



NEWSLETTER

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This issue of the BSH Newsletter reports on the consensus conference on mechanical circulatory support (MCS) programmes in the UK, which took place in Oxford, UK, on 2 July 2004. The day conference included sessions on:

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7th BSH Autumn meeting 2004 – Reports

The newsletter reporting from this meeting (taking place 25–26 November 2004) is estimated to be circulated to members in February/March 2005. There will also be an article in the *British Journal of Cardiology* in the Jan/Feb 2005 issue, focusing on specific issues from the meeting.

British Cardiac Society Conference 2005

This conference will take place in Manchester on 23–26 May 2005 and the BSH is delighted to have received confirmation that we will be involved in even more sessions this time! We will have five sessions, as follows (exact times/dates to be confirmed):

- **Pragmatic diagnosis of heart failure**
Chairs: Henry Dargie/John Chambers/Fran Sivers
- **Heart failure with preserved systolic function**
Chairs: John Cleland/Jackie Taylor
- **Sudden death in heart failure**
Chairs: Mick Davies/Janet McComb
- **Tomorrow's world**
Chairs: Theresa McDonagh/Anne-Marie Seymour
- **How to manage acute heart failure**
Chairs: tbc

Detailed programmes will be posted on the BSH website in December and the printed programmes circulated to BSH members and Friends in the new year.

Development of mechanical circulatory support programmes for the UK: a consensus conference

In November 2003, delegates at the BSH conference 'Heart failure beyond maximum medical management' (see Newsletter Issue 15) agreed that patients in the UK did not have the access to mechanical circulatory support that was available in other national healthcare systems. So it was decided to hold a consensus conference to specifically tackle the issues of mechanical circulatory support in the UK. The conference, held in Oxford, UK, on 2 July 2004, was addressed by some of the leading UK experts in the field and by opinion leaders from the USA, Germany and The Netherlands. The discussion times at the conference were given high priority as delegates sought to establish consensus on how this exciting new technology should be best implemented in the UK. Key points emerging from these discussions were a need to develop effective networks and equity of access to services, establish appropriate funding, improve patient selection and raise standards of care in heart failure in the UK. The organizer of the conference was Mr Stephen Westaby (Oxford).

Although there have been significant developments in heart failure (HF) surgery over recent years, some have been slow to be adopted in the UK. There is a general feeling that current medical therapy is not able to meet the pressing needs of the nearly 700,000 patients with

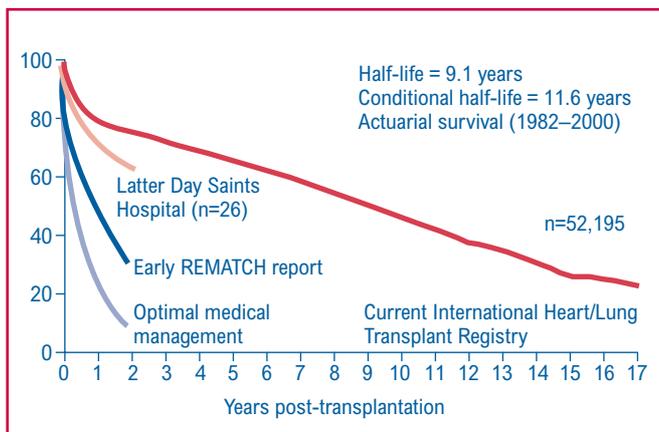
HF (10% of these being stage D) in the UK. This BSH meeting was designed to increase awareness of these surgical advances, and to develop a consensus on the development of mechanical circulatory support (MCS) programmes for HF in the UK.

Background: US perspective

Professor Bartley Griffith (Maryland, USA) provided an overview from the USA, which is a leader in MCS. He noted that in certain centres such as the Latter Day Saints Hospital (Salt Lake City, Utah, USA) the survival and quality of life (QOL) in patients (n=26) receiving a left ventricular assist device (LVAD) as destination therapy is approaching that achieved in transplantation and is an improvement on the results of the REMATCH (**R**andomized **E**valuation of **M**echanical **A**ssistance in **T**reatment of **C**hronic **H**eart **F**ailure) study (Figure 1).¹

LVADs are currently the fastest growing type of medical heart device in the USA, and are predicted by the Healthcare Advisory Board to be first-line therapy by 2010, resulting in a market of US\$11 billion. Professor Griffith concluded that close partnership between surgeon, industry and government is required to ensure the success of this effective therapy. In the discussion that followed, Professor Henry Dargie (Glasgow) commented that although REMATCH was a good start, now is the time to perform further randomized controlled trials of devices to confirm the value of this therapy.

Figure 1. Comparison of survival curves from the Current International Heart/Lung Transplant Registry, a patient series at the Latter Day Saints Hospital (Salt Lake City, Utah, USA), the early REMATCH report¹ and optimal medical management.



