ELSEVIER

European Journal of Cardio-thoracic Surgery 24 (2003) 113–118

EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY

www.elsevier.com/locate/ejcts

Left ventricular assist device as bridge to heart transplantation – lessons learned with the MicroMed DeBakey axial blood flow pump☆

S. Salzberg[a,*], M. Lachat[a], G. Zünd[a], E. Oechslin[b], E.R. Schmid[c], M. DeBakey[d], M. Turina[a]

[a]*Clinic for Cardiovascular Surgery, University Hospital, 8091 Zurich, Switzerland*
[b]*Division for Cardiology, University Hospital, Zurich, Switzerland*
[c]*Clinic for Anaesthesiology, University Hospital, Zurich, Switzerland*
[d]*Baylor College of Medicine, Houston, TX, USA*

Received 9 January 2003; received in revised form 14 March 2003; accepted 17 March 2003

Abstract

Objective: The MicroMed DeBakey left ventricular assist device (LVAD) axial blood flow pump was used as bridge to heart transplantation (HTx) in patients with terminal heart failure. The aim was to evaluate this novel mechanical circulatory support system in regard to overall outcome. **Methods**: Prospective study in 15 HTx candidates (mean age 40 ± 7 years) with terminal heart failure and maximal medical treatment due to ischemic cardiomyopathy (CMP, $n = 5$), dilated CMP ($n = 3$), restrictive CMP ($n = 2$), unclassified CMP ($n = 1$), metabolic CMP ($n = 1$), valvular CMP ($n = 1$) and congenital CMP ($n = 2$). All patients were implanted with a MicroMed DeBakey LVAD. A rescue procedure was necessary in eight critical patients, while seven underwent elective LVAD implantation. Procedures were performed via median sternotomy, in normotherm femoro-femoral CPB (mean duration 59 ± 1 min). Oral Marcoumar© (INR 2.0–3.0) and Aspirin© (100 mg daily) were started as soon as possible. Patients were discharged into a specialized rehabilitation clinic from which it was possible to release them home after a few weeks. **Results**: Successful implantation and discharge from ICU (mean stay 10 ± 7 days) was possible in 11 patients. Seven were transplanted (mean support 50.7 days) and one is awaiting HTx (support >310 days) in the comfort of his home (NYHA I). Survival was 100% among the transplanted patients. Of the seven elective implants, five, and of the eight rescue procedures three patients underwent successful HTx. Four patients died early, while three patients died late on pump support due to intracranial hemorrhage ($n = 2$, 73 and 76 days) and chest infection ($n = 1$, 124 days). All survivors were discharged from hospital, with significant decrease in NYHA class (mean 3.8–2.4 ($n = 11$)). Treadmill testing showed increased exercise tolerance, from 35 to 71 W ($n = 4$). Plasma BNP values (mean 950–162 ng/l ($n = 4$)) and pulmonary resistance (mean 316–194.5 dyne s/cm^5 ($n = 3$)) decreased significantly during LVAD support. **Conclusions**: The MicroMed DeBakey LVAD is simple to implant; outpatient treatment is safe and efficient. Patients' condition and pulmonary resistances normalize within 6 weeks, making previously considered inoperable patients amenable for HTx. HTx can be performed in low-risk situation, allowing better donor–recipient matching and improving overall outcome.

Keywords: Terminal heart failure; Axial blood flow; Heart transplantation; Left ventricular assist device; Mechanical circulatory support

1. Introduction

The incidence of chronic heart failure (CHF) is increasing due to the aging population and its improved medical management. With disease progression to terminal heart failure, therapeutic options become fewer and cardiac transplantation (HTx) presents itself as the last option. HTx is also one of the most limited therapies, not only in regard to the lack of donor hearts (<3000 HTx performed each year worldwide) but also due to the surgical limitations inherent to the clinical aspects of this severely ill patient population. Mechanical circulatory support systems have been developed as effective adjuvant therapeutic options in these terminally ill patients. Since the creation of the artificial heart program by the national institute of health (NIH) [1] in 1964, numerous different mechanical circulatory support systems have been elaborated upon. Copeland and associates [2] performed the first bridging to HTx by mechanical support in 1985. Mortality of terminal heart failure being very high as disease progresses, HTx candidates die while

☆ Presented at the 16th Annual Meeting of the European Association for Cardio-thoracic Surgery, Monte Carlo, Monaco, September 22–25, 2002.

