

# The total artificial heart in a cardiac replacement therapy programme

*The increasing prevalence of heart failure coupled with the shortage of donor hearts has led to an ever-growing demand for mechanical devices that can augment or replace the failing human heart. This article describes the modalities used to treat end-stage heart failure and how these fit into a cardiac replacement therapy programme.*

It is estimated that 900 000 patients in the UK suffer from heart failure. It is a progressive illness and most patients ultimately fail medical therapy. With 4–5% of all emergency admissions in England and Wales coded as heart failure, and as one of the top 10 diagnoses for use of hospital bed days, heart failure places a substantial burden on the NHS budget. Mortality rates for heart failure are high with 11.6% of patients dying during a hospital admission and over 30% dying within 1 year of discharge (McDonagh et al, 2012). With limited numbers of organ donors for heart transplantation, one possible solution to address this population on a large scale is to develop mechanical circulatory support devices.

## Heart transplantation: the best treatment for end-stage heart failure

Data from the International Society of Heart and Lung Transplant registry show that over half of the patients who undergo heart transplantation survive 11 years (Stehlik et al, 2011). For these patients, this post-transplant survival represents a dramatic improvement over their projected survival had they remained on best medical management. Heart transplantation is currently the best treatment for patients with end-stage heart failure. However, it has its limitations, both in terms of the availability of donor organs, and also contraindications to transplantation including the existence of recipient antibodies, high pulmonary vascular resistance, recipient comorbidities and adverse events related to long-term immunosuppression. In the UK adult heart transplantation is provided at six designated centres in Birmingham, Cambridge, Glasgow, London, Manchester and Newcastle. In 2011, the number of heart transplants performed nationally increased by 9% to 131, while the waiting list has been growing steadily and is now 23% higher than it was 10 years previously (NHS Blood and Transplant, 2011).

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## The concept of bridging heart failure patients

The scarcity of donor hearts and the progressive nature of end-stage heart failure mean that many patients slowly deteriorate while on the transplant waiting list and some patients die before a suitable donor heart becomes available. The use of mechanical circulatory support devices has allowed heart failure patients who are running out of time to have a new lease of life. The term ‘bridging’ refers to the use of mechanical circulatory support devices to prolong survival and to allow some stabilization or recovery of health to open up other opportunities.

- ‘Bridging to transplantation’ describes supporting transplant-eligible patients who are unlikely to survive the wait for a suitable donor heart with mechanical circulatory support devices until heart transplantation
- ‘Bridge to recovery’ deploys circulatory support to allow native cardiac function to return to a sufficient level to have the circulatory support device explanted
- ‘Bridge to bridge’ describes the use of temporary mechanical circulatory support devices to allow a patient to be optimized before implantation of a longer-term device
- ‘Bridge to candidacy’ describes supporting a patient to allow him/her sufficient time to meet the criteria for listing for transplantation, e.g. for elevated pulmonary vascular resistance to drop so that the patient can meet transplant criteria
- ‘Bridge to decision’ describes the role of a device in holding a patient over a period of time while assessments can be performed and options explored.

## Left ventricular assist devices

The majority of mechanical circulatory support devices used worldwide are to support a failing left ventricle (Figure 1). Even in the context of biventricular failure, for many patients, the improvements in flow through the systemic circulation achieved by use of a left ventricular assist device are sufficient to achieve a real improvement in quality of life and performance status. For some patients, however, a right ventricular support device will also be necessary (Fitzpatrick et al, 2008) and this moves patients into a higher risk group in terms of increased perioperative mortality and inferior longer-term survival (Kirklin et al, 2012).

