

EXPERT
REVIEWS

The 2013 annual autumn meeting of the British Society of Heart Failure

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16th British Society for Heart Failure Annual Autumn Meeting Queen Elizabeth II Conference Centre, London, UK, 28–29 November 2013

The 16th Annual Meeting for the British Society for Heart Failure took place in the impressive surroundings of the Queen Elizabeth II Conference Centre in Westminster (London, UK). Over the two-day conference, more than 700 delegates attended – the largest number to date. Over 40 talks were delivered by some of the world's experts in heart failure. For 2013, the theme was making sense of acute heart failure – a clinical entity which is frequently encountered, poorly understood, and for which there exists virtually no evidence base for treatment.

Acute heart failure: counting the costs

In the UK, there are around 250,000 hospital attendances per year due to acute heart failure (AHF), with approximately half of patients having a normal left ventricular ejection fraction (LVEF). There are many reasons why patients present with AHF [1]. Given the diverse etiologies that may be responsible, defining 'AHF' as a discrete clinical entity is generally not possible; it is: 'heart failure that results in hospitalization'. AHF can be precipitated by many factors, such as acute coronary syndromes, arrhythmias, hypertension, deteriorating renal function, omission of medications or respiratory infections [2]. In approximately 40%, no cause is clearly identified. John McMurray (Glasgow, UK) presented epidemiological data from the USA of >110,000 admissions due to AHF, which showed that there are increasing numbers of patients with a normal LVEF presenting to hospital with AHF, whereas patients presenting with a reduced LVEF are decreasing [3]. It is not completely understood why the inpatient mortality of patients with heart failure in the USA is between a quarter and a third of the UK rate (9–10%), although hospital stay in the USA is shorter, which may explain the difference somewhat [4]. Despite differences in inpatient

survival either side of 'the pond', mortality rates at 1 year following discharge are similar at 30%. Around 20–30% of patients who present to hospital with AHF are readmitted within 3 months of discharge [2,5].

Despite AHF being one of the commonest conditions in the UK, it is abysmally investigated. Recruiting acutely ill patients to clinical trials as soon as they enter the hospital and before a barrage of treatment is thrown at them is challenging. Added to this are the onerous hurdles of clinical trial approval, monetary support, lack of time and professional inertia in an already overstretched healthcare system. Ian Squire (Leicester, UK) broke the rather unsurprising news that only five patients in the UK are currently recruited in trials which investigate therapy for AHF.

Teresa McDonagh (London, UK) presented the annual findings of the National Heart Failure Audit, which captures about 60% of heart failure admissions in England and Wales (n = 40,050). Seventy-eight percent of patients with heart failure are seen by a specialist in heart failure during their admission. Patients reviewed by a specialist have a longer length of stay compared with patients seen by a non-specialist, but have better survival [4]. In-hospital mortality fell from 11.1% in 2011/12 to 9.4% in 2013/13, and the proportion of



Figure 1. Standing room only at the 2013 Annual Autumn Meeting of the British Society of Heart Failure. Photograph provided courtesy of Roy Gardner (Glasgow, UK).

patients undergoing echocardiography and accessing specialist heart failure care has increased. A more worrying trend (which may reflect hospitals bursting at the seams) is an increase in the number of patients with heart failure whose duration of stay is recorded as zero days. Over-optimistically this may suggest that patients may be seen, referred to community heart failure services and treated at home. However, it is more likely to be the case that patients are not being admitted when really they should.

How to treat AHF

If you consult the 2012 European Society of Cardiology (ESC) Guidelines for the Management of Acute and Chronic Heart Failure, you will find little evidence supporting any of the treatment that is used to manage AHF [1,6]. The UK is set to publish its own set of AHF management guidelines, but it is unlikely that there will be anything significant to add to the pre-existing international ones. Over the last 40 years or so, there has been no shift in the management strategy of opiates, oxygen, nitrates and loop diuretics.

Some patients with AHF may be more complicated than meets the eye and a shot of intravenous (iv.) furosemide backed up by a daily infusion does not do the trick. A series of rapid fire presentations focused on the management of more complex patients with AHF. Martin Thomas (London, UK) reassured the conference that there may be a glimmer of hope for managing complex patients with decompensated heart failure associated with fluid overload, diuretic resistance and renal impairment (creatinine <350). He presented multicenter data comprising a group of 79 patients with decompensated heart failure (60% men; mean age 71 years) who were treated with ward-based ultrafiltration. The mean total volume of fluid removed per patient was 8.1 l, with a mean duration of treatment of 58 h. Ultrafiltration may also be ideal for decompensated heart failure patients with hyponatremia.

