



NEWSLETTER

In this issue...

This issue of the BSH Newsletter reports on three BSH Symposia at the British Cardiac Society (BCS) Annual Scientific Conference, 24–27 May 2004:

Heart failure – delivering evidence-based care in the UK	1
Electrical device therapy in heart failure; unmet need and unmet cost	3
Anti-thrombotic therapy for heart failure: which agent, if any?	6

These BSH sessions were very successful and well attended. Apologies to those who were not able to attend due to rooms being full. We hope this newsletter will give you a summary of the most salient points

BSH Update

7th BSH Annual Autumn Meeting 'Heart failure: translating evidence into practice' and Annual General Meeting (AGM), 25–26 November 2004, London

This joint event, between the BSH and the Coronary Heart Disease (CHD) Collaborative, will take place on the afternoon of 25 November followed by a buffet dinner in the evening and a full day meeting on 26 November at the Novotel West Hotel in Hammersmith, London.

The meeting will focus on improving the outcome for patients with heart failure by implementing guidelines and applying the results of research in front-line practice. Service models that encourage best practice will be

discussed with the aim of sharing innovation. We estimate that there will be 500 participants. The programme, more information and registration forms can be found on the BSH website: www.bcs.com/affiliates/bsh.html. Bookings are taken on a first-come-first-served basis and this year the meeting registration deadline is 30 September.

The BSH AGM will take place prior to the Annual Autumn Meeting on 25 November at 13.30-14.00.

BSH Charity Ball, Friday 26 November, 19.30, The Brewery (Barbican), London

We are looking forward to welcoming our members to the first BSH Charity Ball. This 'black-tie' event should attract up to 500 expected guests both from within and outside the medical field. To find more information and to book your tickets, please visit the BSH website (see above).

The BSH would warmly welcome items donated for the auction and/or raffle, and volunteer helpers.

Development of mechanical circulatory programmes for the UK: a consensus conference, 2 July 2004

The above conference was a great success and we are in the process of producing a BSH newsletter from this meeting, which we expect to circulate in October.

BSH Website

We are still looking to expand the BSH website to include more heart failure-specific information, news and resources. Please would you let us know if you would be interested in becoming involved with the development and the updating of the scientific content within the site (specialist IT knowledge is not required).

Heart failure – delivering evidence-based care in the UK

A BSH session at the BCS Annual Scientific Conference on 24th May 2004, chaired by Martin Cowie (London) and Strat Liddiard (Poole)

This session was aimed at health professionals who wanted to obtain up-to-date information on the diagnosis and treatment of heart failure (HF).

NICE guidelines: forces for good?

In the opening presentation, Professor Martin Cowie (London) asked the question whether the National Institute of Clinical Excellence (NICE) guidelines on chronic HF have been a force for good. He outlined the growing problem of HF in England and Wales which currently accounts for 1-2% (£600 million)¹ of the NHS budget and which will increase as the population ages and as more effective treatments for myocardial infarction are used.

Professor Cowie reminded delegates that although the National Service Framework for Coronary Heart Disease² had set out clear goals for the diagnosis and treatment of HF, the publication of the NICE guidelines in July 2003 provided the specific recommendations for primary and secondary care practitioners based on a systematic review of published evidence.³ The guidelines are designed for healthcare professionals who are not specialists in HF and have been published in 3 forms: the full guidelines, the NICE guidelines and a public version for patients and carers.

The guidelines include input from over 50 stakeholder groups. Patient groups ensured that a number of topics of particular interest to patients with HF, such as self-monitoring, managing depression, and end of life issues were covered in detail. Although designed for the non-specialist, the guidelines make recommendations on appropriate referral when specialist help is required.

Figure 1. Key recommendations from the NICE guidelines: identified as priorities for implementation.³

1. The basis for historical diagnoses of HF should be reviewed, and only patients with a confirmed diagnosis should be managed according to the guidelines
2. Echo should be performed to exclude important valve disease, assess the function of the left ventricle and detect intracardiac shunts
3. All patients with HF due to LVSD should be considered for treatment with an ACE inhibitor
4. Beta-blockers licensed for use in HF should be initiated in patients with HF due to LVSD after diuretic and ACE inhibitor therapy (regardless of whether or not symptoms persist)
5. All patients require monitoring, which should include:
 - A clinical assessment of functional capacity, fluid status, cardiac rhythm, and cognitive and nutritional status
 - A review of medication, including need for changes and possible side-effects
 - Serum urea, electrolytes and creatinine
6. Patients should generally be discharged from hospital only when their clinical condition is stable and the management plan is optimized
7. The primary care team, patient and carer must be aware of the management plan
8. Management of HF should be seen as a shared responsibility between patient and healthcare professional

Among the most important highlights of the guidelines are two simple algorithms describing diagnosis and drug treatments for the non-specialist, and the identification of eight key areas that, if addressed, would have a significant impact on HF care in the UK (Figure 1).

