



Australian Government
Department of Health and Ageing



Australia and New Zealand Horizon Scanning Network

ANZHSN

AN INITIATIVE OF THE NATIONAL, STATE AND
TERRITORY GOVERNMENTS OF AUSTRALIA
AND THE GOVERNMENT OF NEW ZEALAND

Horizon Scanning Technology Prioritising Summary

HeartMate II® left ventricular assist device

August 2008



**Australian
Safety
and Efficacy
Register
of New
Interventional
Procedures -
Surgical**



**Royal Australasian
College of Surgeons**

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ISBN

Publications Approval Number:

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The production of this Horizon scanning prioritising summary was overseen by the Health Policy Advisory Committee on Technology (HealthPACT), a sub-committee of the Medical Services Advisory Committee (MSAC). HealthPACT comprises representatives from departments in all states and territories, the Australia and New Zealand governments; and ASERNIP-S. The Australian Health Ministers' Advisory Council (AHMAC) supports HealthPACT through funding.

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PRIORITISING SUMMARY

REGISTER ID

S000086

NAME OF TECHNOLOGY

**HEARTMATE II® LEFT VENTRICULAR ASSIST
DEVICE**

PURPOSE AND TARGET GROUP

**PATIENTS SUFFERING FROM CONGESTIVE HEART
FAILURE**

STAGE OF DEVELOPMENT (IN AUSTRALIA)

- | | |
|---|--|
| <input checked="" type="checkbox"/> Yet to emerge | <input type="checkbox"/> Established |
| <input type="checkbox"/> Experimental | <input type="checkbox"/> Established <i>but</i> changed indication
or modification of technique |
| <input type="checkbox"/> Investigational | <input type="checkbox"/> Should be taken out of use |
| <input type="checkbox"/> Nearly established | |

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

- Yes
 No
 Not applicable

INTERNATIONAL UTILISATION

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
United State	✓		

IMPACT SUMMARY

Thoratec® Corporation (Pleasanton, CA, USA) provides the HeartMate II® left ventricular assist device (LVAD) as a bridge to transplantation or destination therapy for patients with chronic heart failure. The technology is currently unavailable in Australia.

BACKGROUND

Congestive heart failure occurs when an individual's heart becomes too weak to pump blood through the body effectively. It is a progressive disorder, which gradually damages the heart and weakens the cardiovascular system. The major causes of heart failure are

coronary heart disease, hypertension, cardiomyopathy and other heart diseases. Of these, coronary heart disease is recognised as the most common cause of heart failure. The left ventricle of the heart does not function properly in individuals suffering from congestive heart failure. As a result of this, blood begins to pool within the heart and nearby veins, resulting in fluid retention in the lungs, legs and abdomen. Symptoms of heart failure include fatigue/weakness, rapid or irregular heartbeat, dyspnoea, nausea and decreased alertness. Patients suffering from severe heart failure will eventually succumb to irreversible failure of the heart ventricles. Once this occurs, a heart transplant is the only viable treatment to improve clinical outcomes and increase patient longevity.

With the continued worldwide shortage of heart donors, researchers have attempted to utilise mechanical circulatory support devices as a bridge to transplantation or even destination (chronic support) therapy in end-stage heart failure patients. Pulsatile ventricular assist devices (which utilise positive displacement pumps) were among the first to be approved by the Food and Drug Administration (FDA) in the United States. However, the volume-displacement design of these LVADs had significant limitations related to their size, mechanical durability and high infection rates (Miller et al 2007). In view of this, continuous flow LVADs were developed that have fewer moving parts and are smaller in size, which may extend therapy to adolescents and women.

The HeartMate II LVAD is the latest and most advanced continuous flow device from Thoratec Corporation. It consists of an internal axial-flow blood pump that is connected to an external system driver and power source. The pump itself houses an internal rotor with helical blades that curve around a central shaft. When the rotor spins, it draws blood from the left ventricular apex through the pump and into the ascending aorta (Miller et al 2007). The HeartMate II is implanted in a pocket created below the left hemidiaphragm, the inflow conduit is placed within the left ventricle and the outflow graft is anastomosed to the ascending aorta (median sternotomy and cardio pulmonary bypass required). The driveline is tunnelled subcutaneously and exits via the abdominal wall.

The first HeartMate II design was utilised in a European trial in 2001, but the trial was halted due to incidences of thrombosis relating to the texturing of the internal blood-contacting surfaces (Struber et al 2008). In 2003, a new design of the HeartMate II in which the textured surface within the pump housing had been removed was introduced and clinical trials resumed. This prioritising summary will focus on the updated HeartMate II only.

