt the term 'acute' was unhelpful, as it can be applied to a broad spectrum of clinical presentation, from the rapid onset of acute pulmonary oedema, to the subacute deterioration in chronic HF symptoms (predominantly peripheral oedema) that culminates in hospitalisation. Accordingly, the new 2013 American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) HF guidelines refer to 'the hospitalised patient', rather than 'acute HF'.<sup>1</sup> In contrast to treatments for chronic HF, treatments for acute HF are not supported by randomised-controlled trials (RCTs). Indeed, other than venous thromboembolism prophylaxis, no treatment for acute HF is supported by Class 1 Level A evidence.<sup>2</sup> Nonetheless, he stressed the importance of up-titration of chronic HF therapies, such as angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs), beta blockers and mineralocorticoid receptor antagonists (MRA). Updated National Institute for Health and Care Excellence (NICE) guidelines for acute HF are currently in preparation.

In the 2012/13 National Heart Failure Audit (available at [www.bsh.org.uk](http://www.bsh.org.uk)), in-hospital mortality from acute HF was 9.4%. This is considerably higher than the 3–4% seen in large US registries;<sup>3,4</sup> however, mortality at 30 days (14.9%) is equivalent, and, thus, the observed difference in in-hospital mortality may be artefactual. Importantly, the early risk of death following discharge after a HF hospitalisation was emphasised, with mortality

increasing with the frequency and duration of hospitalisations.<sup>5</sup> Furthermore, there is a high risk of early re-admission (25%), although only 35% of patients are re-admitted due to HF,<sup>6</sup> highlighting the extensive comorbidity of HF patients, and the destabilising effect of acute HF on comorbidities.

Professor John Cleland (Imperial College, London) discussed triggers for hospitalisation. An identifiable cause for decompensation is apparent in 60% of cases,<sup>7</sup> including pneumonia, ischaemia and arrhythmia. The importance of hypertension underlying the development of systolic HF was emphasised.<sup>8</sup> Acute coronary syndromes are a less frequent cause of acute decompensation in patients with pre-existing chronic HF,<sup>9</sup> although troponin is commonly elevated in acute HF and is a marker of worse prognosis.<sup>10</sup>

Professor Theresa McDonagh (King's College Hospital, London) discussed in detail the National Heart Failure Audit, which includes data from 95% of acute trusts in England and Wales. There have been improvements over the last year: in-hospital mortality fell from 11.1% to 9.4%, and the proportion of patients undergoing echocardiography and accessing specialist HF care has increased. However, 6.1% of those who survived to discharge died within 30 days, with the risk doubling in patients not on ACE inhibitor/ARB at discharge.

## Acute heart failure trials update

Professor McMurray summarised recent RCTs in acute HF, which have been largely disappointing. The Diuretic Optimization Strategies Evaluation (DOSE) trial showed no difference in high-dose versus low-dose, or continuous versus bolus intravenous diuretics.<sup>11</sup> Serelaxin reduced dyspnoea but had no effect on early prognosis

(RELAX-AHF – Relaxin in Acute Heart Failure<sup>12</sup>); there was, however, a reduction in all-cause mortality at six months. RELAX-AHF2, a larger study of over 6,000 patients, will evaluate this further. Cardiorenal Rescue Study in Acute Decompensated Heart Failure (CARRESS-HF) demonstrated a paradoxical worsening of renal function, and no improvement in outcomes, with ultrafiltration compared with standard therapy.<sup>13</sup> Similarly, the Renal Optimization Strategies Evaluation (ROSE) trial showed no benefit of low-dose dopamine (or nesiritide) on renal function or diuresis.<sup>14</sup> In the Aliskiren Trial on Acute Heart Failure Outcomes (ASTRONAUT), aliskiren did not improve outcomes following discharge after a HF hospitalisation.<sup>15</sup>

What does the future hold for acute HF? Trial of Ularitide's Efficacy and Safety in Patients with Acute Heart Failure (TRUE-AHF) will investigate the novel natriuretic peptide ularitide following the disappointing results of nesiritide in ASCEND-HF (Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure).<sup>16</sup> ATOMIC-AHF (Acute Treatment with Omecamtiv Mecarbil to Increase Contractility in Acute Heart Failure) and COSMIC-HF (Chronic Oral Study of Myosin Activation to Increase Contractility in Heart Failure) will examine intravenous and oral forms of the cardiac myosin activator omecamtiv mecarbil, which has shown improvement in cardiac function in small studies.<sup>17</sup> Finally, SOCRATES will examine the effect of a novel soluble guanylate cyclase stimulator (BAY1021189).