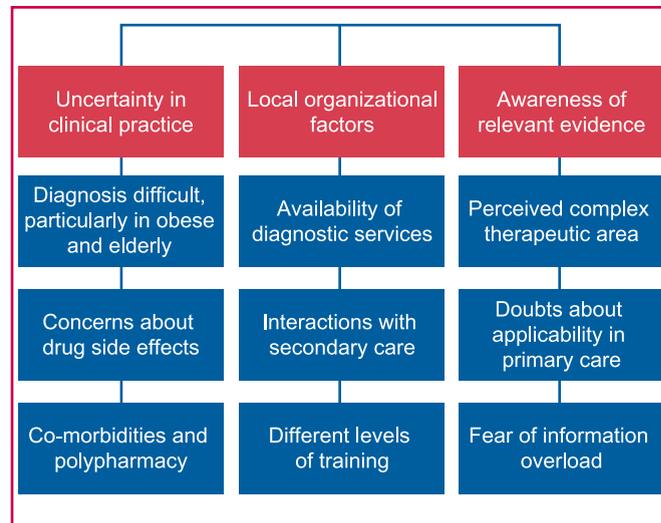
Forthcoming SIGN and ESC guidelines will soon add to the general knowledge base, but Professor Cowie commented that "The NICE guidelines provide a powerful force in raising awareness of current best practice in HF and in highlighting areas that demand the greatest attention". Although he admitted that as the main author of the guidelines he may be biased, he concluded with a strong affirmation of the benefit of the NICE guidelines.

Improving diagnosis

Dr Ahmet Fuat (Darlington) commented that HF presents clinicians with a diagnostic challenge (Figure 2).⁴ Symptoms and signs often do not allow differentiation between cardiac and non-cardiac causes of breathlessness and many patients are falsely diagnosed with HF in primary care (40% in the Framingham Study; 50% in the Kuopio study).^{5,6} Although echocardiography is recommended as the gold standard investigation, it is not readily available to many GPs around the country and it may be difficult to determine left ventricular (LV) function among some, particularly obese, patients.^{4,7}

The NSF for Coronary Heart Disease proposed 3 models for referral from primary care: open access echocardiography (OAE),⁸ specialist HF clinics and general cardiology outpatient clinics.⁹ OAE is defined as echocardiography requested by a GP without prior clinical assessment by a cardiologist.¹⁰ A recent systematic review of 5 observational cohort

Figure 2. Barriers to accurate diagnosis and effective management of CHF⁴



studies of OAE showed that left ventricular systolic dysfunction (LVSD) was confirmed in only 14-23% of patients.⁸ This study concluded that there was a lack of rigorous controlled studies to support the establishment of open access services.

One Stop or Rapid Access clinics may provide a useful alternative to OAE based on experience from South East London and Darlington.^{9,11} A questionnaire survey of GPs revealed that about 65% of GPs preferred the one stop clinic option to OAE⁹ and Dr Fuat concluded that these clinics provide accurate, expedient diagnosis which prevent delays in outpatient care and provide evidence-based therapy.

Hand-held echo has also been suggested as a way of screening patients for HF. Dr Fuat said that portable echo performed by an experienced sonographer is an accurate and reproducible technique for detecting LVSD and other abnormalities and its high predictive value would allow its use in future community based programmes.¹² In addition, the method, combined with NTproBNP measurement, was cost-effective when compared to traditional methods.¹³

Dr Fuat concluded that a HF diagnostic service, with highly trained technicians and based on local needs and resources is central to any HF service. A multidisciplinary approach is essential and he encouraged the aim of seamless integration between primary, secondary and tertiary care.

Improving treatment (in its broadest sense)

Dr Suzanna Hardman (London) presented work from The Whittington Hospital, based in a challenging inner city area, aimed at improving treatment of patients with HF. Five years earlier, there had been no interest or practice around HF in the area. In developing services the ideal was that care should be optimal wherever a patient entered the healthcare system and that there should be a continuity of approach across primary, secondary and tertiary care.

Community-wide guidelines were developed with local GPs and reviewed by the local multidisciplinary

Cardiovascular Disease Reference Group and are now intrinsic to the local coronary artery disease website (www.chd.org.uk). Complimentary hospital guidelines followed to address the needs of those admitted to hospital with a diagnosis of HF. In this high-risk group the idea that a home-based intervention might reduce unplanned re-admissions and mortality was appealing.¹⁴ However, the resource-rich healthcare context in which the Adelaide study (and others) had been conducted meant the benefits seen elsewhere would not necessarily transfer to an inner city London practice. Furthermore, Dr Hardman and colleagues were keen to explore the idea that empowering patients so that they were more involved in their own care and management would translate into a positive spiral of behaviour resulting in fewer hospital admissions and better outcome for these patients.