CLINICAL NEED AND BURDEN OF DISEASE

The health and economic burden of congestive heart failure is expected to increase as the population of Australia ages. However, despite the substantial effect of this condition on the healthcare system, population estimates of the prevalence and incidence of heart failure and left ventricular dysfunction in Australia were practically non-existent until 2006. Prior to this, heart failure was often categorised within a group of heart, stroke and vascular conditions. The Heart Foundation estimates that approximately 1.5% to 2.0% of Australians are affected by congestive heart failure. The incidence and prevalence of

heart failure increases with age, with a prevalence of 1% in people aged 50 to 59 years, 10% in people aged 65 years or older and over 50% in people aged 85 years or older (National Heart Foundation 2006).

The Canberra Heart Study revealed that the overall prevalence of clinical heart failure in Australians aged 60 to 86 years was 6.3%. In addition, nearly 60% of people with left ventricular systolic dysfunction may actually be in the preclinical stage of heart disease (Abhayaratna et al 2006). Thus, diagnosed heart failure cases may only represent a small proportion of the national burden of heart failure and left ventricular systolic dysfunction.

From 2003 to 2004, heart failure was responsible for 41,425 hospitalisations (0.6% of all hospitalisations) in Australia. In addition, the disease was responsible for 2279 deaths in 2004 (1.7% of all deaths) (Australian Institute of Health and Welfare [AIHW] 2006).

DIFFUSION

The HeartMate II LVAD received European CE (Conformité Européenne) Mark approval in 2005 and is available to all European centres for cardiac surgery as a bridge to transplantation or as destination therapy in patients with end-stage heart failure (Struber et al 2008). The FDA provided premarket approval (PMA) for the use of HeartMate II in the United States in April 2008 as a bridge to transplantation in cardiac patients at risk of imminent death from non-reversible left ventricular failure (Food and Drug Administration 2008).

COMPARATORS

At the time of writing, there are several different models of continuous flow ventricular assist devices, all of which are comparators to HeartMate II:

- Novacor® Left Ventricular Assist System (World Heart Corporation, Oakland, CA, USA)
- Incor® VAD (Berlin Heart GmbH)
- Jarvik 2000 Flowmaker ®(Jarvik Heart Inc.)
- VentrAssist™ (Ventracor Limited)
- HeartWare HVAD™ (HeartWare Limited)

SAFETY AND EFFECTIVENESS ISSUES

Three case series studies (level IV intervention evidence) were retrieved for inclusion in this summary. Study design and patient characteristics will be described in the following paragraphs. Results were presented as mean ± standard deviation unless otherwise stated.

Miller et al (2007) compiled the results of a prospective study involving 26 centres in the United States which performed HeartMate II implantations in 133 end-stage heart failure patients from March 2005 to May 2006. All enrolled patients were required to have symptoms of New York Heart Association (NYHA) class IV heart failure and be ill enough to be given high priority for heart transplantation. Patients with severe renal, pulmonary or hepatic dysfunction; active uncontrolled infection; aortic insufficiency; a mechanical aortic valve; aortic aneurysm; other mechanical circulatory support (except

for intra-aortic balloon pump); and high-risk technical obstacles were excluded from the study. The mean patient age was 50.1 ± 13.1 years. All patients were refractory to pharmacological treatment and the major cause of heart failure was nonischaemic cardiomyopathy. Forty-one patients (30.8%) had concomitant intra-aortic balloon pump support (Miller et al 2007).

Struber et al (2008) conducted a retrospective survey of 101 consecutive European HeartMate II recipients from March 2004 to January 2007. The majority of patients had ischaemic (61/101; 60.4%) or dilative (30/101; 29.7%) cardiomyopathy. The mean patient age was 48 ± 13 years. The intention-to-treat was bridge to transplantation in 69 patients, destination therapy in 31 patients, and support following open heart surgery in one patient. The preoperative NYHA class for this patient cohort was class IV (89%), class IIIb (6%) and class IIIa (3%). No NYHA class details were provided for the remaining 2% of patients. There were two major differences between the bridge to transplantation and destination therapy groups. Firstly, the mean patient age was substantially lower for the bridge to transplantation group (44.0 years versus 52.5 years). Secondly, most patients in the bridge to transplantation group had dilated cardiomyopathy, while most destination therapy patients had ischaemic heart disease. It was not stated if these differences were statistically significant (Struber et al 2008).