Background: European perspective

Professor Roland Hetzer (Berlin, Germany) described the development of MCS in Europe which began with introduction of total artificial hearts in 1986 in Berlin, Vienna and Paris. Extracorporeal pulsatile pneumatic VADs (e.g. Berlin Heart Excor, Thoratec PVAD, Abiomed BVS 5000, Medos) were also in use from this time in a number of centres and over 3600 patients have received these devices. Implantable pulsatile pneumatic VADs (e.g. TCI Heart Mate, Novacor, LionHeart) have been used in nearly 1300 patients since 1992. More recently, over 350 patients have received implantable non-pulsatile electric VADs (e.g. Jarvik 2000, Micromed DeBakey, Berlin Heart Incor) since 1998. The routine application of MCS systems differs widely among European countries according to health care regulations and reimbursement; VADs are regularly implanted, when indicated in Germany, Belgium, France, Austria and Italy, whereas other countries including the UK and Switzerland use the devices only in selected patients and in limited investigational series. A number of other countries such as Finland, Greece and Rumania use these devices only very occasionally.

Dr Hetzer said that the bridge-to-transplantation (BTT) approach has provided a useful vehicle to demonstrate the efficacy of devices, to gain valuable experience and to gain acceptance of the techniques in what was initially a sceptical environment. A total of 42 patients have now remained on these devices long-term in Berlin. Although early experience in Germany was less favourable than that observed in the REMATCH trial, there are now patients with more than 4 years' experience on VADs (Novacor, Berlin Heart Excor).

He concluded that mechanical devices have been successful in keeping patients alive till transplantation and noted that some patients prefer a mechanical device to a donor heart. In some patients mechanical unloading can lead to myocardial recovery, although there are as yet no reliable predictive criteria. The experience in Germany is that various systems can improve patients' physical condition and may provide a

good QOL for several years, particularly in those patients with contraindications for heart transplantation.

Current activity in the UK

There are currently six centres in the UK involved in implantations: Birmingham, Glasgow, Harefield, Manchester, Newcastle and Papworth. Professor John Pepper (London) said that between 1995 and mid-2002 approximately 80 VADs were implanted in patients with New York Heart Association (NYHA) class IV HF in the UK. In mid-2002, funding was given for up to 35 implantable devices per year over 3 years as a BTT by the National Specialist Commissioning Advisory Group (NSCAG). This work has taken place in three centres: Newcastle, Papworth and Harefield. A total of 16 devices were implanted in 2002, 28 in 2003 and 12 in 2004 (up till 14 May 2004). The four devices that have been most commonly used are the Thoratec paracorporeal VAD and intracorporeal VAD, the HeartMate I vented electric LVAD and the Jarvik 2000 axial impeller pump.

Subsequent discussion focused on the poor uptake of new technology in the UK, which is severely limited by lack of resources. There were repeated calls for randomized trials to further demonstrate the effectiveness of this therapy. It was suggested that many younger patients with acute myocardial infarction (MI) could be saved by use of this technology. Dr Adrian Banning (Oxford) commented that the UK needs to gear up on a broad front in its provision of healthcare, and highlighted the lack of provision of primary angioplasty.

However, Professor Pepper suggested that there is an exciting future for this technology in the UK with BTT and bridge-to-recovery, with a number of spectacular recoveries seen in patients with myocarditis and with alcoholic cardiomyopathy. Future advances will include use of these pumps as destination therapy² and perhaps as a bridge to novel therapy such as gene therapy. Mr Steven Westaby (Oxford) also suggested that within 20 years the treatment of chronic and acute MI will have changed dramatically with the use of miniature axial flow pumps.

Cost of circulatory support systems

Noreen Caine (Papworth) described a recent systematic review, to be published in early 2005, of the clinical and cost-effectiveness of LVADs for end-stage HF, which has highlighted the limited nature and poor quality of evidence.³ Most published studies are from the USA and all are on first-generation devices. Mean estimated cost for device implantation for BTT in the NSCAG programme is nearly £100,000 per patient, which includes assessment, the device, implantation to discharge and readmissions.⁴

In the REMATCH trial, overall mean cost per patient of randomization and implantation to discharge was US\$210,000. This included the device, at US\$60,000, but not clinical fees as in most cases these were not charged.⁵ Costs ranged widely between US\$72.5K and US\$1.12 million per patient, and sepsis, pump housing

infection and peri-operative bleeding were the most important cost predictors. Since REMATCH, there have been a number of changes to devices aimed at reducing infection, and improvements in surgical procedure to reduce bleeding. Improved device reliability and further attention to patient selection may also reduce costs.

As well as costs, further information is needed on patient survival, functional status and health-related QOL in order to estimate the value of the therapy. The UK VAD evaluation (EVAD) study final report will provide this range of data on approximately 70 VADs and 80 heart transplants, and form the basis for a future central registry of activity, key outcomes and changing costs.

Ms Caine concluded that future studies need to consider a number of issues, including the net cost/benefit of VADs compared to HF treatments, and the impact of BTT on heart transplant waiting lists. Long-term chronic support is the goal: clinicians and industry need to work on improving devices, and clinicians, academics, industry and government need to work together to plan future high-quality studies.

