Chapter 2.

Left ventricular assist device as bridge to transplantation in patients with end-stage heart failure. Eight year experience with the implantable HeartMate LVAS.

JR Lahpor, N de Jonge, HA van Swieten, H Wesenhagen, C Klöpping, JH Geertman, A Oosterom, B Rodermans, JH Kirkels

Heart Lung Center Utrecht: University Medical Center Utrecht and St Antonius Hospital Nieuwegein

Neth Heart J 2002; 10: 267-271
Abstract

OBJECTIVE- To evaluate the use of left ventricular assist devices (LVAD) as bridge to heart transplantation (HTx) in patients with end-stage heart failure.

METHOD- Between March 1993 and December 2001, 38 patients with refractory end-stage heart failure underwent HeartMate LVAD (Thoratec, Pleasanton Calif.) implantation.

RESULTS- 33 of the 38 patients (87%) survived the implantation and perioperative period. There were 5 perioperative deaths (13%), 2 of right ventricular failure, 2 as a result of bleeding and 1 probably due to septic shock at the time of LVAD implantation. Three patients (9%) died late in the postoperative period due to septic shock, mechanical failure of the device and a cerebral embolus resulting from LVAD endocarditis, initiated by an acute cholecystitis. Twelve patients (32%) had one or more infectious episodes during long-term assist, of which 1 patient died. Four patients are still on the device, waiting for heart transplantation. Twenty-six patients (76%) underwent HTx after 206 ± 129 days of support.

CONCLUSION- These results show the efficacy of LVAD support as a bridge to heart transplantation in patients with end-stage heart failure. Major long-term complications are infections and mechanical failure of the device.
Clinical experience with LVAD

Introduction

In the treatment of patients with end-stage heart failure, heart transplantation is still the only option that provides both a better life expectancy and a substantially better quality of life \(^1,2\). It mostly results in a dramatic improvement in general wellbeing and in exercise performance \(^3,4\). However, since the start of heart transplantations in the Netherlands in 1984 the number of procedures has been limited due to shortage of suitable donor hearts. Every year the heart transplant centers in Utrecht and Rotterdam together perform 40-50 heart transplants. This number has been fairly stable during the last decade, despite all measures to improve donation and despite the tendency to accept hearts from older donors.

The low number of heart transplantations is in sharp contrast to the growing number of patients with end-stage heart failure \(^5\). This discrepancy has resulted in long waiting times and a high (15-20%) mortality on the transplantation waiting list. Moreover, many potential transplant candidates not even make it to the waiting list, because of acute hemodynamic deterioration. To reduce this high mortality rate, mechanical circulatory support can play an important role as a bridge to transplantation. Implantable left ventricular assist devices like the HeartMate (Thoratec, Pleasanton Calif.) and the Novacor (WorldHeart, Ottawa) are the most suitable devices as bridge to transplant, because they can support the failing heart for months or even years \(^6-10\).

The Heart Lung Center Utrecht (HLCU) started a bridge to transplantation program in 1993 using the implantable HeartMate pneumatic and later the vented electric left ventricular assist device.

In this article the results of 8 years experience with this device are presented.

Methods

Description of the HeartMate\(^\circledR\) device and mode of implantation.

The HeartMate\(^\circledR\) left ventricular assist system (LVAS) consists of an implantable pneumatic (IP) or a vented electric (VE) left ventricular assist device (LVAD) (fig 1). The pump consists of a titanium housing with a flexible Biomer polyurethane diaphragm bonded to a rigid pusher plate. The diaphragm divides the pump in two halves: a blood chamber and an air chamber in case of the IP system or an electrical motor chamber in case of the VE system. The air chamber of the IP system is connected to an external console by a transcutaneous driveline. By delivering programmed pulses of air the console provides the displacement of the diaphragm propelling the blood through an outflow graft into the arterial
circulation. Both the outflow and inflow graft contain porcine xenograft valves, providing uni-directional flow. Differences in air pressure between this closed system and the ambient air are equalized by manually venting the system on the console, which also has a display continuously showing information about stroke volume, filling status and pump rate.

