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Update on Mechanical Circulatory Support in Heart Failure

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Abstract and Introduction

Introduction

Temporary mechanical support technology has advanced, and the miniaturisation of these devices has permitted their use with less operative morbidity and more rapid functional recovery following operation. At present a broad range of devices are available. The most comprehensive mechanical support for both the systemic and the pulmonary circulation is still best provided by extracorporeal membrane oxygenation for extremely ill patients with lung and heart failure, which remains a cumbersome and invasive but extremely effective form of short term mechanical support.[w1] However, the development of devices such as the Impella and the Tandem-Heart has allowed less invasive forms of temporary support of the systemic circulation typically applied during high risk percutaneous intervention procedures, such as high risk coronary stenting[w2 w3] and cardiogenic shock.[w4 w5] Larger, external pulsatile pumps such as the AbioMed 5000 and the more recent magnetically levitated centrifugal Centrimag pump are used to provide temporary support of either the left or right ventricle or both as a short term rescue strategy post-cardiotomy, or as a bridge to more long term cardiac replacement treatment or recovery.[w6–w9] Counterpulsation technology remains a mainstay of acute care in patients with cardiogenic shock, both before and after surgical or percutaneous intervention. This technology has been developed and miniaturised for potential long term use in ambulatory patients, most notably the Akpulsor (Cardiak, Ltd, Oxford, UK), C-Pulse (Sunshine Heart Inc, New South Wales, Australia), and CardioPlus (CardioPlus, Inc, Detroit, Michigan, USA) devices. None of these devices has been evaluated in a US Food and Drug Administration (FDA) or European CE approved trial. Finally, enhanced external counterpulsation treatment has been established as an effective therapy in intractable angina in non-revascularisable patients with coronary artery disease. The counterpulsation principle and marked left ventricular afterload reduction may also be helpful in congestive heart failure[w10 w11] and this has been evaluated in the Prospective Evaluation of EECP (enhanced external counterpulsation) trial.[w12]

Ventricular Assist Devices as Long Term Cardiac Replacement Therapy

At present the gold standard of long term heart replacement remains heart transplantation, but the number of heart transplants performed is limited by donor organ availability.[w13] Research in genetic engineering and xeno-transplantation, using transgenic animals as donors, has progressed considerably but not yet to the stage of clinical trials.[w14] Although much progress has been made in the understanding of stem cell biology in heart failure, the field is still in its infancy. Therefore, there has been great interest in the development of left ventricular assist devices (LVADs) as lifelong support for end-stage chronic heart failure.

Left Ventricular Assist Devices

LVADs have been in use as a bridge to heart transplantation for 20 years; the HeartMate XVE device, an electrically powered pulsatile pump, was approved for this purpose in 1994.[w15] The Randomised Evaluation of Mechanical Assistance in Treatment of Chronic Heart Failure (REMATCH) study evaluated the long term benefit of HeartMate XVE placement compared with optimal medical treatment in end-stage heart failure patients.[1] The rates of survival at 1 year were 52% in the device group and 25% in the medical treatment group (p=0.002), and at 2 years the survival rates were 23% and 8% (p=0.09), respectively. A 48% reduction in death from all causes was attributable to LVAD treatment compared with best medical treatment in this trial, and on this basis, the HeartMate XVE was approved for use as destination therapy in 2002.

Follow-up studies since REMATCH[2] have shown that uptake of chronic LVAD treatment has been limited because there is an unacceptably high incidence of device failure.[3] In addition, Leitz's work shows that there continues to be a very high early mortality with a continued decline in survival later. Although REMATCH showed that LVAD implantation improved survival compared to medical treatment, both groups had an extremely high early mortality and most were on inotropic support. This underlines the importance of patient selection. In this respect, Leitz and colleagues showed that using a novel operative risk score encompassing severity of heart failure, nutritional status, renal function, and right ventricular (RV) function, the patients with the lowest risk had the best early survival. But, even in the sickest patients, LVAD treatment offered a significant survival advantage, as shown in a subsequent sub-study of the REMATCH population[w16] and in a recent study with the Novacor device (also a pulsatile device) in inotrope dependent patients with end-stage heart failure.[4]