## Philip Poole-Wilson lecture: beta blockers in heart failure

Professor Sian Harding (National Heart & Lung Institute, London) gave the biennial Philip Poole-Wilson lecture, entitled 'beta blockers in heart failure: active agents with unexplored potential'. This fascinating lecture chronicled

Figure 1. Professor Walter Paulus. Photo courtesy of Roy Gardner



over 20 years of research by Professor Harding and Professor Poole-Wilson into the cellular mechanisms through which beta-adrenergic receptor subtypes influence cardiomyocyte function in health and disease, via divergent cardioprotective and cardiodepressive effects. At the time of her initial experiments using isolated human myocytes from failing hearts,<sup>18</sup> beta blockers were contraindicated in HF. She illustrated how understanding of these pathways informed the contemporary use of beta blockers in HF, through landmark RCTs such as COMET (Carvedilol or Metoprolol European Trial).<sup>19</sup> Finally, Professor Harding described recent work in another cause of acute HF, takotsubo cardiomyopathy.<sup>20</sup>

## Heart failure with preserved ejection fraction

The second keynote lecture was given by Professor Walter Paulus (VU University Medical Center, Amsterdam, Netherlands) (figure 1). Via an entertaining case report, he examined the predisposing factors and triggering events that lead to acute decompensation in patients with HF with preserved ejection fraction (HeFPEF). Comorbidities, especially obesity<sup>21</sup> and diabetes mellitus,<sup>22</sup> appear central to the pathophysiology of HeFPEF through the development of a pro-inflammatory state, which promotes myocardial oxidative stress and, subsequently, cardiomyocyte hypertrophy and fibrosis.<sup>23</sup> Furthermore, recent mechanistic studies have shown how

triggering factors, such as salt-loading, can cause elevation in pulmonary capillary wedge pressure,<sup>24</sup> and thus pulmonary oedema.

Professor Alan Fraser (Cardiff University School of Medicine) gave an overview of echocardiographic assessment in HeFPEF. Long-axis systolic function is impaired in patients with HeFPEF.<sup>25</sup> Individual measures of diastolic function, such as E/e' ratio, are specific but lack sensitivity; other markers of elevated left ventricular (LV) filling pressure, such as left atrial volume index, should be taken into account. The concept of measuring diastolic function on exercise (a diastolic 'stress test') was introduced, but this remains a research tool at present.

Professor Martin Cowie (Imperial College, London) discussed treatment of HeFPEF. ACE inhibitors and ARBs, which are beneficial in HF with reduced ejection fraction (EF), do not improve outcome in HeFPEF;<sup>26,27</sup> however, patients with HeFPEF frequently have comorbidities (e.g. hypertension or diabetes) that warrant treatment with these agents. Most recently, the TOPCAT (Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist) trial (presented as a late-breaking clinical trial at the AHA Scientific Sessions, November 2013) demonstrated no effect of spironolactone on the primary composite end point of cardiovascular death or HF hospitalisation, although the secondary end point of HF hospitalisation was significantly reduced. Finally, Dr Luke Howard (National

Heart & Lung Institute, London) discussed the pulmonary hypertension syndromes associated with HF.

## Other sessions in brief

The Young Investigators' Award was contested by Dr Pierpaolo Pellicori, Dr Ahmad Shoaib (both Castle Hill Hospital, Hull) and Dr Donah Zachariah (Portsmouth Hospitals NHS Trust). Three excellent abstracts were presented. Dr Pellicori was awarded the prize for his work in characterising HF patients using cardiac magnetic resonance according to QRS morphology. Dr Jane Cannon (Golden Jubilee National Hospital, Glasgow) was awarded the inaugural BSH Research Fellowship.

Aspects of acute HF service provision were discussed in a stimulating multi-disciplinary session. Dr Nigel Rowell (Endeavour Practice, Middlesbrough) presented his view on ideal practice through the eyes of a commissioner. Dr Gerry Carr-White (St Thomas' Hospital, London) described novel methods using B-type natriuretic peptide to prioritise inpatient specialist services, and Mrs Jayne Masters (Southampton University Hospitals NHS Trust) and Dr Jackie Taylor (Glasgow Royal Infirmary) gave overviews of inpatient HF team models. Dr Angus Nightingale (Bristol Royal Infirmary) discussed HF post-MI, Dr Suzanna Hardman (Whittington Hospital, London) described the workings of a dedicated HF unit, and Dr Jim Moore (Stoke Road Surgery, Cheltenham) and Mrs Annie MacCallum (Gloucester Care Services NHS Trust) presented their successful community-based model.

Two further clinical sessions discussed specific aspects of HF treatment. Dr Martin Thomas (The Heart Hospital, London) addressed diuretic resistance, particularly the role of ultrafiltration, Dr Dominic Kelly (Hampshire Hospitals NHS Foundation Trust) discussed arrhythmias in HF, Dr John Baxter (Sunderland Royal Hospital) gave his amusing take on preventing HF decompensation in patients hospitalised for other reasons, and Dr Simon Williams (University Hospital of South Manchester) summarised the management of myocarditis. Dr Derek Connelly (Golden Jubilee National Hospital, Glasgow) discussed indications for implantable cardioverter-defibrillators, and Dr Carol Whelan (Royal

Free Hospital, London) and Dr Mark Petrie (Golden Jubilee National Hospital, Glasgow) gave overviews on cardiac amyloidosis and peripartum cardiomyopathy, respectively.

