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HEMODYNAMIC AND PHYSIOLOGIC CHANGES DURING SUPPORT WITH AN IMPLANTABLE LEFT VENTRICULAR ASSIST DEVICE

From the Departments of Thoracic and Cardiovascular Surgery, Cardiology, Cardiothoracic Anesthesia, and Biostatistics and Epidemiology, Cleveland Clinic Foundation, Cleveland, Ohio.

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Address for reprints: Patrick M. McCarthy, MD, Department of Thoracic and Cardiovascular Surgery, Cleveland Clinic Foundation, 9500 Euclid Ave., F-25, Cleveland, OH 44195.

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To evaluate hemodynamic effectiveness and physiologic changes on the HeartMate 1000 IP left ventricular assist device (Thermo Cardiosystems, Inc., Woburn, Mass.), we studied 25 patients undergoing bridge to heart transplantation (35 to 63 years old, mean 50 years). All were receiving inotropic agents before left ventricular assist device implantation, 21 (84%) were supported with a balloon pump, and 7 (28%) were supported by extracorporeal membrane oxygenation. Six patients died, primarily of right ventricular dysfunction and multiple organ failure. Nineteen (76%) were rehabilitated, received a donor heart, and were discharged (100% survival after transplantation). Pretransplantation duration of support averaged 76 days (22 to 153 days). No thromboembolic events occurred in more than 1500 patient-days of support with only antiplatelet medications. Significant hemodynamic improvement was measured (before implantation to before explantation) in cardiac index (1.7 ± 0.3 to 3.1 ± 0.8 L/min per square meter; $p < 0.001$), left atrial pressure (23.7 ± 7 to 9 ± 7.5 mm Hg; $p < 0.001$), pulmonary artery pressure, pulmonary vascular resistance, and right ventricular volumes and ejection fraction. Both creatinine and blood urea nitrogen levels were significantly higher before implantation in patients who died while receiving support. Renal and liver function returned to normal before transplantation. We conclude that support with the HeartMate device improved hemodynamic and subsystem function before transplantation. Long-term support with the HeartMate device has a low risk of thromboemboli and makes a clinical trial of a portable HeartMate device a realistic alternative to medical therapy. (*J THORAC CARDIOVASC SURG* 1995;109:409-18)

Patrick M. McCarthy, MD (by invitation), Robert M. Savage, MD (by invitation), Charles D. Fraser, MD (by invitation), Rita Vargo, RN, MSN (by invitation), Karen B. James, MD (by invitation), Marlene Goormastic, MPH (by invitation), and Robert E. Hobbs, MD (by invitation), *Cleveland, Ohio*
Sponsored by Delos M. Cosgrove, MD, *Cleveland, Ohio*

The implantable left ventricular assist device (LVAD) is currently being used as a bridge to heart transplantation. However, a new clinical trial with the portable HeartMate LVAD (Thermo Cardiosystems, Inc., Woburn, Mass.) should begin soon. In this multicenter trial, the HeartMate LVAD will not be used for patients awaiting transplantation, but as an alternative to *medical* therapy for patients with end-stage heart disease who are not candidates for transplantation or other surgical therapy. This trial will be the first clinical use of mechanical circulatory support devices as permanent therapy since the very early use of the pneumatic Jarvik 7 total artificial heart (Symbion Inc., Salt Lake City, Utah).¹

To better understand the hemodynamic and physiologic changes seen during implantable LVAD support, we carefully studied Cleveland Clinic patients who underwent HeartMate 1000 IP pneumatic LVAD support as a bridge to heart transplantation. This article reports our experience and observations regarding hemodynamic and physiologic changes during LVAD support, changes observed in the left and right ventricles, and improvement in patient exercise capacity.

Patients and methods

Twenty-five consecutive patients received the pneumatically driven HeartMate LVAD according to a protocol. The devices were implanted between December 1991 and March 1994. The mean age of the patients was 50 years (range 35 to 63 years) and 21 were men (84%). Seven of the patients had dilated cardiomyopathy and 18 patients (72%) had ischemic cardiomyopathy. The group with ischemic cardiomyopathy included 10 patients who had acute myocardial infarction <7 days before LVAD implantation. Twenty-one patients met inclusion and exclusion guidelines for the experimental device according to the Food and Drug Administration (FDA) criteria.² Four patients were clear deviations from the FDA protocol because of recent myocardial infarction within 1 week of LVAD implantation without preexisting cardiomyopathy (acute myocardial infarction <7 days before LVAD insertion was a FDA exclusion criterion). All patients (or their family members) gave informed consent to LVAD insertion, and the trial was carried out with the approval of the Cleveland Clinic Institutional Review Board.