Frazier et al (2007) examined the outcomes of 43 patients who received the HeartMate II from November 2003. Patient indication for LVAD implantation was bridge to heart transplantation in 26 patients and destination therapy in 17 patients. Of these patients, 30 had idiopathic cardiomyopathy and 13 had ischaemic cardiomyopathy. All patients were classified as suffering from NYHA class IV heart failure. Intra-aortic balloon pumps were present in 14 patients, while six patients were supported by the TandemHeart® (CardiacAssist Inc., Pittsburgh) percutaneous ventricular assist device and 10 patients underwent HeartMate II implantation due to failure of their HeartMate I device (Frazier et al 2007). There is a possible patient overlap between the Frazier et al (2007) and Miller et al (2007) studies.

A) SAFETY

Two of the three included studies (Miller et al 2007; Struber et al 2008) noted that bleeding complications were the most common adverse event post-implantation. In Miller et al (2007) 83.5% (101/133) of patients required some form of treatment for bleeding (41 patients required surgery; 30.8%), while in Struber et al (2008) 20.9% (53/251) of adverse events were related to bleeding complications that required thoracotomy.

The overall death rate was 19% (6 months), 33% (6 months) and 20.9% (average duration of support 258 days) for Miller et al (2007), Struber et al (2008) and Frazier et al (2007), respectively. Miller et al (2007) noted that 18/25 (72%) deaths occurred before hospital discharge while receiving HeartMate II support. Causes of death within the first 180 days after implantation included: ischaemic stroke (n=5), multiorgan failure (4), haemorrhagic stroke (3), anoxic brain injury (2), right heart failure (2) and miscellaneous causes (4) (Miller et al 2007). No details on the cause of death of the remaining five patients who

died were presented. In Struber et al (2008), multiorgan failure was the most frequent cause of death, accounting for 43.3% (13/30) of deaths. Other causes of death were right heart failure (n=5), cerebrovascular accident (5), respiratory failure (3), disconnection of drive lines (2), bleeding after ventricular rupture (1) and suffocation after nasal haemorrhage (1) (Struber et al 2008). In Frazier et al (2007) all nine deaths occurred while the patients were receiving device support. Five patients died due to a combination of right-side heart failure, multisystem organ failure and bleeding complications. One patient died due to bleeding associated with small bowel arteriovenous malformations which required cessation of anticoagulation and antiplatelet therapy. This eventually led to thrombus formation and neurologic death. One patient died due to massive haemorrhagic stroke while the remaining two patients died suddenly with unknown causes (Frazier et al 2007).

Device-related complications were relatively infrequent in the included studies. Miller et al (2007) reported that one death was related to an accidental twisting of the inflow graft during implantation, and device-related infections were observed in 14% (18/133) of patients (all involved the percutaneous lead). A total of five HeartMate II devices were replaced, two of which were due to pump thrombosis. Struber et al (2008) stated that percutaneous lead infections were present in 21/101 patients; of these six experienced recurrent infections. Pocket infections were less common, being observed in only 3% (3/101) of patients. None of the infections were lethal. Pump thrombosis was present in one patient four months post-implantation (Struber et al 2008). Frazier et al (2007) had no incidences of device malfunction, but percutaneous lead infections were evident in 7% of patients (3/43).

B) EFFECTIVENESS

Miller et al (2007) reported that five of the 133 patients (3.8%) received an additional temporary right ventricular assist device 3 to 93 days after HeartMate II implantation. All patients were receiving drugs to increase the heart's pumping action (inotropic support) preoperatively, and the median duration for postoperative inotropic support was 7 days. The investigators observed a significant improvement in cardiac index 24 hours after HeartMate II implantation from 2.0 ± 0.6 min/m² preoperatively to 2.8 ± 0.7 min/m² ($P < 0.001$). In addition, pulmonary capillary wedge pressure decreased from 26 ± 8 mmHg to 16 ± 5 mmHg ($P < 0.001$) and mean pulmonary artery pressure decreased from 37 ± 10 mmHg to 26 ± 7 mmHg ($P < 0.001$). Average pump flow index and mean pump speed remained relatively stable throughout the support period, indicating consistent device function over time. Paired analysis of 67 patients from baseline to 3 months post-implantation indicated significant reductions in levels of serum creatinine (1.4 ± 0.5 to 1.1 ± 0.5 mg/decilitre, $P < 0.001$), blood urea nitrogen (30.3 ± 16.9 to 18.6 ± 9.8 mg/decilitre, $P < 0.001$) and serum alanine aminotransferase (48 ± 41 to 32 ± 29 U/litre, $P = 0.0006$), which indicated that renal and hepatic function improved significantly during HeartMate II support. At 3 months (n=78), 83% of patients (65/78) had improvement in their NYHA functional class by at least two functional classes (from IV to II) and surveys indicated a significant improvement in quality of life at 3 months post-implantation ($P < 0.001$).