Finally, focusing on the most severe end of the HF spectrum, Dr Roy Gardner (Golden Jubilee National Hospital, Glasgow) rationalised management of the hypotensive patient, Dr Peter Cowburn (Southampton University Hospitals NHS Trust) described his experience of cardiac resynchronisation therapy in severely unwell patients, and Dr Steve Shaw

(University Hospital of South Manchester) gave an update on mechanical circulatory support ●

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### Further information

Future BSH meetings:

- 6<sup>th</sup> Heart Failure Day for Training and Revalidation, 20 March 2014

- 4<sup>th</sup> Heart Failure Nurse Study Day, 21 March 2014
- 17<sup>th</sup> Annual Autumn Meeting, 27–28 November 2014

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## References

1. Yancy CW, Jessup M, Bozkurt B *et al.* 2013 ACCF/AHA guideline for the management of heart failure: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation* 2013;**128**:1810–52. <http://dx.doi.org/10.1016/j.jacc.2013.05.020>
2. McMurray JJ, Adamopoulos S, Anker SD *et al.* ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2012;**33**:1787–847. <http://dx.doi.org/10.1093/eurheartj/ehs104>
3. Steinberg BA, Zhao X, Heidenreich PA *et al.* Trends in patients hospitalized with heart failure and preserved left ventricular ejection fraction: prevalence, therapies, and outcomes. *Circulation* 2012;**126**:65–75. <http://dx.doi.org/10.1161/CIRCULATIONAHA.111.080770>
4. Gheorghiade M, Abraham WT, Albert NM *et al.* Systolic blood pressure at admission, clinical characteristics, and outcomes in patients hospitalized with acute heart failure. *JAMA* 2006;**296**:2217–26. <http://dx.doi.org/10.1001/jama.296.18.2217>
5. Solomon SD, Dobson J, Pocock S *et al.* Influence of nonfatal hospitalization for heart failure on subsequent mortality in patients with chronic heart failure. *Circulation* 2007;**116**:1482–7. <http://dx.doi.org/10.1161/CIRCULATIONAHA.107.696906>
6. Dharmarajan K, Hsieh AF, Lin Z *et al.* Diagnoses and timing of 30-day readmissions after hospitalization for heart failure, acute myocardial infarction, or pneumonia. *JAMA* 2013;**309**:355–63. <http://dx.doi.org/10.1001/jama.2012.216476>
7. Fonarow GC, Abraham WT, Albert NM *et al.* Factors identified as precipitating hospital admissions for heart failure and clinical outcomes: findings from OPTIMIZE-HF. *Arch Intern Med* 2008;**168**:847–54. <http://dx.doi.org/10.1001/archinte.168.8.847>
8. Levy D, Larson MG, Vasan RS, Kannel WB, Ho KK. The progression from hypertension to congestive heart failure. *JAMA* 1996;**275**:1557–62. <http://dx.doi.org/10.1001/jama.1996.03530440037034>
9. Torp-Pedersen C, Poole-Wilson PA, Swedberg K *et al.* Effects of metoprolol and carvedilol on cause-specific mortality and morbidity in patients with chronic heart failure – COMET. *Am Heart J* 2005;**149**:370–6. <http://dx.doi.org/10.1016/j.ahj.2004.10.002>
10. Peacock WFT, De Marco T, Fonarow GC *et al.* Cardiac troponin and outcome in acute heart failure. *N Engl J Med* 2008;**358**:2117–26. <http://dx.doi.org/10.1056/NEJMoa0706824>
11. Felker GM, Lee KL, Bull DA *et al.* Diuretic strategies in patients with acute decompensated heart failure. *N Engl J Med* 2011;**364**:797–805. <http://dx.doi.org/10.1056/NEJMoa1005419>
12. Teerlink JR, Cotter G, Davison BA *et al.* Serelaxin, recombinant human relaxin-2, for treatment of acute heart failure (RELAX-AHF): a randomised, placebo-controlled trial. *Lancet* 2013;**381**:29–39. [http://dx.doi.org/10.1016/S0140-6736\(12\)61855-8](http://dx.doi.org/10.1016/S0140-6736(12)61855-8)
13. Bart BA, Goldsmith SR, Lee KL *et al.* Ultrafiltration in decompensated heart failure with cardiorenal syndrome. *N Engl J Med* 2012;**367**:2296–304. <http://dx.doi.org/10.1056/NEJMoa1210357>