Accordingly Dr Hardman described a randomized controlled trial designed to assess the efficacy of a nurse-led self-help intervention using a problem-solving model, for patients admitted to hospital with HF. This approach has proven successful in the management of patients with other chronic conditions such as asthma and diabetes, but to date has not been explored in HF. The study compares standard HF care based on local guidelines with the nurse-led intervention. This intervention involves two visits from the nurse in the 48 hours prior to discharge, and includes a single home visit within 7 days of discharge and a subsequent telephone call. The primary endpoint of the study will be readmission rates and duration at 90 days. Since a single type of intervention is unlikely to suit all patients, an important part of the analysis will be to examine which patient characteristics (demographic, clinical, psychological) predict likely benefit.

Dr Hardman concluded that the priorities in improving HF treatment are:

- Continuity and optimum service provision in primary, secondary and tertiary care (including continuity of guidelines, infrastructure and range of personnel)
- Interventions designed to improve treatment, based on what is feasible in the local area and with a recognition that different models may suit different patients.

Improving multi-professional working

Hayley Pryse-Hawkins (London), a HF nurse specialist, described some key issues that need to be addressed to improve multi-professional work in HF. People with HF frequently have multiple, chronic symptoms that require expert intervention and support from a team of healthcare professionals including doctors, pharmacists, therapists, nurses and voluntary sector agencies. HF is also commonly associated with co-morbidities and may be managed by up to 6 or 7 different teams. Great care needs to be taken to ensure that these patients are treated in a holistic manner and do not receive poly-pharmacy or that there is not an unnecessary overlap and waste of resources.

The patient/carer version of the NICE guidelines stresses that healthcare teams should be listening to patients' feelings, fears, views and beliefs, and that healthcare professionals should work in a constructive partnership with the patient, providing all the information that they require for help and support. Ms Pryse-Hawkins commented that the healthcare team must learn to work in a cohesive manner to meet these objectives in the NICE guidelines. Careful listening to patients' preferences and needs will ensure optimal use of resources and provision of care. Good communication is central to maintaining the ongoing management of patients.

These patients should be aware of their treatment programme and can then direct communication between different healthcare professionals and ensure that databases are maintained. There is a great need for prompt, effective and inclusive communication channels and an integrated IT system should be a central component of this in the future.

Ms Pryse-Hawkins concluded that effective multidisciplinary working will minimize morbidity and mortality and optimize quality of life, and demands a greater understanding of the roles of different healthcare professionals and the facilities available to them.

Electrical device therapy in heart failure: unmet need and unmet cost

A joint BSH/British Pacing and Electrophysiology Group (BPEG) session at the BCS Annual Scientific Conference on 25th May 2004, chaired by Henry Dargie (Glasgow) and Anthony Rickards (London)

This joint session provided delegates with a summary of the different types of electrical devices available for patients with HF and presented the case for their increased use in the UK with the wider financial implications.

What is the unmet need?

Dr Theresa McDonagh (London) set the scene for the session by describing the consequences of left ventricular (LV) dyssynchrony and dysrhythmias in patients with LV systolic dysfunction (LVSD). Ventricular dyssynchrony manifests as electrical, structural and mechanical abnormalities.¹⁵ A useful review describes complex echocardiographic formulae for measuring inter- and intra-ventricular dyssynchrony.¹⁶

Left bundle branch block (LBBB) is a surrogate for LV dyssynchrony and appears to occur in 8% of patients with preserved systolic function, in about 24% of patients with systolic dysfunction, and in 38% of patients with moderate/severe HF.^{17,18} A wide QRS duration in HF is an independent predictor of mortality¹⁹ and LBBB confers a three-fold risk for subsequent mortality in the general population.

Sudden cardiac death (SCD) accounts for approximately 50% of HF deaths. Dr McDonagh commented that nearly a third of the deaths in patients

with severe HF (NYHA III and IV) in the MERIT study were from SCD, demonstrating the real unmet need for electrical device therapy for patients in these classes.²⁰

Patients with HF (NYHA III and IV) have a poor quality of life, substantially worse than that experienced by patients with other chronic cardiac complaints, and are frequently hospitalized. There is much unmet need in HF which will not be met by new drugs alone. The CHARM study showed that even patients (75% NYHA III) treated with maximal pharmacological therapy have a substantial event rate (13% 1-year cardiovascular death or hospitalization).²¹

Patients who may benefit from electrical device therapy mostly include those with systolic dysfunction, in NYHA III or greater, and with a wide QRS complex. Based on extrapolations from three studies from Glasgow and Poole, Dr McDonagh suggested that there could be just under half a million people with HF and systolic dysfunction in the UK, with approximately 165,000 in NYHA III or greater, and 33,000 people with LBBB. She noted that this translates into estimated costs of device therapy of between £99 million and £4 billion according to the various strategies for device therapy (e.g. ICD alone, cardiac resynchronization [CRT], CRT-D), and the subset of HF patients targeted. Whatever the strategy used, there is enormous unmet need.