The HeartMate 1000 IP is a pneumatically driven pusher plate LVAD with pump inflow from the left ventricular apex and pump outflow to the ascending aorta. Descriptions of the device² and implantation techniques³ have been previously published. The device was implanted in a pocket in the left upper quadrant of the abdominal wall underneath the left rectus muscle and on top of the posterior rectus fascia in all patients except the first patient (intraabdominal implantation was used).³ All LVADs were placed in the automatic mode after the

patient was weaned from cardiopulmonary bypass, so that the pump automatically ejected when 90% full.⁴ Typically, the left ventricle is unloaded in this mode of operation and the patient's aortic valve does not open during ventricular systole.

All patients were in severe cardiogenic shock as part of the FDA inclusion criteria, and many were moribund. All patients were receiving inotropic support. Twenty-one patients (84%) were also receiving intraaortic balloon pump (IABP) support. An IABP was not placed because of tachycardia in one patient (heart rate 150 beats/min) and bacteremia during two previous IABP insertions in another patient. Twenty patients (80%) were intubated for pulmonary edema. Nine patients (36%) had undergone previous coronary artery bypass. Seven patients (28%) were in such severe acute cardiogenic shock that they had to be supported with a heparin-coated extracorporeal membrane oxygenator (ECMO) to stabilize their condition and allow evaluation and clearance as transplantation candidates (an important prerequisite before HeartMate LVAD insertion).

Multiple hemodynamic measurements were made: (1) in the operating room before LVAD insertion; (2) after LVAD insertion after weaning from cardiopulmonary bypass, (3) 24 hours after LVAD insertion, and (4) weeks later, just before LVAD explantation and heart transplantation. Left atrial pressure was measured directly before LVAD insertion and explantation and was monitored continuously with a percutaneous catheter for at least 24 hours after insertion. Transpulmonary gradient was measured (mean pulmonary artery pressure – mean left atrial pressure) and divided by cardiac output to determine pulmonary vascular resistance in Wood units. A special fast-response thermodilution pulmonary artery catheter (REF catheter, Baxter Healthcare Corp., Irvine, Calif.) was used to calculate right ventricular end-diastolic volume, right ventricular end-systolic volume, right ventricular stroke volume (end-diastolic volume – end-systolic volume), right ventricular stroke work index, and right ventricular ejection fraction. The right ventricular ejection fraction was correlated with the right ventricular “fractional area of change,” an equivalent measurement to right ventricular ejection fraction, by means of intraoperative echocardiographic techniques with automatic boundary detection via acoustic quantification.^{5,6} The REF catheter and echocardiographic studies provided two independent measurements of right ventricular function.

Hypoxemia and acidosis were assiduously avoided in the early postoperative phase because of their deleterious effects on the pulmonary resistance and subsequently right heart function. Patients' lungs were ventilated to maintain arterial oxygen tension greater than 100 mm Hg, carbon dioxide tension approximately 30 mm Hg, and lowest possible peak inspiratory pressures (typically high-rate, low tidal volume ventilation).

Laboratory values considered *baseline* were obtained within 24 hours of LVAD insertion. Laboratory values were repeated at least weekly while the patients were receiving LVAD support and within hours before LVAD explantation and heart transplantation. Treadmill exercise began shortly after the patients having an LVAD were transferred out of the intensive care unit. The recorded

treadmill distance underestimated the patient's activity level because patients also were ambulating throughout the hospital and grounds, and some minimally supervised additional treadmill exercise sessions were not recorded.

No heparin or warfarin was given for pump anticoagulation. Intraoperative heparin was reversed with protamine after the patient was weaned from cardiopulmonary bypass. Perioperative aprotinin was given to 20 patients. Dextran was not administered to any patients after the operation. One patient had a short course (<5 days) of intravenous heparin for deep vein thrombosis until a vena cava filter was placed. Only antiplatelet agents were given for pump anticoagulation, consisting of one aspirin per day (350 mg) and 75 mg of dipyridamole 3 times a day. Ten patients completed pump support without any anticoagulants (including antiplatelet agents) because of peptic ulcer disease or other clinical concerns.