14. Chen HH, Anstrom KJ, Givertz MM *et al.* Low-dose dopamine or low-dose nesiritide in acute heart failure with renal dysfunction: The ROSE Acute Heart Failure Randomized Trial. *JAMA* 2013;published online. <http://dx.doi.org/10.1001/jama.2013.282190>
15. Gheorghiade M, Bohm M, Greene SJ *et al.* Effect of aliskiren on postdischarge mortality and heart failure readmissions among patients hospitalized for heart failure: the ASTRONAUT randomized trial. *JAMA* 2013;**309**:1125–35. <http://dx.doi.org/10.1001/jama.2013.1954>
16. O'Connor CM, Starling RC, Hernandez AF *et al.* Effect of nesiritide in patients with acute decompensated heart failure. *N Engl J Med* 2011;**365**:32–43. <http://dx.doi.org/10.1056/NEJMoa1100171>
17. Cleland JG, Teerlink JR, Senior R *et al.* The effects of the cardiac myosin activator, omecamtiv mecarbil, on cardiac function in systolic heart failure: a double-blind, placebo-controlled, crossover, dose-ranging phase 2 trial. *Lancet* 2011;**378**:676–83. [http://dx.doi.org/10.1016/S0140-6736\(11\)61126-4](http://dx.doi.org/10.1016/S0140-6736(11)61126-4)
18. Harding SE, Jones SM, O'Gara P, del Monte F, Vescovo G, Poole-Wilson PA. Isolated ventricular myocytes from failing and non-failing human heart: the relation of age and clinical status of patients to isoproterenol response. *J Mol Cell Cardiol* 1992;**24**:549–64. [http://dx.doi.org/10.1016/0022-2828\(92\)91843-T](http://dx.doi.org/10.1016/0022-2828(92)91843-T)
19. Poole-Wilson PA, Swedberg K, Cleland JG *et al.* Comparison of carvedilol and metoprolol on clinical outcomes in patients with chronic heart failure in the Carvedilol Or Metoprolol European Trial (COMET): randomised controlled trial. *Lancet* 2003;**362**:7–13. [http://dx.doi.org/10.1016/S0140-6736\(03\)13800-7](http://dx.doi.org/10.1016/S0140-6736(03)13800-7)
20. Paur H, Wright PT, Sikkil MB *et al.* High levels of circulating epinephrine trigger apical cardiodepression in a beta2-adrenergic receptor/Gi-dependent manner: a new model of Takotsubo cardiomyopathy. *Circulation* 2012;**126**:697–706. <http://dx.doi.org/10.1161/CIRCULATIONAHA.112.111591>
21. Haass M, Kitzman DW, Anand IS *et al.* Body mass index and adverse cardiovascular outcomes in heart failure patients with preserved ejection fraction: results from the Irbesartan in Heart Failure with Preserved Ejection Fraction (I-PRESERVE) trial. *Circ Heart Fail* 2011;**4**:324–31. <http://dx.doi.org/10.1161/CIRCHEARTFAILURE.110.959890>
22. van Heerebeek L, Hamdani N, Handoko ML *et al.* Diastolic stiffness of the failing diabetic heart: importance of fibrosis, advanced glycation end products, and myocyte resting tension. *Circulation* 2008;**117**:43–51. <http://dx.doi.org/10.1161/CIRCULATIONAHA.107.728550>
23. Paulus WJ, Tschope C. A novel paradigm for heart failure with preserved ejection fraction: comorbidities drive myocardial dysfunction and remodeling through coronary microvascular endothelial inflammation. *J Am Coll Cardiol* 2013;**62**:263–71. <http://dx.doi.org/10.1016/j.jacc.2013.02.092>
24. Fujimoto N, Borlaug BA, Lewis GD *et al.* Hemodynamic responses to rapid saline loading: the impact of age, sex, and heart failure. *Circulation* 2013;**127**:55–62. <http://dx.doi.org/10.1161/CIRCULATIONAHA.112.111302>
25. Yip G, Wang M, Zhang Y, Fung JW, Ho PY, Sanderson JE. Left ventricular long axis function in diastolic heart failure is reduced in both diastole and systole: time for a redefinition? *Heart* 2002;**87**:121–5. <http://dx.doi.org/10.1136/heart.87.2.121>
26. Cleland JG, Tendera M, Adamus J, Freemantle N, Polonski L, Taylor J. The perindopril in elderly people with chronic heart failure (PEP-CHF) study. *Eur Heart J* 2006;**27**:2338–45. <http://dx.doi.org/10.1093/eurheartj/ehl250>
27. Massie BM, Carson PE, McMurray JJ *et al.* Irbesartan in patients with heart failure and preserved ejection fraction. *N Engl J Med* 2008;**359**:2456–67. <http://dx.doi.org/10.1056/NEJMoa0805450>