* Corresponding author.
E-mail address: sacha.salzberg@chi.usz.ch (S. Salzberg).

1010-7940/03/$ - see front matter © 2003 Elsevier Science B.V. All rights reserved.
doi:10.1016/S1010-7940(03)00179-9

waiting on long lists [3,4]. According to the recently published REMATCH study [3], the use of left ventricular assist devices (LVAD) resulted in more than twice the survival rate and an improved quality of life, in comparison to optimal medical management. Researchers from the Baylor College of Medicine (Houston, TX) with engineers from NASA have been developing the DeBakey LVAD produced by MicroMed Inc. since 1988 [5]. This implantable continuous axial flow pump creates a maximal flow in excess 10 l/min, hence providing relief to the sick heart by taking over part of the pumping action [6]. As the DeBakey LVAD has been available at our center since October 1999, we evaluated this new device in 15 consecutive patients and report our results in regard to overall outcome in HTx candidates.

2. Materials and methods

From October 1999 until December 2002, 15 patients (mean age 40 ± 17 years, one female, 14 male) have been implanted with a MicroMed DeBakey LVAD (MicroMed Inc, Houston, TX, USA). To qualify, patients had to fulfill institutional inclusion criteria for terminal heart failure (Table 1). All patients were accepted on the transplantation list and gave their informed consent as stated by our local ethics committee, when this was not possible their legal representative did so. Patient's medical history and indication for LVAD implantation are resumed in Tables 2 and 3. A precise description of the DeBakey LVAD was done previously by Noon et al. [5,7].

2.1. Implant procedure

After general anesthesia and median sternotomy, the pericardium was opened, diaphragmatic attachment to the costal margin divided and both extended laterally beyond the apex. Patients were systemically heparinized (Heparin® 100 IE/kg) in preparation for heparinized normotherm CPB with femoro-femoral veno-arterial cannulation. The left ventricular apex was elevated; the insertion site of the inflow cannula selected and an apical fixation ring sewn to the apex. In preparation for insertion of the pump inflow cannula, the heart remained beating in the last five cases, in ventricular fibrillation in the ones prior. A round bladed coring device was used to create a hole in the left ventricular apex permitting insertion of the inflow cannula. The apical insertion site was carefully checked for bleeding, and Flowseal® was applied to the sutures holding the inflow tract in place to insure perfect hemostasis. Then tunneling was performed in order to exit through the skin in a convenient position above the iliac crest. The pump was placed into the abdominal pocket and the length of the outflow graft measured and trimmed. A lateral anastomosis to the ascending aorta was done so as to protect the outflow graft from injury during HTx surgery. After completion of the anastomosis and de-airing of the system, pumping was started at 7500 rpm and adjusted to maintain a cardiac index >2.0 l/min/m^2. Pump output was gradually increased, to unload the heart, while catecholamines were started to increase output. Protamine® was given to reverse heparin (ratio 1:1). Hemostasis and anticoagulation were conducted with a modified Szefner protocol [8].

Table 1
Inclusion criteria

- Left atrial *or* pulmonary capillary wedge pressure >18 mmHg
- Mean arterial pressure <90 mmHg
- Cardiac index <2.0 l/min/m^2
- Left ventricular ejection fraction <25%
- Incomplete response to intravenous drugs
- Intraaortic balloon pump support (IABP)

or: At high-risk of sudden cardiac arrest
And: accepted by Transplantation Committee for HTx

2.2. Post-operative management

Anticoagulation was started with intravenous heparin early post-operative (6–8 h, PTT aim >60 s) with Antithrombine III substitution when <80%. Antivitamin K (Marcoumar®) and Aspirin® were initiated as soon as possible (target international normalized ratio (INR) 2.0–3.0). When anticoagulation was insufficient, low weight heparin (Fragmin® 2500IE s.c. 1 or 2 × daily) was added. Anticoagulation was monitored in the ICU every 4 h, daily on the regular ward (twice daily when abnormal) and on ambulation at least three times per week, of which once in our clinic.