Unlike pulsatile pumps, a continuous flow pump based on either axial or centrifugal motors can be made smaller and more

durable. They can also be converted easily to a totally implantable system. These types of axial flow devices have been in development since 1988 and were first implanted in clinical trials 10 years later (figures 1 and 2). The advantage of these devices is their smaller size and fewer moving parts, which should increase durability. Concerns about non-physiological non-pulsatile output from these devices resulting in possible end-organ damage have been allayed by recent data showing their safety in relatively long term use as a bridge to transplantation when compared with pulsatile devices.[5] An important issue with axial flow devices is their requirement for anticoagulation and the risk of thrombosis and haemolysis. The most commonly used axial device, the HeartMate II, is already FDA approved for bridge to transplantation. A totally implantable LVAD, the Lionheart device, was approved as destination therapy in Europe. The absence of an external drive-line was thought to significantly reduce the risk of infection.[w17] Unfortunately this pump proved to have serious durability problems with the blood sac which tended to rupture, and this only came to light in patients after 1 year. It has now been withdrawn from clinical practice.

In a recently reported randomised trial, Slaughter and colleagues[6] showed that a continuous flow LVAD, HeartMate ll, in patients with advanced heart failure significantly improved the probability of survival free from stroke and device failure at 2 years compared with a pulsatile device. The primary composite end point was survival free from disabling stroke and reoperation to repair or replace the device. This was achieved in more patients with continuous flow than with pulsatile flow devices (62 of 134 (46%) vs 7 of 66 (11%); $p<0.001$; HR 0.38, 95% CI 0.27 to 0.54; $p<0.001$), and patients with continuous flow devices had superior actuarial survival rates at 2 years (58% vs 24%, $p=0.008$). This is a significant achievement, but the risk of stroke, infection and device malfunction remains a reality. In this study 59 of 134 patients (44%) receiving the continuous flow device had a disabling stroke or died within 2 years. While helpful and reliable, LVADs still represent a form of life support with a specific set of burdens and complications.

Figure 1. HeartMate II rotary axial impeller pump.

Biventricular Support

The LVAD alone may be unsuitable for patients with advanced congestive cardiac heart failure with concomitant RV failure. Very often, RV function improves after placement of an LVAD, when RV dysfunction has developed secondary to chronic pulmonary venous congestion, but occasionally persistent right heart failure only becomes apparent after LVAD implantation.[w18] Specifically, in the setting of intrinsic RV myocardial dysfunction due to ischaemic heart disease or infiltrative disease, RV support may prove necessary, with or without additional LVAD support. Recently, risk factors have been identified that may help to better predict patients with ongoing RV failure after LVAD implantation.[w19]

Current Devices in Clinical Trials

Cardiac assist devices that are already approved and being evaluated in clinical trials have been implanted under the rather artificial designations of either a bridge to transplantation or as destination therapy (Table 1). In reality, a significant number of patients who were thought to be poor transplant candidates initially became reasonably good candidates for cardiac

transplantation when their multisystem organ dysfunction improved with effective haemodynamic support on a ventricular assist device (VAD). In addition, LVAD implantation as a bridge to cardiac transplantation permits effective exercise capacity[w19] and weight loss, improvement in end-organ perfusion, and even reversal of pre-existing medically unresponsive pulmonary hypertension.[w20]

Table 1. Implantable cardiac assist devices

Device	Manufacturer	Device type	Approval
HeartMate XVE	Thoratec, California, USA	First generation (pulsatile)	FDA approved as DT and BTT European CE mark approved for all indications
HeartMate II	Thoratec	Second generation (axial flow)	FDA approved as BTT and DT European CE mark for all indications
Jarvik 2000	Jarvik Heart, New York, USA	Second generation (axial flow)	European CE for all indications
Ventr/Assist	Ventracor, Sydney, Australia	Third generation (centrifugal)	European CE for all indications Now withdrawn
Incor	BerlinHeart, Germany	Third generation (centrifugal)	European CE mark for all indications
HeartWare	HeartWare, Florida, USA	Third generation (centrifugal)	Under evaluation for CE mark
DuraHeart	Terumo Heart, Michigan, USA	Third generation (centrifugal)	European CE mark approved for all indications
Synergy	Circulite, Delaware, USA	Micro-pump	Under evaluation in Europe for CE mark

BTT, bridge to transplant therapy; DT, destination therapy; FDA, US Food and Drug Administration.