**Figure 1**: Schematic diagram of the HeartMate VE left ventricular assist device. The inflow canula is implanted in the left ventricular apex. The outflow graft is connected end to side to the ascending aorta. The transcutaneous skin line is connected to the controller.

In case of a VE system the pump is electrically driven and continuously vented through an almost identical driveline connected to a small controller and energized by rechargeable batteries. The LVAD has a maximal stroke volume of 83 ml and a maximal beat rate of 120 beats per minute. The pump can function in a fixed mode or in an automatic mode, allowing the device to vary its flow dependent on the left ventricular filling volume.

The unique feature of the HeartMate® blood pump is the blood-contacting surface. These textured biomaterials are to promote the formation of a thin, well-adhered pseudointimal lining on the inner side of the pump. This non-thrombogenic
neointimal layer reduces the need for anticoagulation, as are the porcine xenografts; only 80 mgr. of aspirin a day is required for antithrombotic prophylaxis.

Implantation of the device is accomplished through a median sternotomy and laparotomy. The pump is implanted in the left upper quadrant of the abdomen, intra-or extraperitoneally. The inlet canula connects the apex of the left ventricle to the pump, while the outlet canula is connected end to side to the ascending aorta using a Dacron® vascular graft. (Fig 1). Both canulae pass the diaphragm.

Since 1997 the driving console has been replaced by a smaller, portable one (HeartPak) (fig 2) which is charged by exchangeable batteries and offers the patients a better and more extended range of mobility.

**Patients.**

From March 1993 to December 2001, 38 patients, (34 males, 4 females, mean age 38±13 years, range 16-62 years) received the HeartMate® LVAD as a bridge to heart transplantation. Indication for implantation was cardiogenic shock refractory to drug treatment in all cases (table 1). Dilating cardiomyopathy was the underlying cause in 23 patients (60%), ischemic heart disease in 15 (40%).

Pre LVAD all patients were on high-dose intravenous inotropic medication (dopamine, dobutamine and milrinon) and 16 patients were also supported by an intra-aortic balloon pump. An external ventricular assist device had been implanted in 3 cases (1 Hemopump and 2 Abiomed BVS 5000). The pneumatic HeartMate IP was used in 32 patients, the electrical HeartMate VE in 6.

**Statistical analysis**

Data are presented as the mean ± SD. Statistical analysis was performed with two-tailed paired Student t test. A p-value < 0.005 was considered significant.

**Results.**

In this group of 38 patients, 33 survived the implantation and early postoperative period (87%). Five patients died in the first 30 days post implant (peri-operative mortality 13%), 3 patients (9%) died late in the postoperative period (Table 2).
Table 1. Characteristics of LVAD patients at the time of implantation (n = 38)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Male / Female</td>
<td>34 / 4</td>
</tr>
<tr>
<td>Age (yr.)</td>
<td>38 ± 13</td>
</tr>
<tr>
<td>DCM / IHD</td>
<td>23 / 15</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>14 ± 5</td>
</tr>
<tr>
<td>Cardiac Index (L/min/m²)</td>
<td>2.0 ± 0.7</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>62 ± 11</td>
</tr>
<tr>
<td>RAP (mm Hg)</td>
<td>13 ± 7</td>
</tr>
<tr>
<td>PCWP (mm Hg)</td>
<td>24 ± 7</td>
</tr>
<tr>
<td>PVR (dyne sec cm⁻²)</td>
<td>196 ± 94</td>
</tr>
<tr>
<td>TPG (mm Hg)</td>
<td>9 ± 4.2</td>
</tr>
<tr>
<td>IABP / other support</td>
<td>16 / 3</td>
</tr>
<tr>
<td>Mean duration support (days)</td>
<td>172 ± 140</td>
</tr>
</tbody>
</table>