After implanting and adjusting of coagulation parameters, the manning of the pump required limited special training. Nurses and patients were informed about practical functions of the external pump controller device and the patients were trained to deal with alarms when on leave from the hospital. Patients were also instructed on how to take care of the exit site wound, and were able to change their bandages themselves. The display screen of the controller device allowed patients to check their pump data themselves. This datum was collected on provided pump data sheets.

As soon as the patients were ambulating, they were released into a specialized cardiovascular rehabilitation clinic or went directly home, returning to our clinic once a week for a full check-up by a multidisciplinary LVAD team (cardiologist and surgeon).

3. Results

3.1. Surgery

Surgery was performed by the same senior surgeon with

Table 2
Pre-operative patient demographics

Patient	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Age	18	47	53	48	51	17	14	55	41	18	37	52	64	61	18
Sex	M	M	M	F	M	M	M	M	M	M	M	M	M	M	M
Height	168	169	171	172	187	169	178	186	176	185	186	182	185	170	152
Weight	49	76	71	67	80	50	60	61	72	94	92	92	64	68	52
HR	96	84	96	100	120	115	96	100	80	88	90	95	88	84	92
BP	98/68	84/52	70/50	105/75	100/50	110/57	96/54	130/75	100/54	95/50	90/60	85/50	80/50	85/65	78/62
GCS	15	15	15	15	10	8	15	10	15	14	15	15	15	15	7
NYHA	IV	IV	IV	III	IV	IV	IV	IV	IV	IV	III	III	III	III	IV
CI	1,5	1,8	n.a.	n.a.	n.a.	n.a.	1,9	1,4	n.a.	n.a.	1.9	n.a.	n.a.	1.5	1.2
Other	Iono	IABP			IABP, Iono	Iono	IABP, Iono	ECMO							ECMO

BP, blood pressure (mmHg); HR, heart rate (bpm); GCS, Glasgow coma scale; NYHA, New York Heart Association; CI, cardiac index (l/min/m^2); IABP, intraaortic balloon pump; Iono, intravenous inotrop support; ECMO, extra corporal membranous oxygenation; M, male; F, female.

a mean duration of 256 ± 4 min, cardiopulmonary bypass (CPB) was 69 ± 1 min with no surgical complications occurring. Fourteen patients were weaned from CPB in the operating room; one was operated under extra corporal membranous oxygenation (ECMO) support. After a mean stay in the ICU of 10 ± 7 days, 11 patients returned to the regular ward. Total mean support duration on the device was 64 ± 61 days. No device related events occurred in 956 patients support days. Six patients were able to be released into a selected rehabilitation facility.

3.2. Clinical outcome

Table 4 resumes complications and outcome. To date, seven patients have been successfully bridged to HTx (mean support 54 ± 22 days). Survival after HTx after a mean follow up of 27 ± 10 months is 100%. One patient is still awaiting a suitable donor organ on LVAD support (>310 support days) discharged from the hospital.

In the presented series, four early deaths occurred during the ICU stay. Three patients died late: two patients suffering fatal hemorrhagic strokes (days 73 and 76) and one patient developing a central graft infection (Germ: *Staphylococcus* coagulase negative) leading to MOF (day 124).