With increasing experience of VAD treatment, other interesting clinical and laboratory observations have been made. Myocytes at subcellular and cellular levels, as well as the heart as an organ, have displayed an ability to recover function. Birks and colleagues have reported on the very promising possibility of meaningful, clinical recovery.[7]

Patient Selection

The landmark findings of the post-REMATCH data highlighted the importance of nutritional parameters, haematological abnormalities, and markers of RV failure and end-organ dysfunction in determining mortality post-LVAD placement.[2] These findings shone a new light on the original REMATCH trial, in that much of the early mortality could have been attributable to patient selection, as these patients were uniformly New York Heart Association (NYHA) functional class IV, with severely low cardiac indices (mean 1.9 l/min/m^2) and evidence of end-organ dysfunction (mean serum creatinine 180 µmol/l). In Leitz's univariate analysis of the post-REMATCH data, highly significant predictors for 90 day mortality post-LVAD placement were thrombocytopenia (<148 000/µl), low serum albumin (<3.3 g/dl) as a measure of nutritional deficiency, elevated aspartate aminotransferase (AST >45 U/ml) reflecting liver congestion, and low haematocrit (<34%). These findings have led to an increased awareness that the previous practice of LVAD implantation as a last resort in severely decompensated patients is not in their best interest, and that either LVADs should be considered earlier in the evolution of advanced heart failure, when nutrition and end-organ function are still optimal, or means should be taken to improve these factors preoperatively where possible.

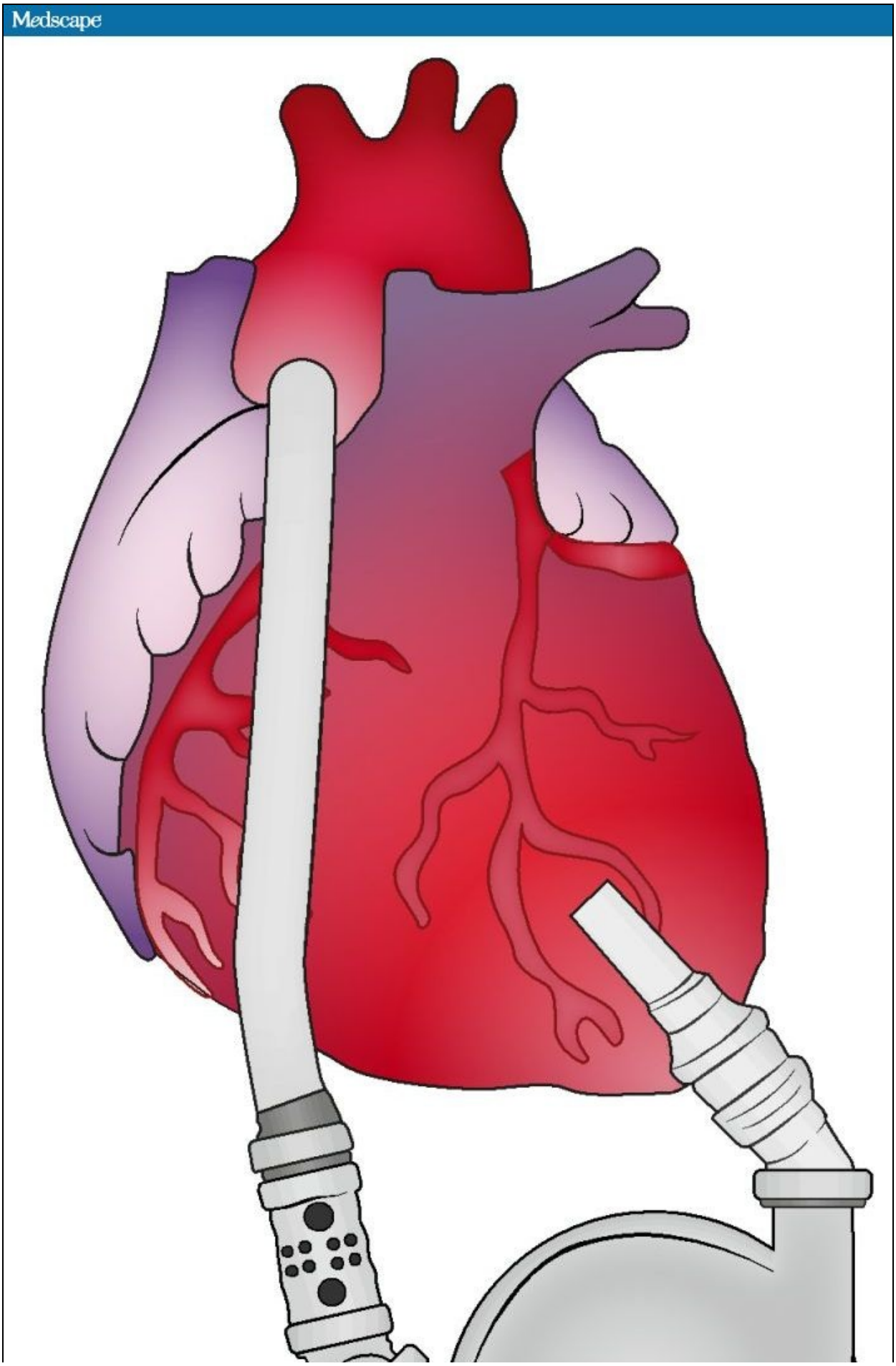
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Figure 2. HeartMate and pulsatile pump.