Percent change from baseline was analyzed with either a paired *t* test or Wilcoxon signed rank test as appropriate. Significance levels of 0.05 or less were considered to be statistically significant. A Wilcoxon rank sum test was used to compare baseline values for patients who survived until transplantation versus patients who died before transplantation. All values are expressed as mean plus or minus standard deviation unless otherwise stated.

Results

Of the 25 patients, 19 (76%) underwent transplantation, including five of seven (71%) who required ECMO support before LVAD insertion and 17 of 21 (81%) of those who met all FDA inclusion/exclusion criteria. The mean duration of LVAD support was 63 days (range 0.2 to 153 days); it was 76 days (range 22 to 153 days) for those who underwent transplantation.

Six patients died during LVAD support (Table I), most of progressive multiple organ failure despite adequate LVAD flow. Autopsies were obtained in all patients. One patient who died had undergone urgent reoperative myocardial revascularization, complicated by cardiac arrest. The patient was supported by ECMO after this operation for 20 hours but with hypotension despite adequate flow. Urgent HeartMate LVAD insertion led to initially adequate flows but persistent hypotension. The patient died shortly after return to the intensive care unit, and autopsy confirmed what was by then our clinical suspicion, extensive cerebral hemorrhage. Two other patients had severe coagulopathy, eventually required a right ventricular assist device (RVAD) for high pulmonary vascular resistance, had multiple organ failure, and died. In one of these patients the RVAD was successfully removed, with good hemodynamics, but late *Candida* mediastinitis contributed to the patient's death. Three other patients had

Table I. Patient deaths during LVAD support

Patient	Age (yr)	Diagnosis	Duration (days)	PI	Comments
1	61	ICM	44	3.6	RVAD, <i>Candida</i> , MOF
2	53	ICM	3	2.1	RVAD, coagulopathy, MOF
3	35	ICM	70	2.5	RHF, <i>Candida</i> , MOF
4	48	ICM	13	3.1	RVAD-ECMO, MOF
5*	63	ICM	0.2	1.9	Intracerebral bleed
6*	46	AMI	12	2.0	MOF

PI, Pump index on support (L/min per square meter); ICM, ischemic cardiomyopathy; DCM, dilated cardiomyopathy; AMI, acute myocardial infarction; RVAD, right ventricular assist device; MOF, multiple organ failure; RHF, persistent right heart failure; ECMO, extracorporeal membrane oxygenation.

*Patients having pre-LVAD ECMO and FDA exclusions.

progressive multiple organ failure, one required RVAD support, and another had chronic right ventricular dysfunction such that the inotropic medications could not be stopped during 70 days of LVAD support. None of the patients who died ever left the intensive care unit or were able to be extubated.

In total, four patients (16%) required RVAD support. These four include two with heparin-coated RVAD-ECMO systems, returning oxygenated blood to the pulmonary artery in one patient and to the left atrium in the other. One patient, who was supported by ECMO before insertion of the LVAD, was hypoxic after being weaned from cardiopulmonary bypass with LVAD support, and this contributed to right heart failure. An RVAD-ECMO system was placed, and a bronchoscopic examination showed that she had aspiration of gastric contents (probably when intubated during a cardiac arrest the day before). She was treated with antibiotics, her lungs improved, and the RVAD-ECMO system was removed. The patient recovered and underwent successful transplantation after 143 days of support. The three other patients requiring an RVAD all died of multiple organ failure, although two RVADs were removed.

Hemodynamic changes with the initiation of LVAD pumping were seen immediately. The changes in this report are described from the left heart first, then pulmonary artery pressures, and then right heart changes.

The cardiac index before LVAD insertion was low (1.67 ± 0.3 L/min per square meter) and the left atrial pressure was high (Table II, Fig. 1). A significant rapid increase in cardiac index ("pump" index from the device⁴) and an immediate decrease in left atrial pressure were seen in the operating room after

Fig. 1. The cardiac index (CI) before LVAD insertion (*pre-implant*) was low (1.7 ± 0.3 L/min per square meter) in these patients with cardiogenic shock. In the operating room during LVAD support (*post-implant*), the cardiac index rose to 3.1 L/min per square meter and stayed at approximately this level at 24 hours and for the duration of support until the time of device explantation and transplantation (*pre-explant*). The left atrial pressure (LAP) dropped from 23 mm Hg to 10 mm Hg with the initiation of LVAD pumping and stayed low at 24 hours and pre-explant. Right atrial pressure (RAP) dropped gradually from a mean of 20 mm Hg down to 12 mm Hg before device explantation and transplantation.