All patients were followed for a minimum of 180 days until transplantation or death (Miller et al 2007). Of the 133 patients, 100 (75.2%) attained the principal outcomes of transplantation (56 patients), cardiac recovery (1 patient) or survival at 180 days with ongoing HeartMate II support and eligibility for transplantation (43 patients). The remaining 33 patients with unsuccessful outcomes included 25 patients who died before the 180-day time point (median time to death was 38 days, range 6 to 144); five patients who suffered irreversible medical complications during device support and were no longer eligible for transplantation; and three patients who underwent replacement of the HeartMate II with a different ventricular assist device (due to surgical complications after pump implantation) and were withdrawn from the study. The overall actuarial survival rate for patients continuing to receive mechanical support was 89%, 75% and 68% at 1 month, 6 months and 12 months, respectively (Miller et al 2007).

In the study by Struber et al (2008), overall patient survival was 67% (68/101) at 6 months post-implantation. Of these, 17 patients underwent transplantation and two patients experienced cardiac recovery so the HeartMate II was removed. Follow-up data of more than 180 days were available for 33 patients. After six months two patients died (6%), one from intracerebral bleeding and the other from an unknown cause (the patient was found with a disconnected drive line cable). Three of the 33 patients underwent successful heart transplantation (9.1%), while the remaining 28 patients continued with device support (84.8%). Struber et al (2008) noted that a significant difference in initial postoperative mortality was evident when survival was stratified by intention-to-treat, such that destination therapy patient survival was 93% while bridge to transplantation survival was 80%. However, beyond 4 months post-implantation the survival rates were similar between both groups.

Frazier et al (2007) observed significant improvements in average cardiac index (1.9 ± 0.27 to 3.5 ± 0.81 l/min/m²) and pulmonary capillary wedge (24.8 ± 11 to 18.5 ± 5.3 mmHg) 48 hours after HeartMate II implantation. Inotropic support was reduced after implantation and all patients were free from such support within one week. In addition, left ventricular diastolic dimension decreased by 16% (from 6.7 cm to 5.6 cm) one month after implantation, indicating improved ventricular dimensions. The overall Kaplan-Meier survival rate was 80%. A total of 18 devices were explanted: three due to transplantation, four due to recovery of cardiac function, one due to damage (skateboarding accident), one because of pump-pocket infection and nine due to death. None of the explanted devices had evidence of thrombus formation and no bearing wear was detected. The authors stated that measurements of function (not detailed) did not reveal any difference in technical function of the pump before or after removal in the first patient of this cohort over a total of 749 days of use.

Two of the included studies provided details of the duration of HeartMate II support. Miller et al (2007) reported a mean duration of support of 168 ± 148 days (range 1 to 600; median 126 days), while Frazier et al (2007) noted an average of 258 days (range 1 to 761).

COST IMPACT

No cost-effectiveness studies on this device are available, and the exact price of the HeartMate II is not known.

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified from the retrieved material.

OTHER ISSUES

Thoratec Corporation is currently developing the HeartMate III which utilises a magnetically levitated rotor. This device is currently undergoing animal testing and is still in the very early stages of development (Farrar et al 2007).

SUMMARY OF FINDINGS

Overall, the included case series studies indicated that the HeartMate II is capable of functioning as a bridge to transplantation or destination therapy in patients with end-stage heart failure. Significant improvements in cardiac index, quality of life, and renal and hepatic function were observed during the period of mechanical support compared with baseline values. However, it is important to note that the use of continuous pump LVADs require higher levels of antithrombotic therapy compared to some pulsatile LVADs. This consequently increases the risk of bleeding complications, which was reflected in the studies presented. The most common device-related complication was percutaneous lead infection, which was evident in all three studies. Serious adverse events were rare, and no incidences of mechanical failure were observed. However, there is evidence that the device drive lines may disconnect and that pump thrombosis may still occur despite the new design of the Heartmate II.

HEALTHPACT ACTION

As a result of the limited evidence available and the lack of comparative studies it is difficult to determine if the HeartMate II offers substantial advantages over other LVADs. Further long-term comparative studies would be helpful. Due to the development of several new generation VADs, a horizon scanning report will be produced on continuous flow ventricular assist devices.

NUMBER OF STUDIES INCLUDED

Total number of studies 3
Level IV intervention evidence

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SEARCH CRITERIA TO BE USED

Heartmate

Thoratec

Ventricular assist device