Whether LVADs are implanted as destination therapy or as a bridge to transplant, full commitment from the patient and optimal support from family or other caregivers is essential. In this respect, the psychological and sociological milieu of the patient is critical and requires detailed assessment by specialised staff before LVAD implantation, as is routinely true in the consideration of patients for cardiac transplantation.[w21 w22]

Complications After LVAD Implantation

The main complications specific to LVAD placement are related to driveline infection, postoperative bleeding, and thromboembolism. Driveline infections are common and serious if allowed to progress to pump pocket infection, which can only be eradicated definitively by LVAD explantation.[w23] These issues underline the importance of patient and care-provider compliance with driveline exit site care. Hopes that total implantability of assist devices and the elimination of a driveline would reduce the risk of infection may be realistic based on recent reports of the Lionheart experience in Europe.[w17] Increased perioperative mediastinal bleeding and spontaneous haemorrhage (commonly gastrointestinal or epistaxis and rarely intracranial) have been associated with LVAD implantation, more than what would be expected based on the anticoagulation regimen alone. Some of the increased gastrointestinal bleeding may be attributable to the formation of arteriovenous malformations, which may be more common with continuous flow devices.[w24] Recent data have shown that the increased bleeding tendency overall may be largely attributable to acquired platelet dysfunction due to high shear rates and abnormal microaggregate formation, and in this regard resemble an acquired von Willebrand's disease.[w25 w26]

The incidence of neurological events and thromboembolism post-LVAD implantation is low (<20%) for both the pulsatile and non-pulsatile devices, and for the HeartMate II, prolonged periods of low or even no anticoagulation due to bleeding concerns may be safe.[w27 w28] RV failure post-LVAD placement is associated with increased perioperative mortality and morbidity but is difficult to predict. Investigations are in progress to define better means of assessing the need for RV support post-LVAD implantation.[8] Other complications seen frequently post-LVAD implantation are exudative pleural effusions.[w29] These effusions occasionally interfere with the rehabilitation of the patient and radiological guided drainage is effective and safe.

Bridge to Recovery

Reports regarding rates of recovery during pulsatile LVAD support are varied (Table 2). The Columbia group reported a 1% rate of sustained cardiac recovery in 111 patients with ischaemic and non-ischaemic aetiology. In contrast, the German Heart Institute reported that 13% of patients with non-ischaemic heart failure demonstrated sustained recovery with a minimum follow-up of 36 months after LVAD explantation. The LVAD Working Group reported on a multicentre prospective study of 67 LVAD patients with both ischaemic and non-ischaemic aetiology. Six per cent of the entire cohort and 7% of all non-ischaemic patients were able to undergo LVAD explantation. There were no reports of the consistent use of pharmacological treatment during LVAD support, until the first Harefield recovery study.[9] In this study, 15 LVAD patients received maximal doses of heart failure drugs, followed by high dose clenbuterol, a β-agonist. All patients had a non-ischaemic aetiology, and 80% had had heart failure for more than 6 months. The authors reported that 75% of patients receiving clenbuterol could undergo LVAD explantation and 46% of all patients with non-ischaemic heart failure could be managed in this way. More recently, Birks and colleagues have reported a similar experience with a continuous flow pump, HeartMate II.[10] Thirty-three patients underwent LVAD implantation at Harefield during the 3 year study period. Twenty-three patients (70%) with non-ischaemic cardiomyopathy were considered appropriate for the recovery protocol at the time of implantation, and 20 patients (61%) who survived LVAD implantation formed the study cohort. Using the same intensive recovery protocol as in their first study, the authors were able to demonstrate that 30% of all patients and 43% of all non-ischaemic patients could be managed to long lasting recovery.