Scope in the UK

Mr Stephen Westaby (Oxford) gave delegates a brief summary of the potential role of MCS in the UK. He commented on the increase in projected demand for end-stage intervention in the UK and noted that, at present, there could be 12,000 patients aged less than 65 years with end-stage HF who require an LVAD on a permanent basis. In the USA, the Healthcare Advisory Board estimates that there will be 100,000 lifetime LVADs by the year 2010.⁶

Mr Westaby recommended that:

- All interventional catheter laboratories and cardiac operating theatres, and patients with acute MI or myocarditis should have access to rescue technology to treat cardiogenic shock
- Transplant centres should have the option of BTT, particularly as the number of available organs decreases
- Regional centres, supported by specialised HF clinics, should develop lifetime implant programmes as part of networks for advanced cardiac care.

Long-term circulatory support with miniature devices that give people good QOL in the community may well be the future of MCS. In the USA, there are already 67 centres for destination therapy with the TCI HeartMate LVAD alone. Mr Westaby encouraged delegates to consider how many centres will be required in the UK to meet a potential demand of 5–10,000 implants per year.

Short-term circulatory assist

This session covered the use of different devices in short-term circulatory assist.

Devices in the catheter laboratory

Increasing numbers of patients in the cardiac catheter laboratory are undergoing immediate angiography,

including those treated with primary angioplasty for acute MI. Many of these patients have impaired left ventricular (LV) function that may be reversible with treatment, and recovery of LV function can be anticipated. Dr Adrian Banning (Oxford) suggested that there will probably be an increasing need for temporary mechanical cardiac support to facilitate treatment and recovery.

He described the ongoing use of the intra-aortic balloon pump (IABP), which has proved the mainstay of temporary support for failing left ventricles over many years. He commented on the cost-effectiveness, ease of use and familiarity of these devices. However, limitations to their use include the difficulty in tracking irregular heart beats, the femoral approach, which requires the patient to lie horizontally and restricts support, the limited ability to supplement blood pressure (max. 25–30%) and problems resulting from tortuous vascular anatomy.

Dr Banning also described other devices under development, which include a pump (TandemHeart™) requiring trans-septal puncture to generate a bypass circuit that increases flow in the descending aorta resulting in rises in cardiac output and reductions in heart rate, wedge pressure and lactate. Limited available data in acute MI suggest that this device will be of use in a number of patients.^{7,8} Another device is an impeller pump (Impella Recover and Impella Acute), which can be sited temporarily to remove blood from the left ventricle out through the device and into the ascending aorta. The mode of insertion is similar to that of a balloon pump. These devices are being trialed in a small number of laboratories but are not currently commercially available. Preliminary results show that the Recover device reverses cardiogenic shock and that there is a reversal of haemodynamics with the Acute device. Dr Banning commented that although these acute interventions are helping many patients, they do not always produce a complete cure and actually result in more patients with chronic HF.

Cardiogenic shock

Mr Steven Tsui (Papworth) reviewed the treatment of patients in cardiogenic shock where there is gross decline in cardiac output due to HF. Cardiogenic shock occurs in 7–10% of patients following MI and has a 70% mortality rate.⁹ Between 2% and 6% of patients undergoing cardiac surgery will develop cardiogenic shock.

Heart transplantation for such patients is a challenge due to the lack of availability of donor hearts, although an urgent listing system benefits up to 20 patients annually across the UK. However, the vast majority of patients with cardiogenic shock will not survive if they do not have intervention with a VAD as a bridge-to-recovery or BTT. Eventually it is hoped that these patients will receive chronic support from these devices.

At Papworth, patients with cardiogenic shock are divided into four groups:

1. borderline haemodynamics
2. end-organ failure
3. failure to wean off cardiopulmonary bypass (CPB)
4. cardiac arrest.

All of these groups benefit from use of a temporary or implantable VAD at different stages of treatment. Patients with borderline haemodynamics form the largest and most challenging treatment group, as a significant number of these patients will deteriorate in function, develop end-organ failure or cardiac arrest, although many will recover. Invasive haemodynamic monitoring is essential to establish response to treatment and to observe trends. Experienced centres intervene early before any end-organ damage becomes established.

Mr Tsui supported the call for short-term VAD support to rescue these patients as mandatory for all cardiothoracic units in the country. He concluded that VADs buy time for cardiac recovery or transplant, and encouraged cardiologists to refer patients with borderline haemodynamics early to improve chances of survival. Aggressive management in these patients, including timely use of VADs, gives patients in cardiogenic shock a 60–75% chance of successful bridge-to-recovery or transplantation.^{10–12}

Support systems for post-cardiotomy cardiogenic shock

Professor Gilles Dreyfus (Harefield) suggested an approach of early implantation of a cost-effective VAD, supported by a network of institutions to optimize the use of limited resources. He recommended the initiation of inotropic support with the use of IABP. Unsatisfactory response should indicate CPB or an extracorporeal VAD (Biomedicus, Levitronix or Abiomed BVS 5000). Professor Dreyfus suggested that preference should be given to devices that are efficient for up to 2 weeks, have potential high flows greater than 5 L/min and minimal blood trauma. He added that early implantation of a VAD (within 1 hour) and efficient support with high flows (>5–6 L/min) would have a dramatic influence on outcome.