### Right ventricular assist devices

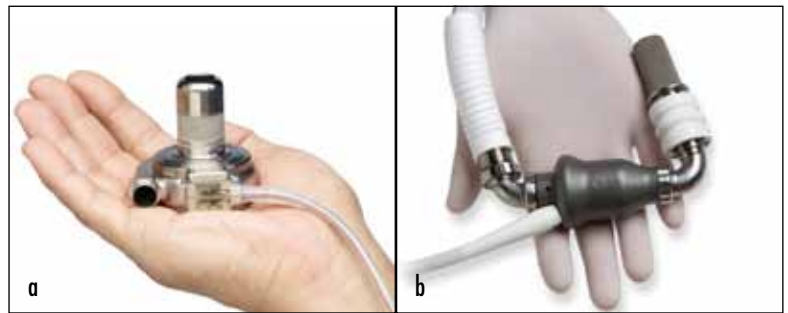
Identification of a right ventricle that is unlikely to cope with left ventricular support alone pre-implant should guide the heart failure team towards planning for biventricular support. In some cases, the need for right ventricular support only becomes apparent after the left ventricular assist device has been implanted. In the past, this used to occur in 10–30% of patients after left ventricular assist device implantation. However, with better patient selection and improved perioperative patient management in recent years, the incidence has fallen to around 5%.

Implanting a right ventricular support device heightens the morbidity and mortality of mechanical circulatory support. Patients requiring biventricular support have a 1-year survival of 55% compared with >80% for patients having left ventricular assist device implantation alone (Kirklin et al, 2012). Preoperative patient and echo variables have been investigated to identify predictors of right ventricular failure after left ventricular assist device insertion (Fitzpatrick et al, 2008; Puwanant et al, 2008) but none of the risk models can reliably identify patients who will require right ventricular support.

Use of right ventricular support devices in patients with isolated right heart failure represents a small subset of the patients who receive mechanical circulatory support devices. This subset is characterized by patients who have developed signs of right ventricular failure and echocardiographic features of right ventricular dysfunction.

### Biventricular assist devices

For patients with clear-cut biventricular failure several options exist. Heart transplantation remains the gold standard therapy for these patients. In terms of mechanical approaches to cardiac replacement therapy, the options include the use of extracorporeal or intracorporeal systems. These can either be continuous flow or pulsatile flow devices. A recent multicentre report from France described biventricular mechanical support with three different approaches in the management of 383 patients with advanced heart failure. This included the use of 90 total artificial hearts, 255 para-corporeal devices and 38 implantable biventricular assist devices. Overall there were no differences in survival between the three modalities of treatment while on support or after subsequent heart transplantation, although patients undergoing prolonged support (>90 days) tended to have better survival when supported with total artificial heart than with biventricular assist devices, which may have been related to a lower incidence of neurological events (Kirsch et al, 2012). This similarity between biventricular support approaches and outcomes is consistent with data from the INTERMACS registry (Kirklin et al, 2012). The advantages of continuous flow biventricular support options are that they are considerably quieter for the patient, and the patient's native heart is left in situ, preventing a contraction of the pericardial cavity which can occur around the total artificial heart, hampering future transplantation.



**Figure 1. Implantable left ventricular assist devices commonly used in the UK. a. The HeartWare ventricular assist device. b. The Thoratec HeartMate II.**

### The total artificial heart

The first artificial heart to be used clinically was the Liotta total artificial heart, which was implanted in 1969 in a patient who was bridged for 48 hours to a heart transplant (Cooley, 2011). Now into the 5th decade since this milestone, over a thousand artificial heart devices have been deployed worldwide. The only device that is currently approved for use in Europe and the United States is the SynCardia total artificial heart (formerly Symbion Jarvik Heart). The SynCardia total artificial heart functions with two separate pneumatically driven pulsatile pumps which assume the role of the native ventricles and are powered by an external driver (Figure 2). The external driver pushes air in and out of the two artificial ventricles. Within each of the artificial ventricles, blood and air are separated by an impermeable diaphragm. Each ventricle also has two mechanical valves, one for inflow and one for outflow (Figure 3). During the ejection phase, a pulse of compressed air inflates the air chamber, pushing the diaphragm towards the blood chamber, thereby ejecting blood into the circulation. During the filling phase, a vacuum is applied to the air chamber, pulling on the dia-