Dominic Kelly (Hampshire, UK) discussed the broad treatment options for patients with AHF and arrhythmia. Sometimes whether the arrhythmia is the cause or effect of the

heart failure is unknown. Treatment strategy will depend on the presenting history, chronicity of the arrhythmia and hemodynamic stability of the patient.

Infrequently, patients may present in AHF due to myocarditis and Simon Williams (Wythenshaw, UK) discussed the management strategy for this. Endomyocardial biopsy is strongly endorsed by the ESC but apart from transplant centers, few places feel they have the skill set to perform these safely [7]. In general, immunosuppression has little effect on improving survival apart from esoteric cases [8]. The TIMIC study showed that a combination of immunosuppressants (prednisolone and azathioprine) in addition to standard heart failure therapy could increase ejection fraction compared with placebo, but the trial was not powered to assess survival [9]. Whether or not the patient with a history of myocarditis who has had recovery of ventricular function should stop their medication remains open to debate.

Non-invasive ventilation (NIV) is frequently used for patients who have pulmonary edema and remain hypoxic despite delivery of high flow oxygen via a rebreather mask. The 3CPO study assessed whether patients with AHF treated with NIV compared with standard oxygen therapy had lower 7-day mortality. NIV was associated with quicker improvement in symptoms but there was no difference in survival [10].

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Trial updates in AHF

John McMurray (Glasgow, UK) presented a quick round up of recent studies in AHF. Unfortunately, almost all randomized trials that have tested treatments in patients with AHF have been neutral or have had negative outcomes. Anecdotally, a continuous infusion of iv. diuretic seems far better than using boluses. The DOSE trial dispels this myth and showed that both methods of diuretic administration are equal in efficacy [11]. Nitrates are arterial vasodilators and reduce afterload. Although they are a logical therapeutic choice for patients presenting with AHF, a recent Cochrane analysis has shown that there is little evidence for the use of iv. nitrate therapy [12]. Patients with AHF, worsening renal function and evidence of fluid overload had no significant benefit from ultrafiltration treatment in terms of weight loss after 4 days of treatment in the CARRESS-HF study and also had greater worsening of renal function and other adverse events compared with patients treated conventionally [13].

Low-dose dopamine has often been used in the hour of need with the expectation that it may enhance renal perfusion and maintain renal function in patients with worsening heart failure. The addition of low-dose dopamine or nesiritide (not licensed in the UK) made no difference to clinical outcome when added to standard treatment in the ROSE AHF trial [14]. The maxim, 'less is more' comes to mind following the results

of the ASTRONAUT trial, which showed that adding the renin inhibitor aliskiren to standard treatment in patients with a recent admission with AHF was of no benefit [15].

One of the few successes to date is the RELAX-AHF study, which showed that recombinant iv. relaxin (serelaxin) improved dyspnea and was associated with a lower mortality by 6 months. However, how short-term use of serelaxin can translate into a mortality benefit is unclear [16]. The statistical robustness of the mortality finding is also open to question, and further studies will follow.

The study named ATOMIC-AHF tested a new type of inotrope called a cardiac myosin inhibitor (omecamtiv mecarbil). Patients with AHF and left ventricular (LV) impairment were recruited and received a 48 h iv. infusion of omeclamtiv mecarbil. The primary end point of improvement in dyspnea response was no different in patients in the active versus control groups. An oral preparation of the same drug is being tested in COSMIC AHF, which will assess safety, tolerability and hemodynamic effects over a 3-month period.

Heart failure in hiding

As we all know, heart failure is predominantly a disease of the elderly. Two-thirds of patients are aged over 75 years at the time of their first admission for heart failure [4]. As the population has increasing life expectancy, a new specialism of 'geriatric cardiology' is in genesis. John Baxter (Sunderland, UK) reminded us all that in the elderly, chronic heart failure (CHF) is frequently nestled among piles of other diagnoses, often ignored and poorly treated until the umpteenth hospital admission. Physicians in elderly medicine and general practitioners are ideally placed to find and treat these. General practitioners and physicians who care for the older person have an important skill that is easy to lose in the sub-specialty, an ability to keep things in perspective and to treat the patient as a whole.