Professor Dreyfus described the aggressive strategy pioneered at Columbia Presbyterian Hospital (New York, USA) based on multiple reassessments and a network approach with a radius of 250 miles converging to a hub.¹³ Patients with post-cardiotomy cardiogenic shock are assessed on the phone and, if patients are adequately managed, they are transferred to the unit and reassessed with close and extensive monitoring.

He urged further discussion on which VADs would be the most appropriate in a cardiac unit, and stressed the early recognition of biventricular vs isolated LV dysfunction. In response to questions about extracorporeal membrane oxygenation (ECMO), Professor Dreyfus said, "I do not believe that there is a place for ECMO to support patients with cardiogenic shock with all the other devices we have today". However, Professor Bartley Griffith (Maryland, USA) suggested that the development of smaller heart–lung pumps in the future will result in wider use of the ECMO approach.

Interhospital networks

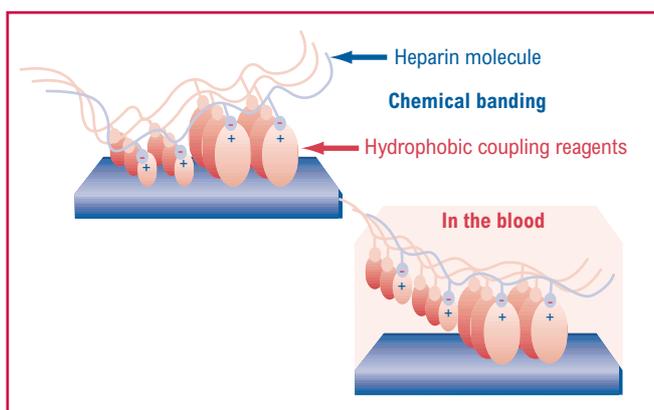
Mr Piet Wassenberg (Abiomed BV, Son en Breugel, The Netherlands) described the importance of interhospital networks between transplant and non-transplant centres, and highlighted the need for these networks in the UK to improve patient outcomes. He commented that therapeutic flexibility, giving more medical options to the patient (including implantable devices, cardiac transplantation and nitric oxide), is a goal of this process. Inexperienced transplant centres are able to network with more experienced centres to allow rapid patient screening and improved access to VADs. Successful networks have been established around a number of US (e.g. Columbia Presbyterian University, New York, USA) and European centres (e.g. Bad Oeynhausen, Berlin, Germany). He commented that early assessment, early implants and early transport are keys for the non-transplant centres in the network. During the meeting there were a number of calls by delegates for a clearly co-ordinated national management plan for these patients.

Mr Wassenberg also described progress with the AbioCor® Implantable Replacement Heart, which has now been implanted in 14 patients. Abiomed are seeking initial FDA market approval this year to treat a defined subset of irreversible end-stage HF patients under a Humanitarian Device Exemption.

New technology

Dr Tomohiro Nishinaka (Oxford) completed the short-term circulatory assist session with a summary of new technology under development. He commented that existing ECMO systems have several limitations including poor durability and poor blood compatibility, resulting in inflammatory responses, thrombus formation and bleeding due to the anticoagulant. Long-term continuous ECMO without anticoagulants has been a significant challenge. Dr Nishinaka described a new system that has the potential for use up to 6 months with no anticoagulant therapy. The system uses a new coating material (T-NCVC), which employs a newly developed heparin-bonding technique (Figure 2), a new membrane oxygenator (Platinum Cube NCVC) and a long-term durable centrifugal blood pump. The system is in use in Japan and is being introduced to a number of European countries.

Figure 2. A new coating material (Toyobo-NCVC) forms part of a newly developed ECMO system.



This new technology has already been used to redesign another ECMO system (QuadroxD) and a paediatric system. These developments were met with enthusiasm by delegates and the new technology should contribute to an improvement in the treatment of patients with severe respiratory and/or circulatory distress, and may lead to a change in concept for ECMO.

Bridge-to-transplantation or -recovery

This session reviewed the use of assist devices in bridging patients to transplant or recovery.

Lessons from the past

Dr Peer Portner (California, USA) described early developments in the 1980s with BTT and total artificial heart BTT, and subsequent experience with over 8000 first-generation devices and 500 newer continuous-flow assist device implants. Despite the debate over the societal benefit of BTT, the technique has provided an invaluable laboratory for device developers and for establishing a basis for destination therapy. Dr Portner described the REMATCH trial as a milestone in the development of this field and commented that its most important contribution was in documenting the natural history of this patient population for the first time.

