VIEWPOINT

The need for artificial hearts

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Summary

Chronic immunosuppression, allograft coronary disease, and restricted availability of donor organs continue to limit the scope of cardiac transplantation. Meanwhile increasingly favourable experience with implantable blood pumps used as a bridge to transplant has reintroduced the concept of permanent mechanical cardiac support. Existing models (for example, the Thermo Cardiosystems Heartmate device) are now used for such support in patients who are not candidates for transplantation. Miniaturised axial flow pumps such as the Jarvik 2000 fit within the failed left ventricle and provide an exciting prospect for the treatment of heart failure in the future. Preliminary experience suggests that the "offloaded" left ventricle may recover. Mechanical blood pumps can be used before the onset of multisystem failure and removed if the myocardium recovers. This "bridge to recovery" concept should be tested in patients with recoverable cardiomyopathy and those with coronary disease and poor left ventricular function where an implantable pump can be used in conjunction with myocardial revascularisation.

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Though cardiac transplantation markedly improves quality of life and provides a cost effective alternative to medical therapy, the number of donor organs is restricted.^{1,2} Overall success is also limited by the complications of chronic immunosuppression, opportunistic infection, and the development of allograft coronary artery disease requiring retransplantation in 40% of patients by six years.^{3,4} In the absence of a realistic alternative, transplantation discards some poorly functioning but potentially recoverable hearts, particularly in dilated cardiomyopathy, viral myocarditis, or protozoal infections. In contrast, modern blood pumps can offload the failed left ventricle and encourage an element of recovery. There

is now the prospect of improved mechanical devices that, without the risks of immunosuppression or organ rejection, will relieve symptoms and prolong life in many heart failure patients. Existing devices for mechanical cardiac support used as a bridge to transplantation function for prolonged periods without blood damage or risk of infection.⁵⁻⁷ The new intraventricular axial flow pumps now under investigation provide better prospects for permanent mechanical support and will become the artificial hearts of the relatively near future. Such devices provide the opportunity to intervene early before multisystem failure develops and to combine coronary or valve surgery with ventricular support. There remains the option to explant the device should the myocardium recover.

Experience with devices used as a mechanical bridge to transplant

The concept of a mechanical bridge to transplantation (for moribund patients awaiting a donor organ) began in the late 1960s with the clinical use of the Liotta pneumatic double ventricle heart by Cooley *et al.*⁸ This first total artificial heart supported the circulation for 64 hours pending acquisition of a donor organ. When the patient died from infection and multisystem failure, intense controversy inhibited further attempts for almost 10 years. In 1978 both Stanford University and The Texas Heart Institute attempted without success to use a left ventricular assist device (LVAD) as a mechanical bridge to transplantation. The same year Reemtsma *et al* used the intra-aortic balloon pump to sustain three patients to transplantation.⁹ All three survived and became the first cases of the successful use of a mechanical bridge to transplant with any type of mechanical device. In 1981 Cooley *et al* used the Akutsu pneumatic total artificial heart to support a patient for 55 hours before transplantation.¹⁰ The patient died 10 days later from sepsis and multiple organ failure; none the less, problems were defined and avoided in future efforts. The first long term LVAD transplant survivor was a 51 year old man sustained for nine days with the Novacor (Novacor Medical Corporation, Oakland CA) system at Stanford University in 1984.¹¹ Soon afterwards Hill *et al*, at Pacific Medical Center,

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Figure 1 The Novacor left ventricular assist device.

San Francisco, used the externally situated Pearce/Donachy LVAD (Thoratec Laboratories Corporation, Berkeley CA) to support a 47 year old man with post-infarction cardiogenic shock. The patient received a donor heart 52 hours later and survived.¹² These operations occurred within a brief time frame and established mechanical bridge to transplantation as an expanding (but expensive) part of cardiac transplantation programmes. An important finding was that chronic offloading of the myocardium often resulted in substantial improvement of native left ventricular function similar to that experienced after prolonged bed rest.¹³

Among the currently available blood pumps are two implantable LVADs specifically designed for long-term circulatory support. The Thermocardio Systems (Woburn MA) and Novacor (Oakland CA) pumps emanate from the mechanical support initiatives of The Texas Heart Institute and Stanford University respectively. Both are pusher plate type LVADs originally designed to function as permanent artificial hearts. The Novacor LVAD (fig 1) is composed of a balanced solenoid energy convertor, dual pusher plate, sac-type blood pump with a microprocessor based control and monitoring console.⁶ The integrated energy convertor and pump are implanted into the abdomen and connected to the patient by Dacron conduits to the left ventricular apex and the ascending aorta. The conduits contain 21 mm Carpentier Edwards pericardial valves which provide unidirectional blood flow. Electrical energy is converted into hydraulic work which ejects blood from the pump. The blood sac has a highly smooth surface which is designed not to require anticoagulation. The electrical power cable is brought out percuta-

neously from the right lower quadrant of the abdomen to connect to an extracorporeal control console and battery power system. Though successful as a bridge to transplantation, the noise of the device, together with the length of the inflow graft and a significant incidence of thromboembolism, limit its potential use as a permanent implant.¹¹