Figure 2: The three models of the HeartMate Left Ventricular Assist System. The Implantable Pneumatic system with the original console and with the portable console (HeartPak), and the Vented Electric device.
Mean duration of support for the 38 patients was $172 \pm 140$ days with a longest duration of 557 days and a cumulative experience of 6522 days (nearly 18 years). Successful implantation of the HeartMate® LVAS resulted in an immediate improvement of the hemodynamic situation in all patients. Cardiac index increased from $2,0 \pm 0,7 \text{ l/min/m}^2$ pre implantation to $3,0 \pm 0,5 \text{ l/min/m}^2$ 24 hours post transplantation ($p < 0.0001$). Renal and hepatic function normalized within 6 weeks (Table 3). Use of the mechanical pump device did not cause hemolysis (normal serum Hb and haptoglobin levels), or thrombocytopenia (platelet count $211 \pm 81.10^9 /\text{L}$ pre-implantation versus $289 \pm 81.10^9 /\text{L}$, 6 weeks post implantation) in any of the patients. Four patients are still on the device. Of the remaining 34 patients, 26 (76%) underwent heart transplantation, after an average of $206 \pm 129$ days on the device. At the time of transplantation all patients were in NYHA functional class 1 and were fully mobilized. After an intensive training and instruction program seven patients have been discharged from the hospital awaiting heart transplantation at home.
Table 3. Hepatic and renal function pre and post implant HeartMate (n = 31)

<table>
<thead>
<tr>
<th>Variable</th>
<th>mean ± SD pre implant</th>
<th>Mean ± SD 6 weeks post implant</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinin (µmol/l)</td>
<td>159 ± 79</td>
<td>74 ± 27</td>
<td>P&lt;0.0003</td>
</tr>
<tr>
<td>Tot.bilirubin (mmol/l)</td>
<td>27 ± 18</td>
<td>14 ± 10</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>ASAT (U/l)</td>
<td>103 ± 129</td>
<td>25 ± 9</td>
<td>p&lt;0.03</td>
</tr>
<tr>
<td>ALAT (U/l)</td>
<td>99 ± 114</td>
<td>23 ± 13</td>
<td>p&lt;0.01</td>
</tr>
</tbody>
</table>

COMPLICATIONS

Right ventricular failure (RVF)
RVF early after implantation occurred in 12 patients (32%). All but 3 patients were successfully treated with positive inotropic agents, vasoactive agents and optimal oxygenation. In three patients temporary support of the failing right ventricle was necessary using an external device (Abiomed®). Weaning of this device was only successful in one single case, 2 patients died in the postoperative course due to complications related to right ventricular failure (air embolism and a hypotensive cerebral infarction).

Bleeding.
Severe postoperative bleeding requiring blood transfusion and reoperation occurred in 5 patients. Two of these died. One patient died due to multi-organ failure after a complicated surgical procedure with long duration of extracorporeal circulation. The other patient died due to an irreparable disruption of the left ventricular apex-inlet canula connection, 7 days after implantation.

Thrombo-embolic complications.
Thrombo-embolic events occurred in only three patients, but resulted in death in two. One patient suffered a massive cerebral infarction resulting from LVAD endocarditis 418 days post implant. The LVAD endocarditis probably originated from an acute cholecystitis. Another fatal thrombo-embolic event occurred due to mechanical failure of the control unit. The third patient suffered episodes of amaurosis fugax and recurring abdominal pain suggestive of embolic renal disease, for which oral anticoagulation was successfully installed. The overall thrombo-embolic complication rate was 7.9 % or 0.014 events per patient month,
Clinical experience with LVAD

despite the use of only low dose aspirin as anti-thrombotic prophylaxis in all cases. If the patients with the device malfunction and the LVAD endocarditis are excluded, the thrombo-embolic complication rate was 2.6 % or 0.005 events per patient month.

Device related infections
Twelve patients (32%) had driveline and pocket infections, primarily staphylococcus aureus. Nine of these patients had positive blood cultures. Treatment in all patients consisted of intravenous antibiotics in combination with local treatment. One patient died as a result of septic shock caused by coagulase negative Staphylococcal infection 45 days after LVAD implantation. In 5 patients surgical treatment was necessary consisting of pocket exploration and transposition of an abdominal rectus muscle flap. One patient was kept on long term antibiotic treatment under suspicion of endocarditis of the porcine xenografts in the device. Explantation of the device, at the time of heart transplantation, however, did not reveal signs of endocarditis.