Table 2. Bridge to recovery

Author	Study population	Aetiology of heart failure	Sustained recovery N (%)	Minimum follow-up (months)
Mancini 1998	111	60 ICM, 51 DCM	1 (1)	15
Dandel 2005	131	DCM	17 (13)	36
Birks 2006	24	DCM	8 (33)	48
Maybaum 2007	67	37 DCM, 30 ICM	4 (6)	12

DCM, dilated cardiomyopathy; ICM, idiopathic cardiomyopathy.

Although this strategy appears very promising, a number of issues remain to be resolved. Different strategies of continuous flow pump management and the challenges of restarting heart failure drugs after LVAD implantation need to be investigated.

Furthermore, the differential effects of the two stages of drug management—phase I: conventional neurohormonal blockade; phase II: clenbuterol—need to be further assessed.

The Total Artificial Heart

The first successful implantation in an animal model took place in 1957; the subject, a dog, survived just 90 min but this was a landmark achievement. The first clinical implant occurred in 1969. The patient was successfully bridged to transplant for 64 h but died of an overwhelming pneumonia. Joyce and his team at the University of Utah subsequently developed the Jarvik-7 Total Artificial Heart (TAH), which was first implanted in 1982. The patient survived 112 days. Several subsequent implants took place in different centres, the longest survivor being 620 days. Due to the unacceptable morbidity and mortality as well as a very poor quality of life while on TAH support, the Jarvik-7 was no longer approved by the FDA from 1990 onward. The updated version, the CardioWest TAH, now known as the SynCardia temporary TAH, was approved by the US FDA for temporary use in patients with irreversible biventricular heart failure who are potential candidates for cardiac transplantation. This approval was granted on the basis of a multi-institutional study of 80 patients.[11]

The survival rate has been 79% to the time of transplantation; 86% of those survivors have lived for 1 year after transplantation. Sixty-nine per cent of the TAH recipients, compared with 37% of a matched control group, have reached the end-point of successful post-transplantation survival ($p<0.01$). Stroke was seen in 10% of patients, but nearly all occurred at the time of implantation or explantation. The stroke rate during device support was <2%.[w30]

Extending VAD Technology to the 'Less Sick'

In many respects, VAD technology has advanced with a view towards engineering devices that are small, totally implantable, and durable for years as a long term cardiac replacement. Currently the most promising features surfacing in technology are third generation, magnetically levitated impellor devices with fewer moving parts and increased durability, and transcutaneous power delivery, which is expected to reduce driveline related device infection significantly.

The provision of chronic ventricular assist at an appropriate stage of a patient's heart failure before they deteriorate to the point of being moribund will be critical to an improved outcome, both in survival and quality of life. As new devices prove to be more patient friendly and durable, shifting the target population to a less ill group would be in the best interest of patients suffering from advanced heart failure. Patients with less severe heart failure are also less likely to require a high output from these devices. The potential need for a device with an output of only up to 2–4 litres/min renders it conceivable to miniaturise the devices and also the route of access required for their implantation. In addition, their lower power requirements would facilitate the development of totally implantable power supply units. Currently, many companies are developing technology for this application, most notably Circulite Inc, whose Synergy device requires minimally invasive access for implantation, delivers up to 4 litres/min of blood to the aorta via the left subclavian artery, and has a completely implantable power supply. Devices of this kind with minimal morbidity related to implantation have already been used successfully as a bridge to transplantation.[w31] They may potentially alter the course of the disease in advancing heart failure, and are the focus of clinical trials. Cardiac assistance such as this in the otherwise reasonably compensated patient may even allow intrinsic myocardial recovery and reverse remodelling, as has been shown for larger LVADs.[12] [w32–w34]