The Thermo Cardiosystems Heartmate vented electric LVAD (fig 2A and B) consists of a positive displacement, pusher plate pump activated by a low speed torque motor that can produce a stroke volume of 83 ml at rates varying from 50 to 120 beats per minute.¹⁴ The electromechanical actuator fits beneath the pumping diaphragm and converts the rotary motion of the torque motor to the linear motion of the pump diaphragm (fig 3). After the motor switches on and makes one complete revolution pushing the diaphragm, blood ejects from the pump. The motor then turns off and the pump passively refills. There is a short inlet conduit which fits directly into the apex of the left ventricle and a longer outlet tube to the ascending aorta. Both the inlet and outlet conduits are fitted with 25 mm porcine valves (Medtronic Blood Systems). The flexing diaphragm is fabricated from biomer polyurethane and has an integrally textured fibrillar surface. All metal components have a sintered titanium/blood interface. This is a counter intuitive approach to thromboembolism whereby the textured surface promotes the formation of a fibre and cellular coagulum that evolves into a blood compatible biological lining.¹⁵ The pseudo-intimal layer obviates the need for anticoagulation. The implanted pump components are situated beneath the diaphragm, either in a retroperitoneal pocket or within the peritoneal cavity. A thick

Figure 2(A) The Thermo Cardiosystems Heartmate vented ventricular LVAD. (B) x-ray of the Heartmate device in situ.

Figure 3 Mechanism of action of the Heartmate LVAD. The torque motor rotates and moves the diaphragm of the blood chamber. Blood is expelled during the systolic phase (C and D) while air is vented outside the body during the diastolic phase (A).

fibrovascular capsule develops around the pump, preventing migration and resisting infection. A percutaneous electric line connects the blood pump assembly to the portable system controller, which easily clips onto a belt (fig 4). The controller contains a microprocessor that regulates motor function and monitors pump performance. The pump can be operated in either a fixed rate or automatic mode, asynchronous with the electrocardiogram. In the automatic mode the device increases output in response to increased venous filling, providing flow up to 10 l/min.

In the ambulant patient the controller is connected to two lead acid gel cells batteries which are contained in a shoulder holster or belt bag worn around the patient's waist. A portable power base unit is used to recharge extra batteries or to power the device when the patient sleeps or sits for prolonged periods. Two batteries used in parallel last up to eight hours and can be exchanged on a rotating basis to provide untethered support indefi-

nately. The external noise from the motor is barely audible and the relatively uncomplicated design of both internal and external components make the device durable and easy to operate.

The fully portable electric system was first used in 1990 after extensive experience with the pneumatically powered pump.¹⁶ Up to September 1995, 435 pneumatic and 49 electric devices have been implanted with maximum duration of support of 344 and 503 days respectively. All have been used as a bridge to transplantation, recently on an outpatient basis.¹⁷ Much useful information was provided by the Food and Drug Administration approved clinical study of 116 patients, who were compared with 46 control patients.¹⁸ The end point was survival at 60 days after transplantation. Seventy one percent of the Heartmate patients survived to undergo transplantation compared with 36% in the control group. After the transplant the group supported by the LVAD had a survival rate of 65% *v* 30% for controls. Improved survival both to transplantation and afterwards was partly the result of dramatic physiological rehabilitation. The improved haemodynamics reversed multisystem organ failure so that patients could resume physical activity and adopt an exercise programme within the hospital environment. Only one patient suffered a device related complication (0.9%); this was because of a loosened connector. Thromboembolism did not occur in the absence of infection.¹⁹ Besides resolution of hepatic and renal failure, prolonged circulatory support reversed the neurohormonal effects of chronic heart failure. Serum aldosterone concentrations, plasma renin activity, and concentrations of atrial natriuretic peptide revert to normal after prolonged support.⁵

In four patients with dilated cardiomyopathy at The Berlin Heart Hospital antibody against the beta I receptor was used as a marker (Personal communication, J Mueller, Berlin Heart Hospital.) Before insertion of the LVAD all had left ventricular ejection fractions less than 15% but with prolonged support (between 160 and 340 days) auto-antibody titres and heart rate fell and left ventricular ejection fraction increased progressively. The patients were weaned by switching their LVAD from automatic mode to fixed rate and reducing this from 90 to 50 beats/min. After removal of the device the patients remained stable on medical treatment (up to 10 months after operation). This encouraging experience gives rise to the concept of a mechanical bridge to recovery.