**Figure 2. The SynCardia total artificial heart.**

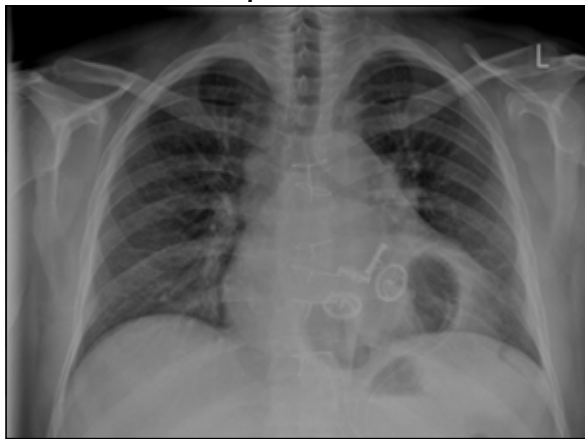


phragm to assist with filling of the blood chamber. Device ejection and forward flow of blood is preload dependent and increases with atrial pressure. With adequate preload, cardiac outputs of up to 10 litres/minute can be generated. A wire-reinforced air driveline which is tunnelled from within the chest through the abdominal wall connects each artificial ventricle to the external driver. The original external console, known as the 'Big Blue', was very bulky and weighed nearly 400 pounds. This used to confine patients implanted with the total artificial heart to hospitals for prolonged periods. The major advance in 2010 was the introduction of a portable, battery-powered driver weighing approximately 6 kg, called the 'Freedom Driver'. This welcome development facilitated patient mobility and enabled discharge from hospital (Figure 4).

### Bridge to transplant

A non-randomized, prospective study in five US centres has been conducted with the use of historical controls to assess the safety and efficacy of the SynCardia total artificial heart in transplant-eligible patients who were at risk of imminent death from irreversible biventricular cardiac failure. The primary end-points included the rates of survival to heart transplantation and of survival after transplantation (Copeland et al, 2004). Eighty-one

**Figure 3. Chest X-ray of a patient implanted with a total artificial heart showing the four mechanical valves and the two air chambers within the two implanted artificial ventricles.**



**Figure 4. The implantable SynCardia total artificial heart attached to the portable external 'Freedom Driver'.**



patients were implanted with the total artificial heart and 79% survived to transplantation compared with only 46% in the control group ( $P < 0.001$ ), with 1-year survival rates of 70% and 31% respectively ( $P < 0.001$ ). One- and 5-year survival rates after transplantation among patients who had received a total artificial heart as a bridge to transplantation were 86% and 64% respectively.

### Total artificial heart vs other ventricular assist devices

Use of a total artificial heart has advantages for patients in terms of immediate reduction in inotrope use, lack of inflow and outflow cannulae and relatively quick patient mobilization. Several studies have looked at the physiological differences between patients according to device types. One study comparing the total artificial heart with left ventricular assist device patients found that patients with a total artificial heart had a tendency towards a greater degree of anaemia, an association with haemolysis, ineffective erythropoiesis, and a higher level of inflammatory markers (Mankad et al, 2012). A further study comparing blood pressure response during exercise found that, although blood pressure did not increase with exercise, patients with a total artificial heart participated in physical therapy and treadmill exercise earlier after device implantation, with increased exercise intensity and duration over time (Kohli et al, 2011).

No trials have directly compared the differences on end organ function of total artificial heart technology against other forms of mechanical circulatory support devices. However, there is evidence that end-organ function in patients on long-term circulatory support with continuous or pulsatile flow assist devices is comparable (Radovancevic et al, 2007). The drawbacks of the total artificial heart include its relatively large size, larger diameter air drivelines and a higher noise level compared with continuous flow ventricular assist devices.

### Indications for use of the total artificial heart

The total artificial heart is indicated for use as a bridge to transplantation in cardiac transplant candidates at risk of imminent death from non-reversible biventricular failure (Table 1). The total artificial heart circumvents some of the limitations of using a left ventricular assist device alone, including right ventricular failure, refractory arrhythmias and surgical issues arising after myocardial infarction such as post-infarct ventricular septal defects. Patients in whom a total artificial heart would be considered are usually those who have contraindications to the use of a left ventricular assist device.