Mechanical complications
Few minor mechanical defects such as driveline electrical wire fractures, display dysfunction, and driver sensor dysfunction occurred, not causing pump function to cease. Major dysfunction of the device occurred in 2 patients. In one case pump function ceased because the pneumatic driving console got jammed, resulting in the nursing staff having to drive it manually for a short period. The console had to be replaced and the patient did not suffer any adverse effects. Mechanical dysfunction of a pneumatic device in a second patient however happened to be fatal (patient # 3 in table 2). A combination of a failing sensor and the vent valve not closing properly after a routine venting procedure at 19 weeks’ post implantation, resulted in a low stroke volume, while the patient was asleep and the devices low flow alarm not going off, due to the failing sensor. This low flow state caused the patient to suffer a fatal stroke due to cerebral embolism originating from an intraventricular thrombus.

Surgical complications during heart transplantation
The presence of a LVAD resulted in a more complex heart transplant procedure. In five patients (19%) this lead to increased bleeding requiring re-operation. In one patient a hepatic laceration due to adhesions had to be oversewn. The abdominal wall could be closed primarily in all patients; the diaphragm had to be reconstructed in some.
Discussion.

The use of implantable left ventricular assist devices as bridge to transplantation for heart transplant candidates, who deteriorate while waiting for a donor heart, is now widely accepted \textsuperscript{11-13}. The results are very encouraging, especially considering the poor condition of the patients at the time of LVAD implantation, who were facing imminent death. This treatment not only leads to increased survival, but also to complete restoration of renal and liver function and impressive improvement of functional class, comparable to the situation after heart transplantation, as we have reported previously \textsuperscript{4}.

Our preference for the HeartMate LVAD over other implantable devices was based on its blood-contacting inner surfaces, promoting the formation of a biological lining, not necessitating the use of anticoagulants and diminishing the risk of thrombo-embolic complications\textsuperscript{14}. This study and studies by others confirm the low risk for thrombo-embolism with this device \textsuperscript{7, 12, 14, 15}.

The overall patient survival until transplantation of 79\% in this study is promising, considering the long mean duration of support (172±140 days). The latter is the reflection of the long waiting time for heart transplantation in our transplant program.

Given this, our policy in the last 2 years has been to discharge patients from the hospital while on the device after they had been fully recovered and after they had been extensively trained to use the device\textsuperscript{16}. This requires good cooperation of the patient and intensive follow-up and support facilities of the hospital.

Considering survival in this study one has to bear in mind the young mean age of the patients, which is younger than in other published studies \textsuperscript{6-8}.

Right ventricular failure has been reported a serious problem after LVAD implantation with risk of air-embolism during the implantation procedure and inadequate filling of the device resulting in low output thereafter. This problem is inherent to the fact that only the left ventricle is supported and it did occur in almost one third of the patients in this study, as has been reported by others\textsuperscript{12, 17, 18}. Predictors of right ventricular failure are high right atrial pressure, high transpulmonary gradient and an acute decrease in pulmonary artery pressure with LVAD implantation\textsuperscript{17}. Growing experience and better patient selection is probably the explanation that no fatalities due to RVF occurred in the second half of the study.

Device-related infections, partly due to the presence of transcutaneous drivelines are reported to be another major problem \textsuperscript{19-22}. The rate of 32\% device-related infections in our patients corresponds to reports in literature. In two patients an infectious episode turned out to be fatal. Therefore, the infection problem needs
careful attention. Totally implantable devices with transcutaneous energy transmission, which are currently being clinically investigated, may decrease the risk of driveline related infections.

There were various mechanical problems, especially of the pneumatic driving consoles, but except for one case, these were not fatal. The need for continuous support by an experienced technical department, however, proves to be increasingly mandatory.

In conclusion, this study shows promising results using the HeartMate IP and VE LVAD as a bridge to transplantation in patients with end-stage heart failure. The main drawbacks are the mechanical complications and the high risk for infections, partly related to the transcutaneous driveline. Future devices may diminish these problems, allowing longer periods of event-free support. Based on the present experience and future technical improvements, LVAD’s may not only be used as a bridge to transplantation, but also as an alternative to transplantation. The recently reported results of the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) Study Group, showing a significant improvement of survival one year after LVAD implantation vs. the medical-therapy group, support this idea.\(^\text{23}\)
References


Clinical experience with LVAD