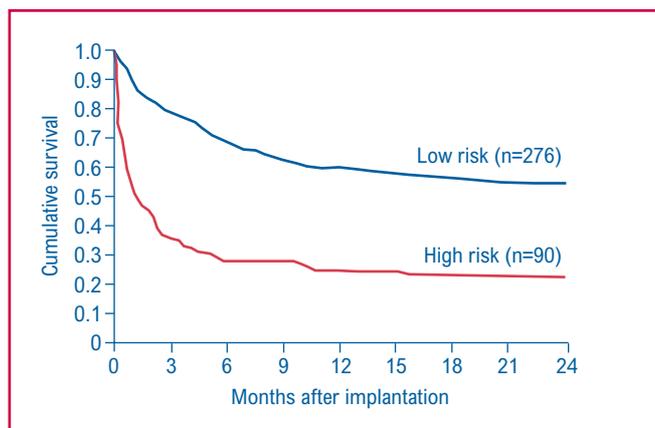
Research and development over recent years have provided critical lessons about thromboembolism, infection and patient selection. A retrospective analysis shows that patients at high risk (with sepsis and respiratory failure, post-cardiotomy, acute MI, previous right HF and age >65 years) have a lower survival outcome (Figure 3).¹⁴ Other important features of this study were improved survival when implantation took place before secondary organ failure, and that highest risk was seen in the first 3 months. Dr Portner noted that myocardial recovery, seen in most VAD recipients, has allowed elective weaning from mechanical support in some patients, giving the option of a bridge-to-recovery.

Despite the important lessons already learned, Dr Portner called for a greater involvement by HF cardiologists, particularly as destination therapy is being explored. Further challenges include the need for a global registry, cost-reduction and reimbursement. In response to a question about available facilities in the UK he commented, "In the USA, it would be seen as inadequate or even malpractice not to have the ability to bridge patients."

Outcome with pulsatile and non-pulsatile systems

Dr Aly El-Banayosy (Bad Oeynhausen, Germany) presented data from his centre's extensive experience with a variety of devices. He reminded delegates of the increasing prevalence of HF and commented that in Germany, in 1999, nearly 7000 patients with cardiogenic shock aged under 65 years died in hospital. The Heart Centre's first implant was in 1987; now over 820 devices have been implanted, representing probably the largest and most diverse experience of any centre in the world.

Figure 3. Effect of patient selection and implant timing on outcome: patient survival after implantation. Retrospective analysis of 366 patients (Novacor European Registry). (Published with permission from reference 14.)



Data were presented on the Centre's out-of-hospital programme, patients with cardiogenic shock and initial experience with third-generation devices such as Lionheart (CUBS trial) and the DuraHeart. Dr El-Banayosy commented that significant improvements in results have been seen in recent years and that the ultimate goal is to use these devices for destination therapy. There followed an extensive discussion on the benefit of these devices for chronic HF patients, and the role of randomized controlled trials, but it was made clear that the majority of patients treated in the German centre were acutely ill and at immediate risk of death rather than suffering from chronic disease. Professor Henry Dargie (Glasgow) commented that LVADs are not yet accepted as the standard of care for destination therapy in patients with chronic HF, and that a randomized controlled trial is needed in the UK. Dr Portner (California, USA) noted that, in the USA, the FDA is requiring any new device to be randomized against the HeartMate – a very expensive way to move forward, with two trials currently underway requiring over 300 patients each.

The NSCAG trial

Mr Stephen Large (Papworth) discussed the national NSCAG trial of BTT outcomes. NSCAG was established by the UK government in 1996 to support low volume, high-cost technology, and aims to improve patient access to this technology and maintain expertise in dedicated centres. NSCAG collaborated with Papworth, Newcastle and Harefield to review a disenfranchised group of patients with chronic HF and deteriorating symptoms who were denied cardiac transplantation despite the presence of the urgent allocation system. This patient population has been described in a recent paper.¹⁵

The group estimated that about 100 patients per year were dying with acute HF across the UK and it was agreed that a BTT programme would be carried out from 2002 in these patients with the restriction that the annual activity did not exceed 10% of the annual transplant activity. Over a 3-year review period the programme aimed to compare mortality in three

groups of patients eligible for transplantation: those on VAD support (Group A, n=105), on inotrope support (Group B, n=55) and those stable on the waiting list (Group C, n=105). The study also aimed to measure QOL at 3-monthly intervals and to construct a measure of cost-effectiveness. Recruitment has been a challenge with Group A recruiting 54 patients and Groups B and C combined recruiting 41 patients to date.

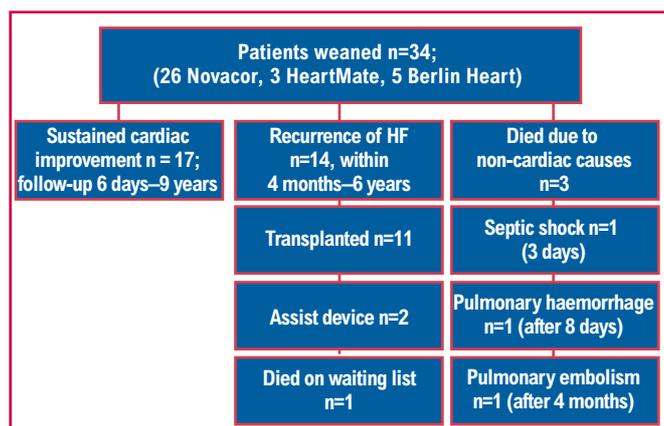
It is too early to draw conclusions from this study but other studies in the UK and USA show similar survival post-transplant for patients previously supported with inotropes or VAD resulting in no disenfranchisement for this patient group.^{16,17} Likewise with QOL, other studies suggest patients' perception of health status and QOL post-VAD implant to be generally stable, with moderate stress levels and acceptable ratings of coping ability. Lack of ambulation and self care were strong indicators of poor outcome.¹⁸ Mr Large urged delegates to proceed carefully in the development of BTT and said that the NSCAG trial will be a foundation for the use of MCS in the UK.