Single centre experience

Dr Jonathan Clague (London) described his centre's experience with implantation of over 400 CRT devices. Most of the patients were in NYHA class III or IV, aged 60-70 years, and the majority had ischaemic HF with a large number of co-morbidities.

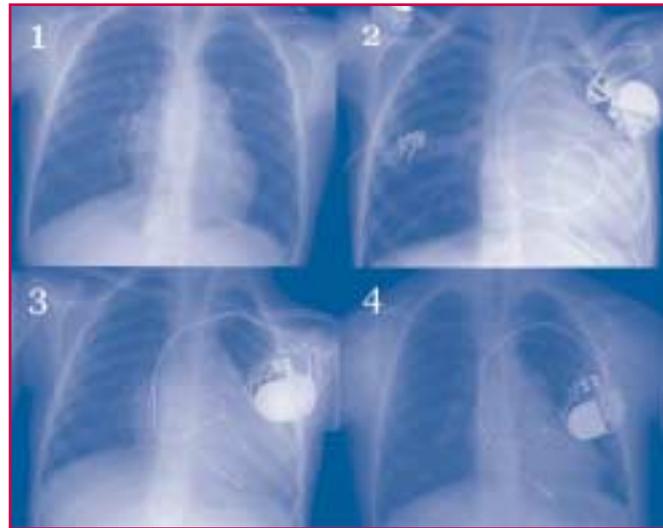
Implantation resulted in a significant shift to NYHA II (NYHA III/IV pre-implantation 82%, post-implantation 25%), a trend towards a higher ejection fraction, but with no significant change in QRS duration or LV dimension.

Interestingly, procedure time decreased significantly with operator experience and improvement in technology. The centre used only Guidant and Medtronic devices. Complications included one procedurally related death from cardiogenic shock, one patient with infection who required re-implantation on the right side, and 8.2% LV lead displacement. Failure to implant was only 2.9% which included two successes on the second attempt, one 5-year old girl, one with no CS access and one patient with no good pacing position.

Comparison with another series showed similar successful implant rates, lead displacement rates, and a similar effect of NYHA class but with a faster procedure time at Dr Clague's centre.²²

Dr Clague highlighted his group's work on biventricular pacing in 4 children aged between 5-9 years, three of whom have improved ejection fraction post procedure. A year after implantation of an endocardial pacemaker, one patient (a 9-year old boy with congenital complete heart block) re-presented in severe HF and underwent standard bi-ventricular pacemaker implantation. He showed significant improvement in radiological appearance, immediately after implantation

Figure 3. Clinical course following implantation of a bi-ventricular pacemaker in a 9-year old boy.



and more recently (Figure 3). Dr Clague concluded that CRT can be safely performed in children and can be effective in improving clinical course.

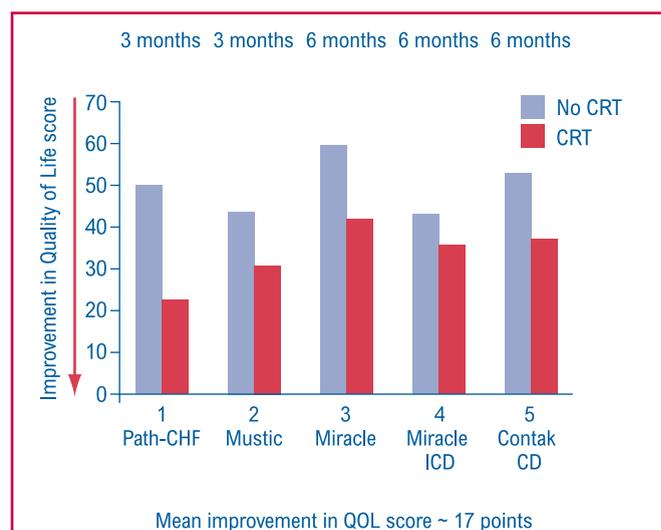
Another interesting study in a sub-group of Dr Clague's patients (n=30) found that patients with a restrictive LV filling physiology are less likely to benefit from CRT.²³ He suggested that this may be due to cycle inefficiency, but larger studies and mortality data are required to confirm this.