3.3. Clinical data

Clinical improvement was seen in all survivors, as testified by the decrease in NYHA classification (mean 3.8–2.4, $n = 11$). Plasma BNP values as markers of CHF normalized within 6 weeks (from mean 950 to 162 ng/l, $n = 9$). In regard to right ventricular hemodynamics, pre- and post-operative invasive cardiac monitoring was routinely performed in the last four elective patients of this series. This showed a significant decrease of pulmonary vascular resistance (PVR) (from mean 316 to 194.5 dyne s/cm^5) over the whole LVAD support period. The increase in exercise tolerance was reported by the patients themselves and documented by treadmill ergometry (from mean 35 to 71 W) in six. Cardiac echocardiography showed increased contractility with significant flow through the aortic valve and increased left ventricular ejection fraction in all patients.

End organ perfusion normalized under LVAD support in

Table 3
Indication for LVAD implantation and disease history

Patient	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Disease	DIL	DIL	ISC	RES	NC	CONG	MET	ISC	ISC	CONG	ISC	ISC	VLV	DIL	RES
Nicotine	No	Yes	No	No	Yes	No	No	Yes	No	No	Yes	Yes	Yes	Yes	No
DM	No	Yes	No	No	No	No	No	No	No	No	Yes	No	No	No	No
HR	R	AR	R	R	R	AR	AR	AR	R	R	R	AR	AR	R	AR
Prev. surg.	No	Yes	No	No	No	Yes[a]	No	Yes[b]	No	Yes[c]	Yes[b]	No	Yes[d]	No	Yes
Surg.	U	U	E	E	U	U	U	U	E	U	E	E	E	E	U
Other	K.B.	GI	MI ×2	Amyl	ARCA	ARCA	x	Stroke	Cor	Cor	x	x	x	x	X

Prev. surg, previous surgery; DIL, dilatative cardiomyopathy (CMP); CONG, congenital CMP; VLV, valvular CMP; MET, metabolic CMP; GI, gastrointestinal bleeding; MI, myocardial infarcts; Cor, coronary disease; K.B., Kiener–Becker muscle dystrophy; ARCA, cardiac arrest 24 h prior; D.Sy., Danon syndrome; Amyl., severe cardiopulmonary amyloidosis; DM, diabetes mellitus; CM, cardiomyopathy; E, elective implantation; U, urgent/rescue procedure; RES, restrictive CMP; NC, not classified CMP, X.

[a] Blalock Shunt.
[b] CABG, coronary aortic bypass graft.
[c] Atrial inversion by senning.
[d] Aortic valve 1987, PM DDD 2000.

Table 4
Complications and outcome

Patient	Type of surgery	Minor events	Major events	Outcome
1	U	Hemolysis	None	HTX on day 60
2	U	UTI, renal infarct	Stroke	Death on day 73
3	E	GI bleeding	None	HTX on day 32
4	E	Hemolysis	Iatrogenous bleeding[a]	HTX on day 81
5	U	Reintubation	None	HTX on day 80
6	U	None	Right ventricular failure	Death on day 7
7	U	Reintubation	Massive chest infection[b]	Death on day 124
8	U	None	MOF	Death on day 16
9	E	None	Cardiac Tamponade[b]	HTX on day 25
10	U	None	None	HTX on day 58
11	E	Renal insufficiency	None	HTX on day 42
12	E	None	None	Awaiting transplant, >220 support days
13	E	None	Ventricular fibrillation, stroke	Death on day 76
14	E	None	Diffuse severe bleeding	Death on day 26
15	U	None	MOF	Death on day 6

E, elective implant; U, urgent/rescue procedure; UTI, urinary tract infection; GI, gastrointestinal; MOF, multiorgan failure.
[a] Due to pleura punction requiring surgery.
[b] Requiring surgery.

all patients (Figs. 1 and 2). Only two patients developed significant organ failure: one during massive liver dysfunction following acute right heart failure (day 7) and one other developed acute renal failure following a renal infarct, resolving spontaneously.

No infections at the exit site of the power cables appeared in any patients.

Four patients showed biological signs of hemolysis, one developed a fatal stroke (day 73), the second a pericardial bleeding requiring surgical drainage and two others were managed by decreasing the pump revolutions per minute (rpm). Fig. 3 shows hemolysis parameters in 11 patients over a period of 4 weeks after implantation.