Current outcomes in bridge-to-recovery

Dr Johannes Müller (Berlin, Germany) discussed his group's clinical experience in 34 patients (aged 14–64 years) weaned from implantable and extracorporeal devices (Figure 4) and attempts to identify parameters that could predict cardiac improvement. The mean time after device removal was 6.5 years, with a sustained improvement in cardiac function more than 2 years after weaning seen in 61% of patients. Five-year survival after device removal was 81%. Kaplan–Meier survival curves showed that the probability of surviving more than 9 years after weaning was nearly 70% in these patients. Dr Müller commented that his centre's policy is that every patient fitted with a VAD is a potential candidate for weaning.

Dr Müller said that parameters that are highly predictive for long-term restored cardiac function at the time of removal of the device include LV ejection fraction (EF) greater than 45%, left ventricular internal diameter (LviDD) less than 55 mm and duration of HF less than 5 years. Patients are also more likely to be successfully weaned if they have increased levels of neutral soluble collagen and acid soluble collagen at

Figure 4. Long-term results of patients weaned from assist devices at the Berlin Heart Centre.



the time of implantation, and a lower percentage of tryptase-positive degranulating mast cells in heart tissue. Patients who were successfully weaned tended to be younger and with an ability for rapid improvement of heart function after device placement.

He concluded that the condition of the extracellular matrix is the predominant factor affecting improvement in cardiac function, and attempts should be made to influence the extracellular matrix by optimising loading conditions or by the electrical stimulation of myocytes. Another option may be to enhance repair mechanisms using novel technologies such as stem cell or myoblast implantation.

Long-term treatment of heart failure

The final session looked at the potential for MCS in long-term or permanent use.

Selection of patients

Professor Philip Poole-Wilson (London) said that there was a desperate need for clinical trials in this area because the prediction of outcomes in patients with chronic HF is still poor. Although the REMATCH trial was an important step, he commented that it did not answer a number of vital questions, such the magnitude of effect, how we should treat, and which patient group to treat, and does not yet provide justification for the use of expensive device therapy in patients in the UK with chronic HF. He said, "REMATCH should be regarded as a brilliant pilot study, and before we advise government on the use of VADs we have to have further evidence."

He proposed a UK clinical trial to discover whether the use of LVADs as lifetime treatment is beneficial for patients with advanced HF given optimal treatment by physicians. It is hoped that all transplant centres will be involved in the trial. Entry criteria are:

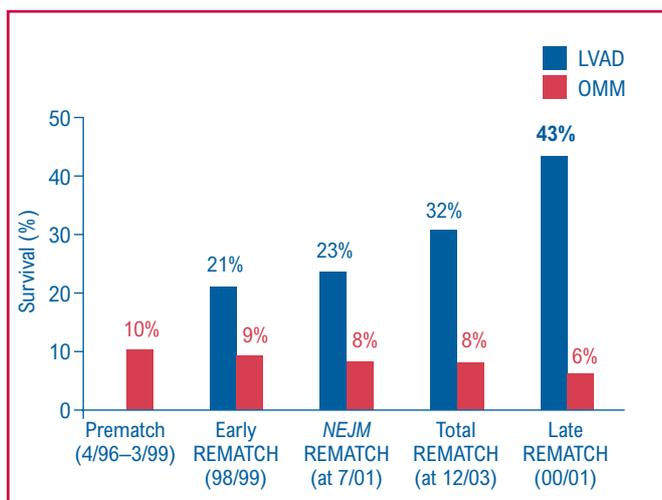
1. Dilated cardiomyopathy; no evidence of ischaemia
2. Ineligible for, refuse or unlikely to undergo, transplantation
3. Myocardial oxygen consumption (MVO₂) less than 12 ml.kg⁻¹.min⁻¹ and RQ greater than 1.
4. NYHA IIIb or IV; in hospital or frequent attendance
5. EF less than 35%
6. Surgeons and physicians agree the patient is suitable
7. Informed consent.

The most important of the proposed entry criteria is that surgeon, physician and patient agree that this treatment is likely to be beneficial. Endpoints will be mortality and a cumulative measure of exercise capacity over time (metre.months over the period of the trial) which takes into account QOL and mortality.