High vs low voltage CRT in heart failure

Dr John Boehmer (Hershey, Pennsylvania, USA) described his experience of CRT in the USA. CRT has been shown in many clinical trials to improve symptoms and exercise capacity in patients with LV systolic dysfunction (LVEF <35%), conduction system disease (QRS >120 ms) and advanced HF (NYHA class III/IV). A review of early CRT trials shows the consistency of statistically significant improvement in quality of life scores from use of CRT in NYHA class III/IV patients (Figure 4).²⁴⁻²⁸ These improvements are echoed in improvements in peak oxygen consumption.

A recent review of primary prevention implantable cardioverter defibrillator (ICD) trials (CABG – Patch,

Figure 4. Impact of CRT on quality of life in CRT trials.



CAT, MADIT, MADIT-II and MUSTT) shows a consistent and substantial reduction in the risk of SCD following ICD use.²⁹ Although the MADIT II trial raised concerns that there could be adverse events associated with ICDs, many of the devices were set to pace the right ventricle and it was thought that dysynchrony was the cause of worsening HF.³⁰ The recently reported SCD-HeFT study showed that ICD therapy reduced all-cause mortality at 5 years by 23% in patients with predominantly NYHA class II HF and LVSD, but that amiodarone was ineffective.³¹ Although a meta-analysis has not been performed on all such trials, there is now in excess of 5000 patients enrolled in primary prevention clinical trials with 1000 endpoints suggesting a 25-30% reduction in all-cause mortality. However, there remain some inconsistencies; for instance, the DEFINITE trial has recently shown that patients with NYHA class II (with low EF, a history of symptomatic HF, non-ischaemic dilated cardiomyopathy and some evidence of ambient arrhythmias) had similar survival with standard therapy when compared with ICDs.³²

The question remains whether CRT should be applied as a pacemaker alone (low voltage CRT) or in combination with an ICD (high voltage CRT or CRT-D). The COMPANION trial showed that CRT and CRT-D produced similar reductions in the combined endpoint of death and all-cause cardiovascular or HF hospitalizations.³³ However, although CRT was associated with a trend for mortality reduction (24% event rate reduction in 12 months) the addition of ICD to CRT improved the mortality reduction to a statistically significant decrease of 36% ($p=0.002$). The preponderance of evidence now supports the use of CRT-D devices for reduction in mortality, although important information will be forthcoming in future clinical trials such as CARE-HF.

UK device implant trends

Dr David Cunningham (Glasgow) described the increasing use of CRT devices in the UK. In 2003 just over 200 CRT devices were implanted, with a greater increase in the use of CRT-D devices with nearly 900 implanted. The implant rate of nearly 18 per million in the UK in 2003 (Northern Ireland 27, Scotland 25, England 17 and Wales 8) compares poorly with the implant rate in Western Europe of 24 per million population.

Patients receiving CRT-D therapy were younger than those with CRT therapy (61.8 vs 66.1 years) and the age distribution of all CRT patients is approximately 10 years younger than the average pacemaker population. Of all patients receiving CRT therapy 27% were in NYHA class I, 26% in class II, 40% in class III and 7% in class IV. The LV ejection fraction was <30% in over 70% of these patients.

There was a dramatic difference in implantation rates in different regions of the UK with some areas (Grampian, W. Yorkshire, Bedfordshire and Hertfordshire) being >30 per million, and others (Trent, Birmingham) being <5 per million. There is a clear South-North divide with underprovision for southern regions.

Dr Cunningham analysed survival data from 553 CRT and 1589 CRT-D patients with HF, both groups having a 5-year survival of about 60%. There was a small improvement in survival with CRT-D over CRT but this disappeared after 3 years. However, there was a clear survival benefit in all-cause mortality over medical therapy of approximately 30% after 5 years.

Dr Cunningham concluded that UK practice compared badly with the rest of the world, being low compared to other European countries and especially low compared with the estimated 270 per million implant rate in the USA. He also highlighted the significant regional differences in implant rate in the UK.

Service implementation

Professor Martin Cowie (London) discussed how device therapy can be moved forward in the UK. He commented on how much time is spent in researching devices compared with time spent on implementation. Drivers to the process of change include a robust evidence base, an increased emphasis on best practice and guidelines, clinical networks to develop equity in delivery of services, management structures, and change in social attitudes. Despite these many other influences, doctors still dominate the decision-making process.

Government and professional bodies are trying to speed up adoption of technology with many initiatives such as the National Service Framework, and Professor Cowie suggested that societies such as the BSH could take a more vocal role in this process. He also emphasized the importance of expert opinion in the hierarchy of evidence, reminding delegates that even the most robust clinical trial data need to be extrapolated through careful judgement and experience to apply to the individual patient in the clinic.