4. Discussion

The evermore present organ shortage for HTx leads to an increasing necessity of therapeutic options for patients with terminal heart failure. Several other studies have concluded that LVAD support is an excellent tool as bridge to transplant [9,10]. As shown by the REMATCH study [3], the role of LVAD support is not only limited as bridge to HTx but destination therapy presents itself as a promising option. The increasing demand for LVAD support has lead to the development of different systems with the main difference being their flow characteristics (pulsatile vs. continuous). Bleeding and thromboemboli are present with any kind of disease progression in terminal heart failure (natural course, LVAD support, total artificial heart). The main complication of mechanical circulatory support in these patients is bleeding. As seen with other systems the DeBakey LVAD comes with a high incidence of bleeding [4,9], our results indicate no significant differences with previously reported figures [11].

Survival of HTx after bridging was 100% in our series.

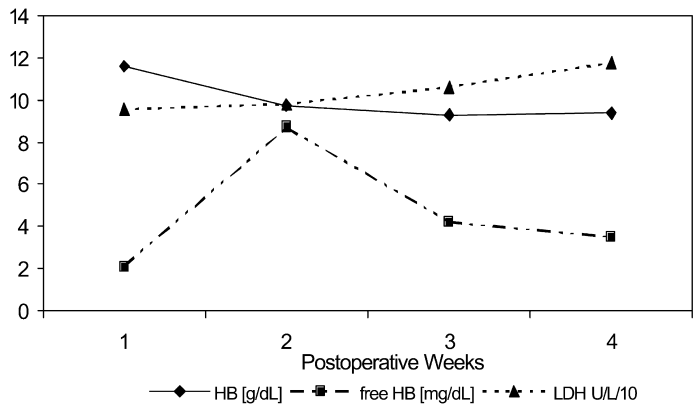

Fig. 1. Liver function ($n = 11$, mean values).

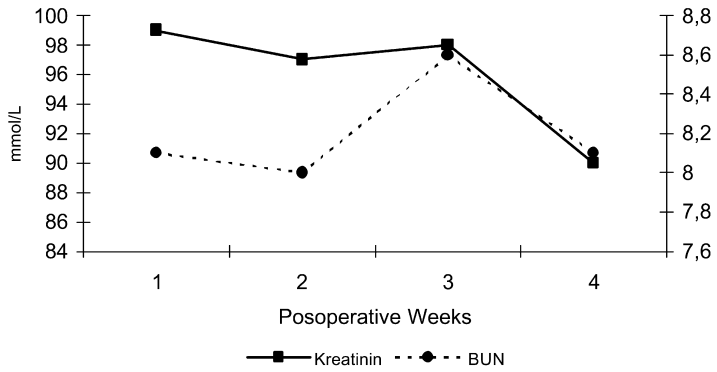

Fig. 2. Kidney function ($n = 11$, mean values).

None of the bridged patients was unsuitable for HTx after LVAD support. In total, seven patients died on LVAD support; one in MOF (day 16), one following a massive chest infection (day 124), one during emergency redo-surgery after which it was impossible to wean him from CPB due to acute right heart failure (day 7), one other never recuperated from pre-operative MOF (day 6), both these patients were on ECMO support prior to device implantation. Of the three late deaths, two patients developed major hemorrhagic strokes (day 73 and 76) while one other patient died following severe diffuse non-controllable post-operative bleeding (day 26).

The high overall mortality of 46% ($n = 7$) can be related to the following factor: eight emergency implantations were performed in critical patients. Of these eight patients, three were successfully bridged to HTx and are doing well to date. In the group of seven elective implants, mortality was low considering the bad general state of terminal heart failure patients.

These results show the importance of the timing of implantation. As seen in other series, elective implant and clinical status both determine positive outcome [12]. It is our belief that early referral and elective implant bring a higher benefit to this patient population. The three early deaths in the group of emergency implants can clearly be attributed to the poor clinical state prior to implant (Table 4).

