Left ventricular assist device as bridge to transplantation in patients with end-stage heart failure

Eight-year experience with the implantable HeartMate LVAS

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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. **A total of 33 of the 38 patients (87%) survived the implantation and perioperative period. There were five perioperative deaths (13%), two due to right ventricular failure, two as a result of bleeding and one 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 one patient died. Four patients are still on the device, waiting for a 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. (*Neth Heart J* 2002;10:267-71.)**

Key words: heart failure, heart transplantation, left ventricular assist devices

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 centres 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 do not even make it to the waiting list, because of acute haemodynamic 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 Centre Utrecht (HLCU) started a bridge to transplantation programme in 1993 using the implantable HeartMate pneumatic and later the vented electric left ventricular assist device.

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

Methods

Description of the HeartMate® device and mode of implantation

The HeartMate® left ventricular assist system (LVAS) consists of an implantable pneumatic (IP) or a vented electric (VE) left ventricular assist device (LVAD) (figure 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 the case of the IP system or an electrical motor chamber in 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 equalised by manually venting the system on the console, which also has a display continuously showing information about stroke volume, filling status and pump rate.

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 energised 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 do the porcine xenografts; only 80 mg 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 extra-peritoneally. 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. (figure 1). Both canulae pass the diaphragm.

Since 1997 the driving console has been replaced by a smaller, portable one (HeartPak) (figure 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

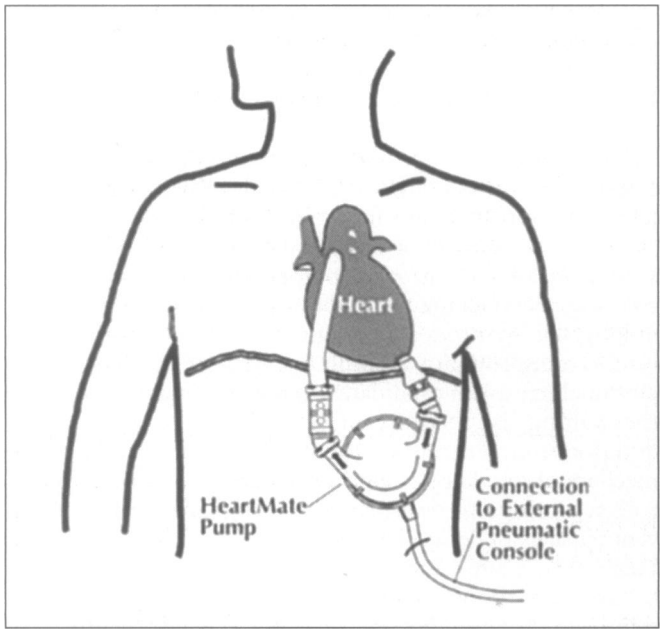

Figure 1. Schematic diagram of the HeartMate Implantable Pneumatic left ventricular assist device. The inflow canula is implanted in the left ventricular apex. The outflow graft is connected end to side to the ascending aorta. The transcutaneous driveline is connected to the external pneumatic console.

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.

Table 1. Characteristics of LVAD patients at the time of implantation (n=38).

Male/female	34/4
Age (years)	38±13
DCM/IHD	23/15
LVEF (%)	14±5
Cardiac index (L/min/m^2)	2.0±0.7
MAP (mmHg)	62±11
RAP (mmHg)	13±7
PCWP (mmHg)	24±7
PVR (dyne sec cm^{-5})	196±94
TPG (mmHg)	9±4.2
IABP/other support	16/3
Mean duration support (days)	172±140

LVAD=left ventricular assist device; DCM=dilated cardiomyopathy; IHD=ischaemic heart disease; LVEF=left ventricular ejection fraction; MAP=mean arterial pressure; RAP=right atrial pressure; PCWP=wedge pressure; PVR=pulmonary vascular resistance; TPG=transpulmonary gradient (mean pulmonary artery pressure minus PCWP).

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%), ischaemic 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 three cases (1 Hemopump and 2 Abiomed BVS 5000).

The pneumatic HeartMate IP was used in 32 patients, the electrical HeartMate VE in six.

Statistical analysis

Data are presented as the mean±SD. Statistical analysis was performed with two-tailed paired Student's 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 (perioperative mortality 13%), three patients (9%) died late in the postoperative period (table 2).

Table 2. Patient mortality and cause of death (n=8).

Patient	Sex	Age	Survival/ days	Cause of death
# 3	M	42	133	Mechanical failure
# 5	M	20	3	RVF
# 6	F	52	8	RVF
# 10	M	62	0	Bleeding
# 18	M	38	435	Cerebral embolus
# 23	M	49	35	Septic shock
# 25	M	25	6	Bleeding
# 30	M	24	0	Septic shock at time of implantation

RVF=right ventricular failure

Mean duration of support for the 38 patients was 172±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 in the haemodynamic situation in all patients. Cardiac index increased from 2.0±0.7 l/min/m^2 pre-implantation to 3.0±0.5 l/min/m^2 24 hours post-transplantation (p<0.0001).

Renal and hepatic function normalised within six weeks (table 3). Use of the mechanical pump device did not cause haemolysis (normal serum Hb and haptoglobin levels) or thrombocytopenia (platelet count 211±81.10^9/L pre-implantation versus 289±81.10^9/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±129 days on the device. At the time of transplantation all patients were in NYHA functional class 1 and were fully mobilised. After an intensive training and instruction programme, 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).

Variable	Mean±SD pre-implant	Mean±SD 6 weeks post-implant	p value
Creatinine (µmol/L)	159±79	74±27	p<0.0003
Total bilirubin (mmol/L)	27±18	14±10	p<0.01
ASAT (U/l)	103±129	25±9	p<0.03
ALAT (U/l)	99±114	23±13	p<0.01

Complications

Right ventricular failure (RVF)

RVF early after implantation occurred in 12 patients (32%). All but three 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, two 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 five 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 disrupture of the left ventricular apex-inlet canula connection, seven days after implantation.

Thromboembolic complications

Thromboembolic 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 thromboembolic 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 thromboembolic complication rate was 7.9 % or 0.014 events per patient month, despite the use of only low-dose aspirin as antithrombotic prophylaxis in all cases. If the patients with the device malfunction and the LVAD endocarditis are excluded, the thromboembolic 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 five 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 due to suspected 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. These did not cause pump function to cease. Major dysfunction of the device occurred in two 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 but the patient did not suffer any adverse effects. Mechanical dysfunction of a pneumatic device in a second patient, however, was 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 device's 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 an 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, but 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 are deteriorating while waiting for a donor heart, is now widely accepted.[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 with the situation after heart transplantation, as we have reported previously.[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 thromboembolic complications.[14] This study and studies by others confirm the low risk for thromboembolism with this device.[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 programme.

Given this, our policy in the last two years has been to discharge patients from the hospital while on the device, after they have fully recovered and after they

have been extensively trained to use the device.[16] This requires good cooperation from 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.[6-8]

Right ventricular failure has been reported to be 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 occurred in almost one third of the patients in this study, as has been reported by others.[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.[17] Growing experience and better patient selection is probably the explanation why 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.[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, LVADs may not only be used as a bridge to transplantation, but also as an alternative to transplantation. The recently reported results of the Randomised 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.[23] ■

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