The NICE HF guidelines, published in July 2003, make a strong recommendation of CRT even before the publication of positive results of recent clinical trials – “Resynchronisation therapy should be considered in selected patients with LV systolic dysfunction (LVEF <35%, drug refractory symptoms and QRS duration > 120 ms. The results of ongoing trials will help guide appropriate patient selection (R47)”. Professor Cowie commented that this statement opens the door for local health communities to decide where this therapy fits in their strategy and that this should be built into local 3-year plans. More detailed health economic comments in the full guidelines are favourable to the further introduction of CRT, although a Health Technology Assessment on these devices is not planned until 2006.

A number of policy initiatives could impact significantly on HF services. HF, like diabetes and asthma, is a chronic disease and cardiologists should play an important role in the development of chronic disease management. In addition, PCTs could make significant budget decisions, and implementation of the new GMS contract and lobbying of government could help considerably. Partnership with industry is also vitally important in developing this new technology for the benefit of patients.

Anti-thrombotic therapy for heart failure: which agent, if any?

A BSH session at the BCS Annual Scientific Conference on 25th May 2004, chaired by John Cleland (Hull) and Gordon Lowe (Glasgow)

This session focused on the role of anti-thrombotic therapies in patients with HF. Speakers argued for and against their use in different patients based on the available evidence.

Vascular biology

Dr David Newby (Edinburgh) presented some of the background to vascular biology in HF. He commented that clear understanding of the vascular and endothelial contributions to the regulation of haemostasis and fibrinolysis provides pathophysiological insights into the thrombotic consequences and mechanisms of HF.

He highlighted the vital role played by the endothelium in the control of tissue perfusion, local haemostasis and endogenous fibrinolysis, mediation of inflammatory responses, and in atherogenesis and plaque rupture. It is well known that the vascular dysfunction seen in HF has important thrombotic consequences. HF is associated with disturbed homeostatic mechanisms and pathways including increased basal nitric oxide, endothelin and angiotensin II generation and induction of inducible nitric oxide synthase. Dr Newby commented that these increases in procoagulant and antifibrinolytic factors and reductions in anticoagulant and profibrinolytic factors may contribute to the potential thrombotic consequences of HF.

Dr Newby summarized that in HF the vasculature and vascular biology is abnormal, but that appropriate therapy can interact with that abnormality and cause changes within the local vasculature. Basal and stimulated blood flow regulation is perturbed and that this can be influenced particularly by neurohumoral activation. One important aspect of vascular function, endogenous fibrinolysis, is very relevant to HF and its treatment.

Haemostatic dysfunction

Professor Gordon Lowe (Glasgow) described the clinical evidence for haemostatic dysfunction associated with HF. Elevated plasma levels of platelet activation markers such as β -thromboglobulin, coagulation markers such as fibrinopeptide A, fibrinolysis markers such as tissue plasminogen activator (tPA), P-selectin, and von Willebrand factor provide evidence for a systematic prothrombotic state.³⁴

Professor Lowe discussed some of the potential causes of these abnormalities. For some of these markers there are trends towards correlation with clinical severity of NYHA class, but there remain no conclusive data on the relationship of haemostatic dysfunction with LVEF.³⁵ Coronary and peripheral atherosclerosis is known to be associated with haemostatic changes, but does not appear to be the sole reason for these effects as similar effects are seen in HF patients with CHD and dilated cardiomyopathy.

Another possible cause is change in intracardiac blood flow, especially in patients with atrial fibrillation who have higher levels of hypercoagulability and thrombotic events, especially stroke.³⁶ Spontaneous echo contrast in patients with atrial fibrillation has also been shown to be related to the risk of stroke and to the degree of systemic hypercoagulability.³⁷ Even in those patients with HF without atrial fibrillation, it is recognized that thrombotic events are associated with HF as a complication of cardiomyopathy and LV aneurysm.³⁸

Neuroendocrine activation has been proposed as another cause. von Willebrand factor has been correlated with plasma levels of angiotensin II and endothelin, and cytokines (plasma IL-6) have been shown to be disturbed in HF and to predict mortality.³⁹ Endothelial dysfunction is known to be associated with HF and may be associated with altered levels of endothelial release products.