The MicroMed DeBakey LVAD is a non-pulsatile assistance for the left heart, in the early support periods flows are continuous, but with myocardial recuperation pulsatility returns. Through the active continuous unloading of the left ventricle and the aspiration created by the inflow cannula, the trans-pulmonary gradient is increased. It is observed that pulmonary wedge pressures are decreased and increased right heart output is achieved. In comparison to pulsatile assist devices, the continuous flow created by the DeBakey LVAD does not depend on native cardiac ejection. Even with constant rpm, the flow through the LVAD increases with patients exercise and physical activity.

In one patient who survived 7 h of ventricular fibrillation before returning to our clinic (recorded by his pace-maker, most likely cause being hypokaliemia), we documented absence of heart output by echocardiography. This patient survived solely by the force of the DeBakey LVAD until he could be electroconverted (case report in press).

The results of this study indicate that non-pulsatile flow allows for continuous reduction of post-capillary load inducing normalization of PVR in patients otherwise not considered as HTx candidates [7,13].

As seen in other studies, quality of life is improved and

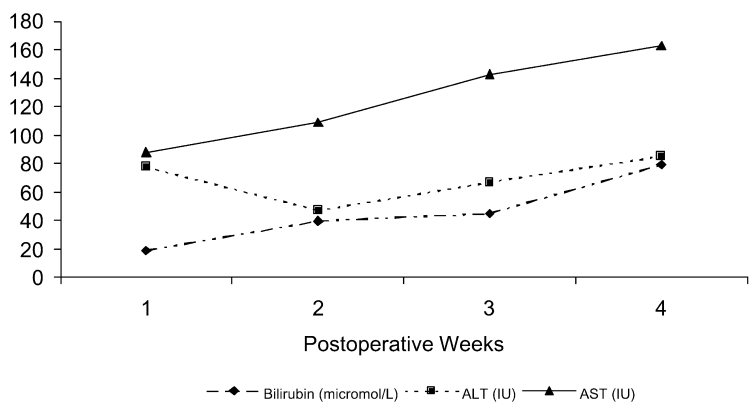

Fig. 3. Parameters of hemolysis ($n = 11$, mean values).

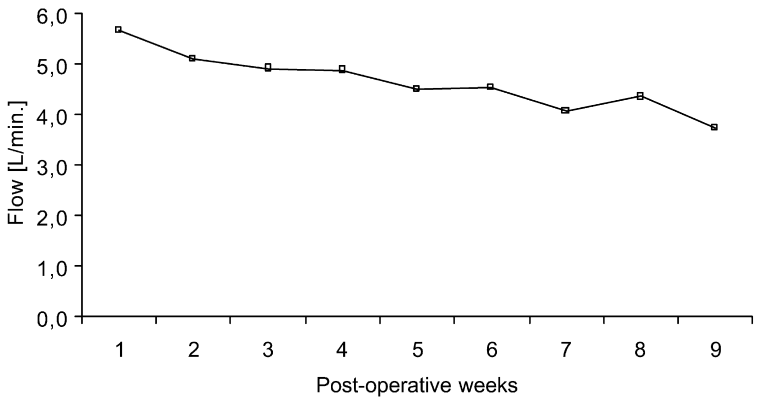

Fig. 4. Pump output ($n = 8$, mean values).

patients increase their exercise capacities and oxygen uptake [13]. Moreover the personal discipline necessary for the management of the LVAD can increase patient's medical compliance in the post-HTX phase [14].

Sustained outpatient treatment is straightforward with this device. The only settings which can vary on the MicroMed DeBakey LVAD are the rpm of the impeller pump, these can only be changed on the clinical data acquiring system (CDAS®) in our institution. It appeared that the rpm and subsequent flow provided by the LVAD could constantly be reduced with increased support duration. Fig. 4 shows the trend observed in eight survivors over 9 weeks, the constant decrease of rpm not only reflects underlying myocardial recuperation, but also the good tolerance of this continuous flow hemodynamic support.