### Ongoing patient care after implantation of mechanical circulatory support devices

Possibly one of the most critical factors in determining long-term outcome for patients who have mechanical circulatory support devices support is the follow-up care

and surveillance that they receive. Regular follow up addresses mechanical circulatory support device-specific and general medical issues, evaluates equipment and continues to support patient education regarding their device. Symptoms of heart failure, chest pain, arrhythmia, neurological changes and gastrointestinal bleeding are screened along with looking for evidence of equipment faults.

Patients on mechanical circulatory support device support are anticoagulated to avoid thromboembolic complications, usually with warfarin and aspirin, with an aim of achieving international normalized ratios of 2.0–3.0. Great care is taken to avoid damage to the driveline and to minimize trauma to the exit site from the skin. Patients need to be aware of their fluid balance and avoid both fluid overload and dehydration. Blood pressure is monitored with the aim of maintaining mean arterial pressures of between 70 and 90 mmHg. Hypertension is a risk factor for neurological events and end organ damage, and must be prevented.

### The story of total artificial hearts at Papworth Hospital

Sir Terence English relates the story of the first total artificial heart in the UK in his memoirs. In December 1982 Dr Williams DeVries inserted a Jarvik artificial heart into a 64-year-old dentist named Barney Clark in Salt Lake City as a permanent implant. Barney Clark survived 112 days with an effective circulation provided by the artificial heart. Robert Jarvik then proposed that the artificial heart could be useful in transplant programmes and approached Sir Terence English to discuss using this device at Papworth Hospital. At the time one third of the patients on the heart transplant waiting list were dying before a donor heart was available and Sir Terence could see an application for the device to bridge these patients to their transplant. However, this was inhibited by cost. Ultimately a US company funded the training required for the surgical team, equipment costs and the patient hospital stay to initiate the programme at Papworth Hospital.

#### Patient 1

On 4 November 1986 a Jarvik artificial heart was implanted into a patient at Papworth Hospital who had had a massive heart attack 10 days earlier. This was the first patient to be implanted with a total artificial heart in the UK. The patient was in low cardiac output heart failure and, despite all pharmacological support, was deteriorating quickly. After implantation the patient was smoothly disconnected from the heart lung bypass machine and he woke up within a few hours of surgery. A donor heart became available just 2 days after the total artificial heart was implanted and this patient was successfully bridged to heart transplantation. The transplant was technically challenging and there was prolonged bleeding at the end of the operation (English, 2011). The patient had a more difficult recovery than after his initial operation but after leaving hospital improved steadily

and thereafter remained in good health until he died suddenly from an infection nearly 2 years later.

Involvement with the Jarvik artificial heart then ended as there was a perception that the procedures associated with using the artificial heart as a bridge to transplant were too complicated to be practical as well as being very expensive and restricting the patient's mobility. The large size of the original pneumatic driver to which the patient was connected to power the total artificial heart meant that patients would effectively be confined to the hospital while they awaited a suitable donor organ.

In 2010 SynCardia introduced the aforementioned portable 'Freedom Driver' which permitted patient discharge from hospital while awaiting transplantation. This rekindled interest in the use of the total artificial heart at Papworth Hospital to complement other mechanical circulatory support devices as a bridge to heart transplant. Discussions were immediately initiated with the National Specialist Commissioning Team and NHS funding for the programme was secured by December 2011.