Meta-analyses of prospective studies show that many of the haemostatic variables are associated with increased risk of both arterial (fibrinogen, tPA/PAI, D-dimer) and venous thrombosis (von Willebrand factor fibrinogen, D-dimer) in the general population and in people with baseline cardiovascular disease.⁴⁰ Professor Lowe concluded that there were probably multiple causes of the association between HF and 'sticky blood'. These associations have potentially pathogenic roles but further large, prospective studies are required to assess their significance.⁴¹

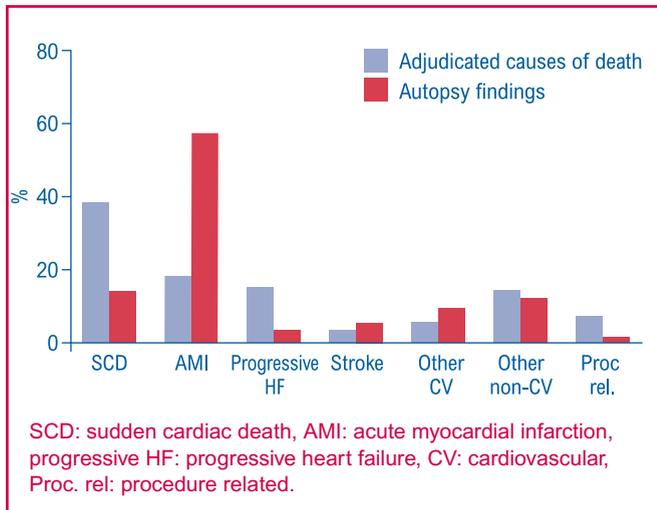
How do vascular events contribute to HF progression?

Dr Iain Squire (Leicester) described the significant impact of HF on hospitalization in Leicestershire which amounts to 60,000 bed days in a population of 1 million in one calendar year. Both ventricular remodelling and recurrent myocardial ischaemia appear to contribute to the progressive deterioration in cardiac function seen in HF.

Vascular events are very common in HF and contribute directly to mortality and morbidity. The pathway for a patient following first admission with HF is not predictable; there is a wide spectrum of cardiovascular disease recorded in these patients which contributes to hospitalization, but HF remains the most common reason for readmission. Approximately 5-15% of patients experiencing their first HF hospitalization have a history of prior MI. Few patients have a prior history of atrial fibrillation. Subsequent to the first HF hospital episode, the most common single reason for admission is HF. In less than 5% the next admission is with MI and in 7-8% chest pain or angina. Therefore subsequent hospital admission in HF is common, and cardiovascular admission is associated with a poor outcome. However, reasons for these admissions vary, with HF predominating over acute coronary syndromes or other major vascular thromboembolic events.

Data from the ATLAS trial show that of 83 patients experiencing sudden death, 42% had evidence of a recent MI.⁴² In the recent OPTIMAAL trial, 180 patients dying during follow up underwent post mortem

Figure 5. Causes of death in all autopsied patients (n=80) in OPTIMAAL before and after the result of autopsy was used to determine cause of death.⁴⁴



examination which changed the prevalence of MI from 18% to 57% and resulted in a significant change for most causes of death (Figure 5).⁴³ Conversely the proportion of deaths felt due to progressive HF fell from 15% to 3%. There is clear evidence that these patients are having acute coronary vascular events as part of HF progression contributing to death.

In conclusion, it is clear that MI is a common event in HF and is frequently 'missed' by clinicians. Later presentations discussed whether anti-thrombotic agents have a role to play in HF.

Does anti-thrombotic therapy reduce events in HF?

Professor Gregory Lip (Birmingham) presented data on the effectiveness of anti-thrombotics in HF. He said that HF is associated with considerable morbidity and mortality, including a high risk of venous thromboembolism and stroke. Framingham data show over a four-fold increase in the incidence of stroke in patients with HF.⁴⁴ In addition, up to 50% of HF sufferers die suddenly, a major mechanism of which may be thrombotic coronary occlusion leading to MI.

Anti-thrombotic therapy may, therefore, be expected to provide mortality and morbidity benefit to these patients, although current evidence is limited. Retrospective analyses of large randomized trials such as the SOLVD study suggested a 24% reduction in all-cause mortality and an 18% reduction in hospitalization with use of warfarin.⁴⁵ A meta-analysis suggests that aspirin in combination with ACE inhibitors is not a preferred option in HF, a trend that is confirmed in the SOLVD-Prevention, SOLVD-Treatment and HOPE trials.^{46,47}

Two recent Cochrane reviews of anticoagulation and antiplatelet therapy for HF in sinus rhythm concluded that the evidence from trials demonstrated a reduction in mortality and cardiovascular events with oral anticoagulant therapy and little evidence for antiplatelet therapy in HF.^{48,49} However, these findings were largely based on data that were over 50 years old.

These results support the need for large, randomized controlled trials comparing aspirin with other anti-

thrombotic therapies and one ongoing trial (WARCEF; Warfarin vs Aspirin in Reduced Cardiac EF) should provide more information.⁵⁰ The WATCH trial, the largest trial in this area to date, is in press and is described in the next presentation.

Which anti-thrombotic agent is preferred?