Meyns and colleagues[w31] have reported on long term partial support with the Synergy Pocket Micro-pump (CircuLite Inc, Saddle Brook, New Jersey, USA) (figure 3). The operation uses a minimally invasive incision below the right clavicle that allows for pump outflow to the axillary artery and provides pump inflow through the interatrial groove into the left atrium. They introduced the pump into 17 patients (14 men), aged 53 (±9 years) with an ejection fraction of 21±6%, mean arterial pressure 73±7 mm Hg, pulmonary capillary wedge pressure 29±6 mm Hg, and cardiac index 1.9±0.4 l/min/m^2. The duration of support ranged from 6–213 (median 81) days. Nine patients underwent follow-up right heart catheterisation at 10.6±6 weeks. These patients showed significant increases in arterial pressure (67±8 mm Hg vs 80±9 mm Hg; $p<0.01$) and cardiac index (2.0±0.41 l/min/m^2 vs 2.8±0.61 l/min/m^2; $p=0.001$), with large reductions in pulmonary capillary wedge pressure (30±5 mm Hg vs 18±5 mm Hg; $p=0.001$).

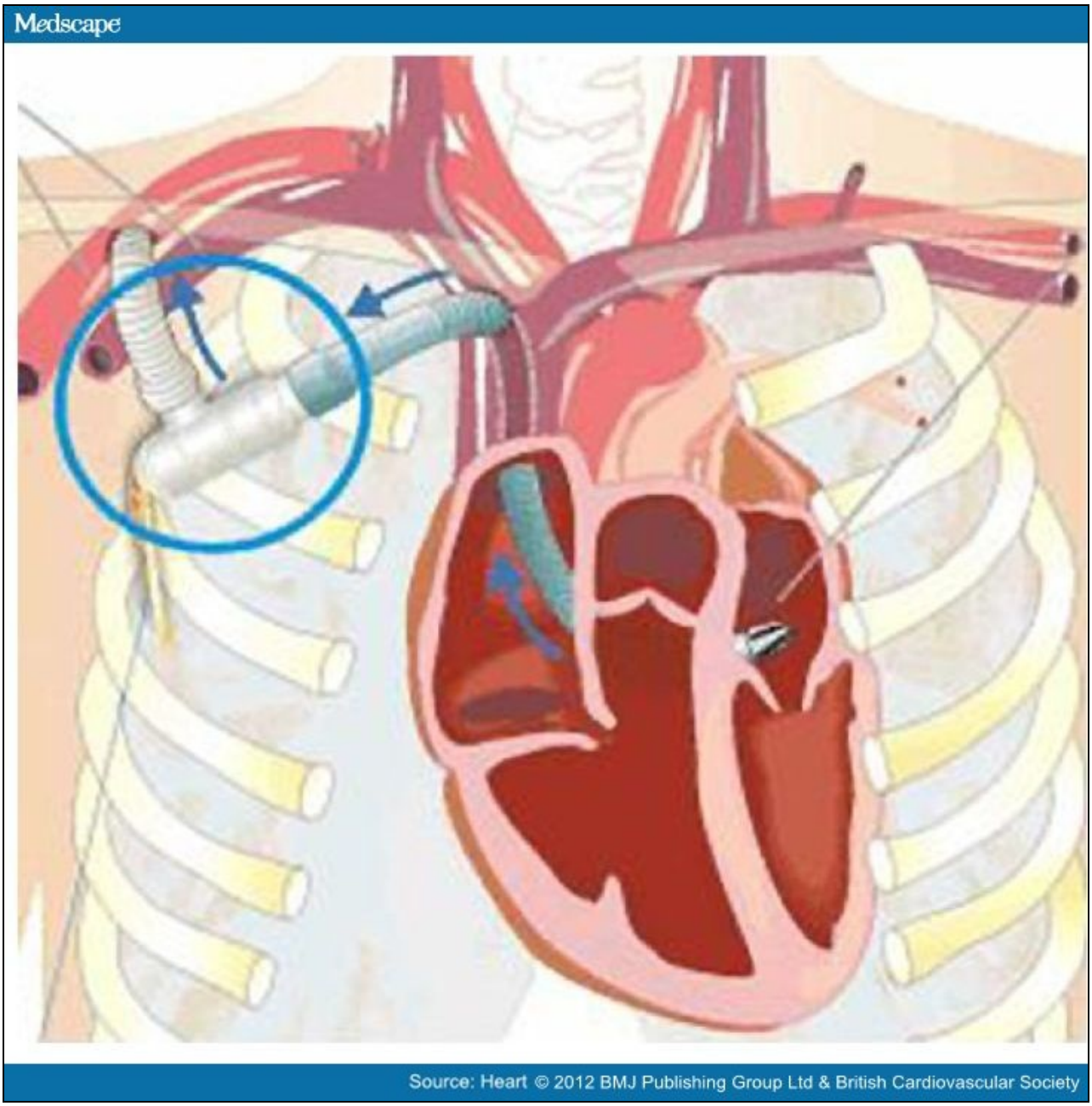

Figure 3. Synergy micro-pump for partial left ventricular assist.