#### Patient 2

In June 2011 a 42-year-old patient was implanted with a SynCardia total artificial heart as a bridge to transplantation at Papworth Hospital (Figure 3). He had been admitted to hospital 30 days earlier with decompensated heart failure. The procedure was complicated by post-operative tamponade and renal dysfunction requiring haemofiltration but the patient subsequently made a good recovery and was discharged home 54 days post-operatively. He is able to mobilize freely using the

**Table 1. Indications for use of the total artificial heart**

NYHA class IV, INTERMACS level I or II*	
Refractory haemodynamic insufficiency	
Irreversible biventricular failure	
Contraindications for left ventricular assist device	Right ventricular failure
	Stone heart
	Left ventricular thrombus
	Transplant rejection or failure
	Refractory arrhythmias
	Ventricular assist device failure
	Mechanical aortic valve prosthesis
	Surgical issues with massive acute myocardial infarction
	Ventricular septal defect
	Left ventricular assist device poor outcome predictors: severe renal and hepatic dysfunction
Ventilator-dependent patients	
<small>INTERMACS = International Registry for Mechanically Assisted Circulatory Support Classification of Heart Failure; * Level I 'Critical cardiogenic shock' (patient has life-threatening hypotension and profound low cardiac output with rapidly escalating inotropic support); level II 'Progressive decline' (patient has demonstrated 'dependency' on inotropic support but nonetheless shows signs of continuing deterioration); NYHA = New York Heart Association classification of heart failure class IV 'symptomatic at rest'.</small>	

Freedom Driver and became the first patient in the UK to be discharged home supported by an artificial heart. He has now been on total artificial heart support for over 450 days and is currently awaiting heart transplantation.

### Patient 3

In July 2011 a SynCardia total artificial heart was implanted into a 45-year-old patient who had a history of dilated cardiomyopathy. He was admitted to Papworth intensive care unit with severe biventricular heart failure. He suffered a cardiac arrest and required cardiopulmonary resuscitation with central veno-arterial extracorporeal life support. Five days later a SynCardia total artificial heart was implanted. Pulmonary oedema developed on weaning the patient from cardiopulmonary bypass and extracorporeal life support was continued for a further 2 days to help with oxygenation. The postoperative course was complicated and the patient developed multi-organ system failure and died after 30 days of total artificial heart support.

In summary three patients have been implanted with artificial hearts at Papworth Hospital to date, of whom one was successfully bridged to transplant after 2 days, one is awaiting transplantation after more than 15 months of total artificial heart support and one patient was implanted with the total artificial heart but did not survive the postoperative recovery period.

### Future developments

The 70cc SynCardia temporary total artificial heart fits a majority of men and some women, but is limited for use in patients with a body surface area of 1.7 m<sup>2</sup> or greater. Currently patients suffering from end-stage biventricular failure who are too small to receive the total artificial heart are considered for a biventricular assist device instead. However, SynCardia is now in the process of developing a 50cc total artificial heart that is designed for smaller patients with body surface area of 1.2–1.7 m<sup>2</sup>.

A number of groups have experimented with excising the diseased native heart and using two continuous flow left ventricular assist devices in sequence as an artificial heart. Smaller left ventricular assist devices such as the Jarvik 2000 and the HeartWare ventricular assist device which permit intrapericardial placement lend themselves to such approaches.

A French group is developing an orthotopic and bio-compatible artificial heart with biological valves. The CARMAT device will be innovative in its use of miniature embedded sensors within the patient to assess physiological demands and adjust pump delivery to maintain aortic pressure at optimal levels. The CARMAT artificial heart is yet to be tested in a patient, but subject to French Health Product Safety Agency approval in 2012, pilot studies in patients are being planned.

The costs of mechanical circulatory support devices are currently high, but with advances in technology, reductions in hospital stays and reductions in complication rates, mechanical circulatory support devices will undoubtedly continue to play a key role in the management of end-stage heart failure. With improved portability and its various unique attributes, the total artificial heart is an important complement to left ventricular assist devices and biventricular assist devices as a mechanical solution for cardiac replacement therapy. **BJHM**

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## KEY POINTS

- Heart transplantation is currently the best treatment for end-stage heart failure.
- Mechanical options of cardiac replacement can be life saving in certain situations
- Patients with biventricular heart failure require simultaneous support of the systemic and pulmonary circulation. This can be accomplished with paracorporeal biventricular support devices, implantable biventricular support devices or the implantable total artificial heart.
- Limitations of mechanical blood pumps include the needs for percutaneous drivelines and systemic anticoagulation, and the risk of device infection and thromboembolic complications.