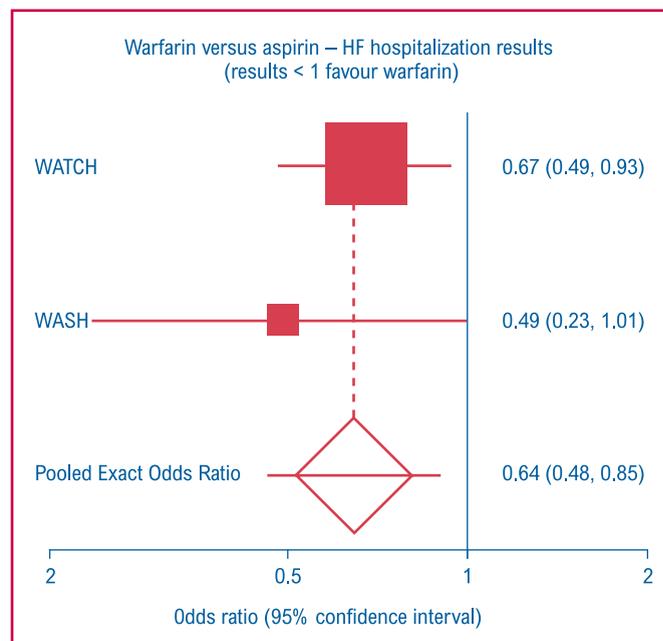
Professor John Cleland (Hull) described the results of recent randomized controlled trials – WASH and WATCH – that assessed the effects of chronic anticoagulation therapy on clinical outcomes in HF.

The WASH (Warfarin, Aspirin study in HF) study is the largest contemporary trial of anticoagulation in HF in sinus rhythm and shows no benefit from the use of aspirin or warfarin over no therapy.⁵¹ Warfarin showed benefit when compared with aspirin, in terms of patients hospitalized and numbers of hospitalizations which were reduced by 41% and 31%, respectively. However, patients who received no anti-thrombotic therapy did just as well as those who received warfarin, suggesting that the difference between aspirin and warfarin reflects harm from aspirin. However, the medical community has such a positive bias in favour of aspirin that it took 5 years and seven rejections to get the paper published.

The WATCH (Warfarin and Antiplatelet Therapy in Chronic Heart Failure Trial) enrolled 1587 patients between 10/99 and 6/2002 and compared warfarin (INR 2.5-3.0), aspirin (162 mg/day) and clopidogrel (75 mg/day) and was followed to allow 3068 patient-years of exposure.⁵² Results were presented at the meeting.

A meta-analysis of the WASH and WATCH trials shows the benefit of using warfarin rather than aspirin (Figure 6).³¹ Professor Cleland commented that one of the most effective ways to reduce morbidity in patients with HF would be to withdraw aspirin. This would reduce HF hospital admission rates by about one third. Also, as up to one third of all major gastro-intestinal

Figure 6. Meta-analysis of warfarin vs aspirin: heart failure hospitalizations.



haemorrhage in patients over 65 years can be attributed to prophylactic aspirin and because HF is also a risk factor for such bleeds, withdrawing aspirin may improve both cardiovascular and gastro-intestinal well-being. He repeated Professor Lip's comments about uncertainty on the efficacy of aspirin. Earlier large, long-term mortality trials of aspirin post-MI (AMIS [500 mg b.d.] and PARIS-II [330 mg t.i.d.]) showed no significant benefit of aspirin over placebo.

Professor Cleland concluded by providing the options for anti-thrombotic agents in HF. He commented that there is no evidence that routine anti-thrombotics are useful for patients with HF in sinus rhythm even if they have coronary disease, although this may reflect an inadequate number of patients randomized. Health economic analysis suggests that warfarin may be the least expensive option, as it is associated with a reduced number of hospitalizations but further data may be required to convince doctors that warfarin is the preferred choice. Future options may include clopidogrel and ximelagatran.

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Obituary

Dr Anthony F Rickards (1945-2004)

It was with great sadness that the BSH learned of the death of Tony Rickards, one of the world's most eminent cardiologists, in late May 2004. He will be sadly missed.

Acknowledgements

The BSH is grateful to Bayer Healthcare, GlaxoSmithKline, Roche and Takeda for providing a meeting-specific grant and to the 'Friends of the BSH': A Menarini, AstraZeneca, Bayer Healthcare, GlaxoSmithKline, Medtronic, Pfizer, Roche, Servier UK and Takeda.

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Rose-Marie Wilkinson/Michelle Glanville

BSH Secretariat

'Nought' The Farthings

Marcham, Oxfordshire

OX13 6QD, UK

Telephone: +44 (0)1993 846475/+44 (0)1865 391215

Fax: +44 (0)1865 391836

E-mail: bsh@medical-interaction.com

Website: www.bcs.com/affiliates/bsh.html

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