A major concern with partial support has been that pumps might be more liable to develop pump thrombosis at low flow. The pump was modified after stopping the clinical trial and performing bench testing, and then a new pump was released with enhanced washing within the rotor and a new target international normalised ratio (INR). With the new design and anticoagulation strategy, there have had been no further episodes of pump thrombosis with 29 implants over a period of support of 14 months.

Cost Effectiveness

Heart failure is associated with substantial morbidity and mortality, leading to frequent admissions to hospital and long term drug costs. As a consequence it is a major cost to the NHS and increasingly the focus of policy initiatives. Clegg and colleagues[13] reported on the clinical outcome and cost effectiveness of LVADs as a bridge to heart transplantation. They conducted a systematic review and an economic evaluation according to internationally recognised methods. They found that LVADs appear beneficial, improving survival, functional status and quality of life, but adverse events were a serious concern. The economic evaluation showed that LVADs had a cost per quality adjusted life year of £65 242 (€78 410, US$100 585). They concluded that it is unlikely that they will be cost effective unless costs decrease or the benefits of their use increase.

A report from Duke University[w35] examined long term outcomes and costs of VADs among all Medicare claimants for the period 2000 to 2006. Overall 1 year survival was 51.6% (N=669 out of 1476) in the primary device group and 30.8% (N=424 out of 1467) in the post-cardiotomy group. Among primary device patients, 815 (55.2%) were discharged to home with a device. Of those, 450 (55.6%) were readmitted within 6 months and 504 (73.2%) were alive at 1 year. Of the 493 (33.6%) post-cardiotomy patients discharged to home with a device, 237 (48.3%) were readmitted within 6 months and 355 (76.6%) were alive at 1 year. The authors concluded that improving patient selection and reducing perioperative mortality will be critical for improving overall patient outcomes.

Conclusion

LVADs have been shown to be efficacious as a bridge to transplantation and as destination therapy in advanced heart failure. The threshold level of heart failure beyond which patients will benefit from the insertion of an LVAD needs to be determined. Currently, LVADs are indicated in patients with advanced heart failure who cannot be weaned from inotropic support and who have a cardiac index <2.0 l/min/m^2, a systolic blood pressure <80 mm Hg, and a pulmonary capillary wedge pressure >20 mm Hg (Hunt 2001[14]). As the technology improves and as LVADs get smaller, more efficient and safer, it is likely that this threshold level will change such that patients with less advanced heart failure may also benefit from an LVAD (Birks 2010[15]).

Sidebar

Key Points 1: Overview of Implantable Left Ventricular Assist Device Treatment

- Continuous flow rotary blood pumps eliminate the need for a blood pumping chamber and volume compensation.
- A lighter, smaller pump is better suited for patients with a smaller body size.
- Simple designs involve only one moving part, the rotor, and no internal valves. This allows for enhanced device durability.
- They are silent in operation.
- The potential benefits of the smaller percutaneous lead include a reduced risk of infection and greater patient comfort.

Key Points 2: Patient Selection

Patient selection and timing of implant are two major determinants of success. The most influential pre-implant measures are:

- Improving nutritional status.
- Lowering pulmonary vascular resistance.
- Aggressive management of volume to minimise right ventricular workload and liver congestion.
- Optimise coagulation.
- Optimise renal, hepatic, pulmonary, and neurological function.
- Treat any infection

The patient's support system, psychosocial status, compliance with care, and ability to operate and care for external system components require careful consideration.

Key Points 3: Outpatient Management

- Success depends on comprehensive care from a multidisciplinary team.
- Effective patient education and support are key components.
- Target international normalised ratio (INR) for patients receiving the HeartMate II is 1.5 to 2.5 with warfarin.
- Stabilise the INR before discharge from hospital.
- Hypertension must be controlled to avoid reduced left ventricular assist device support and cardiac output, and to avoid stroke and transient ischaemic attack.
- Immobilising the percutaneous lead to prevent exit trauma reduces infection risk. Care of this lead is a priority for outpatient management.