This study shows promising results, as the device is reliable and poses no difficulties to implant and explant during HTx surgery. By achieving increased end organ perfusion, organ recuperation as a consequence contributes in creating a low-risk environment for HTx. Donor–recipient matches can be more precise, thanks to the comfort of hemodynamic stability of patients on LVAD support.

Following the analysis of our data, negative predictive factors regarding final outcome are: pre-implant ionotropic cardiovascular support, IABP and general clinical status. As always in surgical specialties, patient selection determines overall outcome. Most importantly in our opinion is timing of implantation.

The precise effect on the brain blood barrier and thrombocyte function of intravenous heparin, oral anticoagulation and continuous flow seem to be an important aspect of continuous flow LVAD support needing to be further assessed in the future as duration of support will increase.

References

[1] Nose Y. Tribute to Dr C. William Hall, founding director of U.S. Artificial Heart Program at NIH (1922–1992). Artif Organs 1993;17:71–2.

[2] Copeland JG, Emery RW, Levinson MM, Copeland J, McAleer MJ, Riley JE. The role of mechanical support and transplantation in treatment of patients with end-stage cardiomyopathy. Circulation 1985;72:II7–II12.

[3] Rose EA, Gelijns AC, Moskowitz AJ, Heitjan DF, Stevenson LW, Dembitsky W, Long JW, Ascheim DD, Tierney AR, Levitan RG, Watson JT, Meier P, Ronan NS, Shapiro PA, Lazar RM, Miller LW, Gupta L, Frazier OH, Desvigne-Nickens P, Oz MC, Poirier VL. Long-term mechanical left ventricular assistance for end-stage heart failure. N Engl J Med 2001;345:1435–43.

[4] Farrar DJ, Holman WR, McBride LR, Kormos RL, Icenogle TB, Hendry PJ, Moore CH, Loisance DY, El-Banayosy A, Frazier H. Long-term follow-up of thoratec ventricular assist device bridge-to-recovery patients successfully removed from support after recovery of ventricular function. J Heart Lung Transplant 2002;21:516–21.

[5] Noon GP, Morley D, Irwin S, Benkowski R. Development and clinical application of the MicroMed DeBakey VAD. Curr Opin Cardiol 2000;15:166–71.

[6] Noon GP, Morley D, Irwin S, Abdelsayed S, Benkowski R, Lynch BE. Turbine blood pumps. Adv Card Surg 2001;13:169–91.

[7] Noon GP, Morley DL, Irwin S, Abdelsayed SV, Benkowski RJ, Lynch BE. Clinical experience with the MicroMed DeBakey ventricular assist device. Ann Thorac Surg 2001;71:S133–8. [discussion p. S144–S146].

[8] Szefner J. Control of bleeding in total artificial heart implants. Philadelphia, PA: Hanley and Belfus, Inc; 2000.

[9] Farrar DJ, Hill JD. Univentricular and biventricular Thoratec VAD support as a bridge to transplantation. Ann Thorac Surg 1993;55:276–82.

[10] Wieselthaler GM, Schima H, Hiesmayr M, Pacher R, Laufer G, Noon GP, DeBakey M, Wolner E. First clinical experience with the DeBakey VAD continuous-axial-flow pump for bridge to transplantation. Circulation 2000;101:356–9.

[11] Piccione Jr W. Left ventricular assist device implantation: short and long-term surgical complications. J Heart Lung Transplant 2000;19:S89–S94.

[12] Kavarana MP-M, Urtecho J, Catanese K, Flannery M, Oz M, Naka Y. Right ventricular dysfunction and organ failure in LVAD recipients: a continuing problem. Ann Thorac Surg 2002;73:745–50.

[13] Demers C, McKelvie RS. Exercise training for patients with chronic heart failure reduced mortality and cardiac events and improved quality of life. West J Med 2000;172:28.

[14] Dew MA, Kormos RL, Winowich S, Harris RC, Stanford EA, Carozza L, Griffith BP. Quality of life outcomes after heart transplantation in individuals bridged to transplant with ventricular assist devices. J Heart Lung Transplant 2001;20:1199–212.