Building a heart failure service is not easy and requires organization and team work. Managing the swathes of patients with heart failure cannot be done alone. Patients can be found by various means and Gerry Carr White (London, UK) discussed two models of identifying patients to the heart failure service, using either N-terminal pro-brain natriuretic peptide (NTproBNP) or echo screening. Measuring NTproBNP or BNP is sensitive at finding new cases of heart failure, but it is not a very specific test and the level is elevated in patients with all manner of other co-morbidities such as atrial fibrillation and renal failure. Using NTproBNP too liberally may create a lot of work, particularly echocardiograms, many of which will be unremarkable.

Heart failure & normal ejection fraction

Walter Paulus (Göttingen, Amsterdam) (FIGURE 2) delivered a fascinating talk about heart failure and normal ejection fraction (HeFNEF), which he views as being pathologically distinct from the more usual heart failure with reduced ejection fraction. Several key factors contribute to cause HeFNEF in over 80% of patients: age, female sex, hypertension, obesity, diabetes, salt ingestion,

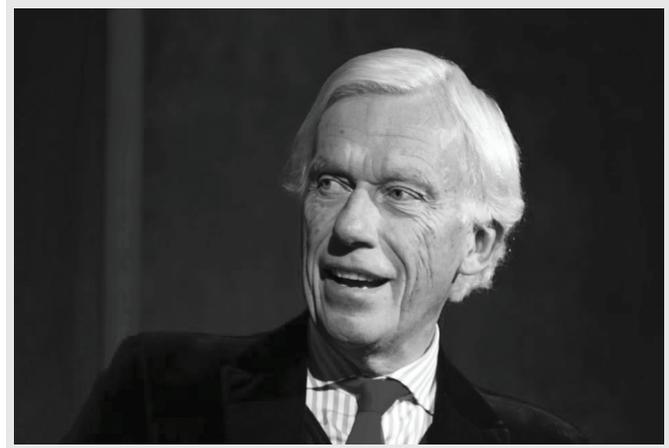


Figure 2. Professor Walter Paulus discusses the paradigm of HeFNEF. Photograph provided courtesy of Roy Gardner (Glasgow, UK).

smoking and lack of exercise [17]. At the myocardial level, such risk factors, alone or in combination, cause a systemic inflammatory state leading to coronary microvascular inflammation. The latter results in lower nitric oxide, cyclic guanosine monophosphate and protein kinase G levels, which promote myocyte hypertrophy and interstitial fibrosis [18]. Since there are many different causes for HeFNEF, it should come as no shock that hoping for a tablet to work as a blanket treatment for all is just illogical. The TOPCAT trial assessed whether spironolactone could reduce mortality in patients with HeFNEF. It is the latest of a long list of other studies that have failed to show any benefit of medical therapy in patients with HeFNEF [19]. The ESC guidelines have nicely summarized the situation as: "no treatment has yet been shown convincingly to reduce morbidity and mortality in patients with HeFNEF" [7]. Weight control, smoking cessation, regular exercise, blood pressure control and reduction of salt intake should be first line of defense for preventing patient developing HeFNEF, not prescription of drugs that work in heart failure with reduced ejection fraction.

Diagnosing patients with HeFNEF, with or without the help of a BNP/NTproBNP measurement, is easier said than done. The echocardiographic assessment of diastolic function is not easy. Alan Fraser (Cardiff, UK) pointed out that no single index to assess 'diastolic function' can be used in isolation. In patients with HeFNEF, the ejection fraction is 'preserved' and since longitudinal function decreases, there is a compensatory increase in radial function. Echo analysis of diastolic function can be split into assessment of LV relaxation and suction versus LV compliance and filling. Left atrial volume is an important measurement to make since HeFNEF is likely to be absent if left atrial volume is normal. Where possible, pulse-wave analysis of the pulmonary vein should be taken and the often quoted E/E' ratio is specific but insensitive.

The patient with HeFNEF has increased LV end-diastolic pressure, which causes a rise in left atrial pressure and pulmonary artery wedge pressure (PAWP) (measured during right

heart catheter). Luke Howard (London, UK) discussed the topic of pulmonary hypertension (PH) due to left heart disease, which is quickly becoming another possible target for treatment. PH is defined as a resting mean pulmonary artery (PA) pressure ≥ 25 mmHg [20]. PH together with a PAWP ≤ 15 mmHg defines pre-capillary PH. New research studying right ventricular (RV)-pulmonary vascular coupling has shown that as the PAWP increases, PA compliance decreases which leads to an increase in RV afterload. Consequently, this may result in impairment of RV function, reduced LV pre-load and culminate in symptoms such as dyspnea [21].