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References

1. Rose EA, Gelijns AC, Moskowitz AJ, *et al*. Long-term mechanical left ventricular assistance for end-stage heart failure. *N Engl J Med* 2001;345:1435–43.
   • This is the classic study of long term untethered LVAD support in extremely sick patients.
2. Leitz K, Long JW, Kafoury AG. Outcomes of left ventricular assist device implantation as destination therapy in the post-REMATCH era: implications for patient selection. *Circulation* 2007;116:497–505.
   •Many of the units contributing patients to the original REMATCH study were inexperienced. This study shows the benefit of gaining experience in treating these very challenging patients.
3. Hunt SA. Mechanical circulatory support: new data, old problems. *Circulation* 2007;116:461–2.
   • An excellent review by an international authority.
4. Rogers JG, Butler J, Lansman SL. Chronic mechanical circulatory support for inotrope-dependent heart failure patients who are not transplant candidates: results of the INTrEPID Trial. *J Am Coll Cardiol* 2007;50:741–7.
   • This destination therapy study illustrates the significant haematological problems which arise in the management of these patients.
5. Radovancevic B, VrtovecdeKort B, deKort E. End-organ function in patients on long-term circulatory support with continuous or pulsatile flow assist devices. *J Heart Lung Transplant* 2007;26:815–18.
   • This study highlights the contrast between pulsatile and non-pulsatile devices, and indicates the level of safety.
6. Slaughter MS, Rogers JG, Milano CA, *et al*. Advanced heart failure treated with continuous-flow left ventricular assist device. *N Engl J Med* 2009;361:2241–51.
   • This paper brings the REMATCH study into the current era by the use of a rotary pump and has set the stage for life-long VAD treatment as an alternative to heart transplantation.
7. Birks EJ, Hall JL, Barton PJ. Gene profiling changes in cytoskeletal proteins during clinical recovery after left ventricularassist device support. *Circulation* 2005;112:157–64.
   • This gives an intriguing insight into some of the molecular pathways involved in ventricular remodelling.
8. Matthews JC, Koelling TM, Pagani FD. The right ventricular failure risk score, a preoperative tool for assessing the risk of right ventricular failure in left ventricular assist candidates. *J Am Coll Cardiol* 2008;51:2163–72.
   • The right ventricle is often overlooked in the assessment of left ventricular failure. This study highlights the importance of optimising right ventricular function as much as possible before insertion of an LVAD.
9. Birks EJ, Tansley PD, Hardy J, *et al*. Left ventricular assist device and drug therapy for the reversal of heart failure. *N Engl J Med* 2006;355:1873–84.
   • This is one of the most successful reports of recovery of patients with end-stage heart failure.
10. Birks E, George RS, Hedger M, *et al*. Reversal of severe heart failure with a continuous-flow left ventricular assist device and pharmacological therapy. A prospective study. *Circulation* 2011;123:381–90.
    • This study reports on a high success rate of recovery in end-stage heart failure using a non-pulsatile rotary pump.
11. Copeland JG, Smith RG, Arabia FA. Cardiac replacement with a total artificial heart as a bridge to transplantation. *N Engl J Med* 2004;351:859–67.
    • The total artificial heart is again in the news, but this is the group who have, almost alone, pioneered this device. Currently it is used as a bridge to transplant only.
12. Klotz S, Barbone A, Reiken S. Left ventricular assist device support normalises left and right ventricular beta-adrenergic pathway properties. *J Am Coll Cardiol* 2005;45:668–76.
13. Clegg AJ, Scott DA, Loveman E, *et al*. Clinical and costeffectiveness of left ventricular assist devices as a bridge to heart transplantation for people with end-stage heart failure: a systematic review and economic evaluation. *Eur Heart J* 2006;27:2929–38.
    • There is very little information on cost effectiveness or cost benefit in the use of VADs. This is one of the few studies and has interesting conclusions.
14. Hunt SA, Baker DW, Chin MH. ACC/AHA Guidelines for the evaluation and management of chronic heart failure in the adult: executive summary. A report of the American College of Cardiology/American Heart Association Task force on Practice Guidelines (Committee to revise the 1995 Guidelines for the Evaluation and management of heart Failure). *J Am Coll Cardiol* 2001;38:2101–13.
15. Birks EJ. The comparative use of ventricular assist devices: differences between Europe and the United states. *Texas Heart Inst J* 2010;37:565–7.

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