The REMATCH and INTREPID trials

Professor Bartley Griffith (Maryland, USA) commented on the difficulty of conducting the REMATCH trial and the number of centres involved, and said that any future trials will be faced with significant challenges. Poor patient selection, sepsis and failure of the VAD

Figure 5. Two-year LVAD survival from the REMATCH trial showing the results of improved patient selection and device design. *As-treated analysis as of December 2003 dataset.



accounted for the majority of mortality in REMATCH. Improved surgical methods, post-operative care and device design resulted in improved 2-year mortality in the same patient group (Figure 5). With such dramatic improvements and constant change in devices, clinicians will have to pay close attention to the design of any future trials. Professor Griffith encouraged clinicians to pay close attention to the improving results in destination therapy seen in centres such as the Latter Day Saints Hospital (Utah, USA) (>50% survival at 2 years), and to try to emulate them.

Professor Griffith provided some data from the INTrEPID (Investigation of Non-Transplant Eligible Patients who are Inotrope Dependent) trial, the results of which have not been published. The baseline characteristics of patients (n=44, 29 LVADs, 15 controls) were similar to those of patients in the REMATCH trial. Results were similar in terms of outcomes, but there were significant embolic problems with the device used. The RELIANT (Randomized Evaluation of the Novacor® LVAS in a Non-Transplant Population) trial has been proposed with a 2:1 randomisation of WorldHeart (NovaCor) to HeartMate devices and will be similar to the REMATCH trial of destination therapy in sick patients. These trials, while difficult from the perspective of their organisation, financing and enrollment, have provided a unique opportunity to understand the true merits of this technology.

Continuous flow pumps

Mr Stephen Westaby (Oxford) described the large number of continuous flow pumps available today, which include the DeBakey VAD (MicroMed Technology Inc.), HeartMate II LVAS and HeartMate III (Thoratec Corp.), Incor VAS (BerlinHeart),¹⁹ DuraHeart (Terumo Inc.), CorAid VAS (Arrow International), VentrAssist LVAS (Ventracor), HeartQuest (MedQuest Products Inc.) and the HeartWare LVAD. He emphasised the dramatic and rapid improvements in device design and reminded delegates that a range of devices are required to suit different types of patients.

There was some discussion about problems with large abdominal drivelines causing infection problems and Mr Westaby described the Jarvik improvements with a driveline attached to a skull pedestal to reduce infection. Other systems now employ fine drivelines exiting through the abdomen that cause fewer infections, although in the future systems will most probably operate with no drivelines.

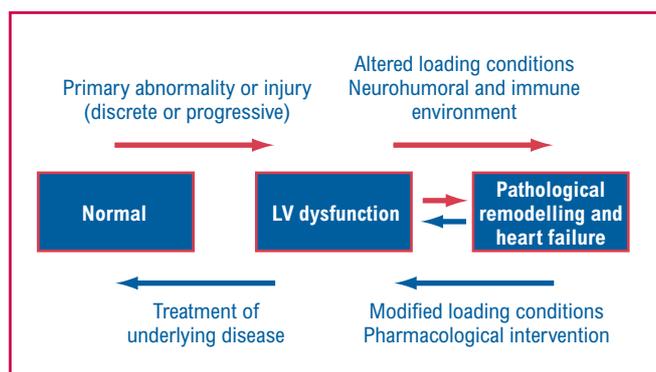
He reminded delegates that when a patient is not suitable for transplantation they will have an unacceptably high risk for LVAD surgery. He commented that with safer, more user-friendly devices and less invasive implant procedures the use of these pumps will be brought out of the end-stage arena.

Adjuvant treatment

Dr Nicholas Banner (Harefield) discussed some of the adjuvant treatments to support MCS in HF patients with dilated cardiomyopathy (DCM). About half of these patients in his centre experience recovery in LV function during LVAD support and he commented that adjuvant drug therapy may contribute to such recovery. He described the Harefield experience in which patients (all transplant candidates aged 20–60 years) were given standard anti-HF drugs once they had recovered from the VAD implant and been discharged from the intensive care unit (ICU). Once patients had shown signs of ventricular recovery (LVEF >45%) the β-blocker was changed from carvedilol to a more cardioselective drug (bisoprolol) plus clenbuterol (a β₂-agonist with actions on skeletal and cardiac muscle). If the device was then explanted, patients went back to the standard drug regimen.

Dr Banner described a model for chronic HF in which there is a primary abnormality that leads to LV dysfunction and neurohormonal activation, an increase in wall stress and alteration of the immune environment leading to pathological remodelling and HF (Figure 6). He suggested that by modifying loading conditions it may be possible to shift patients back to a more normal LV function, although the optimal regimen and durability of recovery remains unknown. Dr Banner suggested that these observations hold the promise that many patients with DCM may be able to avoid the problems of transplant immunosuppression and of long-term LVAD support.

Figure 6. Model for combined mechanical and pharmacological therapy of heart failure.
© Dr Nicholas Banner 2004.



How to proceed in the UK health system

The meeting ended with a brief discussion on the way forward.

Establishment of a national network

There was great enthusiasm for a national network, and a recognised need to develop effective local networks and equity of access to HF services. A number of speakers stated that there was a case for expansion of LVAD provision. It was suggested that information technology will have a major impact on planning services and allowing equitable care. One speaker highlighted the importance of the infrastructure within each centre, which requires labour-intensive medicine to implant and sustain patients in the community.