The transpulmonary gradient (TPG) = ([mean PA pressure] – [PAWP]) is one factor that is often used to decide suitability for patients for heart transplantation or mechanical assist devices (if the TPG is low, then the PH ‘passively’ reflects raised left atrial pressure; where the TPG is high, there must be ‘reactive’ PH). New data suggest that we should be using the diastolic pulmonary difference (DPD) = ([diastolic pulmonary pressure] – [PAWP]) instead of the TPG, which can be influenced by many factors [22]. Two arbitrary types of PH *due to left heart disease* are now described: ‘isolated post-capillary PH’ (PAWP > 15 mmHg and DPD < 7 mmHg) and ‘combined post-capillary PH and pre-capillary PH’ (PAWP > 15 mmHg and DPD ≥ 7 mmHg) [20].

Keep taking the tablets

Doggedly looking for new treatments, medical- or device-based, with the ultimate aim of reducing mortality, may be subject to the law of diminishing returns. Medical therapy for CHF is already very good and to find even an incremental treatment benefit requires ever larger and longer trials. For example, non-invasive ventilation for patients with pulmonary edema may not reduce mortality (i.e., treatment failure), but most would agree that the reduction in need for invasive ventilation and admission to the intensive care unit is a treatment success [23]. One of the key points highlighted by the National Heart Failure Audit is that we must continue striving to improve prescribing of recommended medical therapy. Equally important is titration of therapy and Dawn Lambert (Portsmouth, UK) showed in her case presentation that patience and perseverance can be needed. A low blood pressure is a common reason for not up-titrating medication. Roy Gardner (Glasgow, UK) reminded us that the patient is hypotensive only if symptomatic.

In another of the case presentations, Parminder Chagger (Manchester, UK) raised the age-old question about what is the role of digoxin in the treatment of CHF [24]. Apart from even more *post hoc* analyses and observational study data, there is only one way to answer the question, a large randomised controlled trial. Low-dose digoxin therapy is generally speaking safe, associated with better survival and may be as beneficial as ivabradine [25]. LV assist devices are often considered for patients with heart failure when medical and other device treatments have failed. Although assist devices offer a lifeline, Steve Shaw (Wythenshaw, UK) shared with us the sobering reality that 1-year mortality following implantation is 28%, increasing to 36% at 2 years.

The Phillip Poole-Wilson lecture

One of the cornerstones of therapy for CHF is β -blockade. Professor Sian Harding (London, UK) gave a fascinating insight into her lifelong work investigating β -adrenergic receptor function. In the clinical world, ligand bias agonism is little known about but is an important mechanism in the cascade of reactions when β_2 -adrenoreceptors are stimulated. The 2012 Nobel Prize for Chemistry was awarded for work in this field, which describes the mechanism of action of G-protein coupled receptors, of which β -adrenoreceptors are one type. Ligand bias agonism is the process, whereby an increase in concentration of epinephrine outside the cell increases the affinity of the β_2 -adrenoreceptors to epinephrine. The normal response to adrenergic stimulus is positive inotropy. Professor Harding’s research has investigated the pathophysiological mechanisms that mediate Takotsubo cardiomyopathy. Her work suggests that ligand bias antagonism may be a valuable protective mechanism, whereby supranormal epinephrine levels cause negative inotropy [26]. In time, this work may contribute to the development of new drugs to treat heart failure.

Final thoughts

The 16th British Society of Heart Failure Meeting was thought provoking and information-packed. There was standing room only for most of the conference. This is encouraging since heart failure is one of the most expensive conditions for the National Health Service to treat and needs an ever-increasing number of specialists to help treat it properly. Huge numbers of people in the UK have heart failure, but since other illnesses are marketed to the public more effectively, the general public still knows very little about it. This year’s conference demonstrated that we are making small but steady steps toward understanding what AHF and HeFNEF are, but large gaps remain in our understanding of how they should be managed properly. One of the strongest messages from the conference was that the patient with AHF should be seen by the right person, at the right time and in the right place, in order to get the right treatment.

Future Meetings

20 March 2014: Heart Failure Day for Training and Revalidation

21 March 2014: Heart Failure Nurse Study Day

27–28 November 2014: 17th Annual Autumn Meeting

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