THE PROSPECT FOR PERMANENT MECHANICAL DEVICES

The drive towards a permanently implanted artificial heart began in 1982 when DeVries implanted the Jarvik 7 pneumatic total artificial heart in a 61 year old dentist (fig 5).²⁰ Three further Jarvik 7 total artificial hearts were implanted by DeVries between November 1984 and April 1985 and, though the haemodynamic function was encouraging,

Figure 4 The Heartmate device in situ with external system controller and batteries. Reproduced with the permission of Thermo Cardiosystems.

thromboembolism and infection were serious problems. With technological improvements the incidence of neurological complications and haemolysis were substantially reduced and one patient was sustained for 620 days at the Humana Heart Institute. Subsequently, the Jarvik 7 was used as a bridge to transplant in patients with biventricular failure.²¹ The largest series was that of Cabrol in Paris where 24 (60%) of 40 consecutive patients received successful transplants.²²

About 80% of the haemodynamic work of the heart is performed by the left ventricle. Right ventricular failure can usually be treated medically after implantation of an LVAD and may be avoided by earlier intervention. The use of a biventricular artificial heart is then unnecessary. It is now clear that moribund heart failure patients can improve to NYHA I and return to the community with an LVAD. Pilot programmes in the United States show that well-motivated LVAD patients can return to work or higher education while they wait for a transplant. In some instances use of the device has reduced inpatient costs from \$5000

per day in the intensive care unit to less than \$50 per day with the patient at home.

The success of the outpatient LVAD programme provides a powerful argument for the use of the electric LVAD as an alternative to cardiac transplantation. In the United States in 1991 3797 patients were registered on the heart transplant waiting list with a median waiting period of 198 days: 2107 patients underwent heart transplantation and 778 patients died waiting.²³ Data from the United Network for Organ Sharing have shown that a male with type O blood group, weighing more than 90 kg will wait a mean time of 595 days for a donor organ.²³ Half of this patient group die before transplantation. Consequently, as many as 66 000 end stage cardiac patients per year may be candidates for mechanical circulatory support in the USA alone.²⁴ Unlike the supply of donor hearts, the availability of LVADs is limited only by the industrial capacity for production.

Ultimately, long-term mechanical cardiac assistance may prove less expensive than cardiac transplantation or the intensive medical

Figure 5 The Jarvik 7 pneumatic total artificial heart.

treatment of patients in NYHA classes III and IV. Medically treated patients are admitted to hospital a mean of 2.25 times during their last six months of life, at an average cost of £15 000 per patient. This amount does not cover home care, medical staff costs, or lost income. There are many patients between the ages of 60 and 75 who have an expected mortality of about 40% per year on conventional medical treatment. This is a large and rapidly growing population who are in need of an alternative treatment.²⁵ For these patients it is important to assess whether the use of a permanent LVAD can improve symptoms and prolong life in the current environment of constrained health care resources. A prospective randomised clinical trial of LVAD versus con-

ventional medical treatment will answer this question. Meanwhile efforts are directed towards the development of improved mechanical devices.

The Jarvik 2000 intraventricular artificial heart provides an innovative approach to the development of a permanent, fully implantable system (fig 6). This miniature, self-contained axial flow pump—a little larger than the patient's thumb—is implanted into the apex of the failing left ventricle and retained in place with a cuff sutured to the myocardium. The electromagnetic pump rotor lies within a titanium-lined motor bore. The rotor is supported on blood-immersed miniature bearings by inflow and outflow stators. The mechanism is simple, silent, reliable, and efficient with a projected power requirement in the range of 6–8 W for most patients. The Jarvik 2000 device weighs 85 g and is 25 cc in volume compared with the Heartmate pump which weighs over 800 g and is about 600 cc in volume. It is capable of providing a cardiac output of 10 l/min at a mean aortic pressure greater than 80 mm Hg. Blood entering the dilated left ventricle through the mitral valve is withdrawn via a Dacron graft to the descending thoracic aorta. The normal anatomical relations of flow into and out of the heart are retained but an additional second outlet is provided across the apex to the descending thoracic aorta. The pump unloads the natural left ventricle and allows the diseased heart to provide part of the cardiac output and pulsatility. In its apical position the device does not interfere with the papillary muscles or chordae tendineae and because there are no valves and only one moving part it has a potential life span of several decades. The principal issues of system reliability involve the durability of the blood-immersed bearings, flex fatigue of the electric wires, and the reliability of the

Figure 6 The Jarvik 2000 ventricular artificial heart. The Jarvik 2000 Oxford model is implanted into the apex of the left ventricle and conveys blood to the descending aorta through a vascular graft. There is a percutaneous electrical system attached to batteries.

electronic system including the batteries. Preliminary work in Oxford and The Texas Heart Institute suggests that the Jarvik 2000 can function free of thrombus formation and with insignificant heat generation or haemolysis. Patient mobility is expected to be entirely normal and those implanted with this system would require only anticoagulation with warfarin (international normalised ratio between 2.0 and 3.0). No immunosuppressive agents are needed and the risks of infection are small. Since an organ donor is not required, the system should be implanted before the onset of multisystem organ failure and might prevent further deterioration in left ventricular function. This will be the first implantable device suitable for use in children.

These and other developments over the past decade indicate that mechanical support can provide effective treatment for congestive heart failure. There is every likelihood that mechanical blood pumps will become as applicable to the treatment of heart failure as the pacemaker is to rhythm disturbances.

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