Improved patient selection

Although the best results with VADs have been seen in patients with DCM, it was noted that most HF patients are ischaemic, have many other complex problems and may not be suitable for implantation. However, other speakers suggested that there are significant opportunities for using LVADs in a broader population such as younger patients with acute MI.

Appropriate funding

Although there was concern that health managers would not provide sufficient funding for current needs, it was suggested that the UK system is well designed to allow the development of excellent national trial protocols to assess the efficacy of LVADs and guidelines.

Raising standards of care

It was recommended that more effort is required on HF prevention and noted that optimal medical management is very patchy across the country. An additional benefit from a national network may be to increase the standard of care across the country. It was recommended that the National Institute of Clinical Excellence (NICE) should produce guidelines on HF and then the regulatory authority should comment on the appropriate devices to be used. The BSH are currently drawing up standards for care of patients with HF under the auspices of the BCS.

Mr Stephen Westaby concluded the meeting by restating the recommendation, agreed by the delegates, that:

- All front-line cardiac centres performing high-risk angioplasty and cardiac surgery should have rescue devices in addition to balloon pumps
- These centres should all be able to support BTT
- Regional specialised HF centres should start destination therapy programmes initially within the transplant community but should expand to include the broader HF population.

References

1. Rose EA, Gelijns AC, Moskowitz AJ. Long-term mechanical left ventricular assistance for end-stage heart failure. *N Engl J Med* 2001;345:1435-43.
2. Stevenson LW, Miller LW, Desvigne-Nickens P *et al.* Left ventricular assist device as destination for patients undergoing intravenous inotropic therapy: a subset analysis from REMATCH (Randomized Evaluation of Mechanical Assistance in Treatment of Chronic Heart Failure). *Circulation* 2004;110:975-81.

3. Clegg AJ *et al.* Southampton HTA Centre. 2004; in press.
4. NSCAG – UK VAD Programme cost estimates. 2004; in press.
5. Oz MC, Gelijns AC, Miller L *et al.* Left ventricular assist devices as permanent heart failure therapy: the price of progress. *Ann Surg* 2003;238:577-83.
6. Healthcare Advisory Board.
7. Thiele H, Lauer B, Hambrecht R *et al.* Reversal of cardiogenic shock by percutaneous left atrial-to-femoral arterial bypass assistance. *Circulation* 2001;104:2917-22.
8. Goldstein A, Pacella J, Clark R. Predictable reduction in left ventricular stroke work and oxygen utilization with an implantable centrifugal pump. *Ann Thorac Surg* 1994;58:1018-24.
9. Barron HV, Every NR, Parsons LS *et al.* The use of intra-aortic balloon counterpulsation in patients with cardiogenic shock complicating acute myocardial infarction: data from the National Registry of Myocardial Infarction 2. *Am Heart J* 2001;141:933-9.
10. Magliato KE, Kleisli T, Soukiasian HJ *et al.* Biventricular support in patients with profound cardiogenic shock: a single center experience. *ASAIO J* 2003;49:475-9.
11. Khot UN, Mishra M, Yamani MH *et al.* Severe renal dysfunction complicating cardiogenic shock is not a contraindication to mechanical support as a bridge to cardiac transplantation. *J Am Coll Cardiol* 2003;41:381-5.
12. Samuels LE, Holmes EC, Thomas MP *et al.* Management of acute cardiac failure with mechanical assist: experience with ABIOMED BVS 5000. *Ann Thorac Surg* 2001;71:S67-72.
13. Oz MC *et al.* Presented at the Society of Thoracic Surgeons, 35th Annual Meeting, San Antonio, Texas, January 1999.
14. Deng MC, Loebe M, El-Banayosy A *et al.* Mechanical circulatory support for advanced heart failure: effect of patient selection on outcome. *Circulation* 2001;103:231-7.
15. Stevenson LW, Rose EA. Left ventricular assist devices: bridges to transplantation, recovery and destination for whom? *Circulation* 2003;108:3059-63.
16. Birks EJ, Yacoub MH, Banner NR *et al.* The role of bridge to transplantation: should LVAD patients be transplanted? *Curr Opin Cardiol* 2004;19:148-53.
17. Morgan JA, John R, Rao V *et al.* Bridging to transplant with the HeartMate left ventricular assist device: the Columbia Presbyterian 12-year experience. *J Thorac Cardiovasc Surg* 2004;127:1309-16.
18. Grady KL, Meyer PM, Dressler D *et al.* Longitudinal change in quality of life and impact on survival after left ventricular assist device implantation. *Ann Thorac Surg* 2004; 77:1321-7.
19. Hetzer R, Weng Y, Potapov EV *et al.* First experiences with a novel magnetically suspended axial flow left ventricular assist device. *Eur J Cardiothorac Surg* 2004;25:964-70.

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Becoming a Member or a Friend of the BSH

Membership is open to anyone involved in the diagnosis, management or science of HF.

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