Table II. Hemodynamic changes during LVAD support

	Pre-LVAD	Post-LVAD	p Value pre-LVAD vs post-LVAD	24 hr	Pre-explant	p Value pre-LVAD vs pre-explant
CI	1.7 ± 0.3 (1.7)	3.1 ± 1.0 (3.1)	$p < 0.0001$	3.1 ± 0.6 (3.0)	3.1 ± 0.8 (2.8)	$p < 0.0001$
LA	23.1 ± 7.1 (22)	10.4 ± 4.7 (11)	$p < 0.001$	13.0 ± 4.5 (13)	9.0 ± 7.5 (8)	$p < 0.001$
PA sys	52.5 ± 13.9 (50)	40.0 ± 12.1 (37)	$p = 0.003$	36.2 ± 10.4 (35)	30.2 ± 9.4 (28)	$p < 0.0001$
PA mean	38.5 ± 7.9 (38)	28.7 ± 7.7 (28)	$p < 0.0001$	28.9 ± 9.5 (27)	21.6 ± 7.7 (20)	$p < 0.0001$
PA _D	30.2 ± 8.2 (29.5)	21.2 ± 7.2 (21)	$p < 0.0001$	22.5 ± 9.3 (21)	15.0 ± 6.7 (14)	$p < 0.0001$
TPG	14.5 ± 7.6 (14)	18.3 ± 8 (17)	$p = 0.05$	15.3 ± 8.6 (14)	11.7 ± 5.1 (10)	$p = 0.30$
PVR	4.4 ± 2.7 (3.8)	3.5 ± 2.2 (2.9)	$p = 0.16$	3.0 ± 2.5 (2.6)	2.2 ± 1.1 (1.8)	$p = 0.001$
RVEF	16.5 ± 9.3 (16.5)	31.6 ± 9.4 (33)	$p < 0.0001$	29.2 ± 10.3 (27.5)	38.1 ± 14.5 (41)	$p < 0.0001$
RVAQ	21.6 ± 9.6 (20.4)	35.4 ± 11.6 (34)	$p < 0.0001$	NA	43.5 ± 9.7 (44)	$p < 0.0001$
RVEDV	302 ± 178 (226)	221 ± 78 (202)	$p = 0.06$	243 ± 103 (211)	174 ± 74 (151)	$p = 0.002$
RVESV	266 ± 178 (189)	142 ± 77 (135)	$p = 0.002$	184 ± 98 (152)	110 ± 65 (87)	$p = 0.001$
RVSWI	4.7 ± 2.4 (4.3)	5.3 ± 3.5 (5.6)	$p = 0.93$	4.4 ± 2.6 (3.9)	4.2 ± 3.1 (3.5)	$p = 0.19$
RA	20.1 ± 6.4 (21)	16.9 ± 6.4 (17)	$p = 0.07$	15.3 ± 3.8 (15)	12.3 ± 6.2 (12)	$p < 0.0001$

All values are expressed as mean $\pm$ standard deviation (median). CI, cardiac index (or pump index on LVAD) (L/min per square meter); LA, left atrial pressure (mm Hg); PA sys, pulmonary artery systolic pressure (mm Hg); PA_D, PA diastolic pressure (mm Hg); TPG, transpulmonary gradient (mm Hg); PVR, pulmonary vascular resistance (Wood units); RVEF, right ventricular ejection fraction (%); RVAQ, right ventricular acoustic quantification area of change (%); RVEDV/RVESV, right ventricular end-diastolic/end-systolic volumes (ml); RVSWI, right ventricular stroke work index (5-10 gm/m² per beat); RA, right atrial pressure (mm Hg); NA, not available.

the start of LVAD flow. The cardiac index and left atrial pressure remained virtually normal at 24 hours and when measured before explantation.

The pulmonary artery pressures were elevated before LVAD insertion, consistent with severe heart failure. The pulmonary artery pressures rapidly decreased (Fig. 2) with LVAD pumping and the decrease in left atrial pressure. For example, the pulmonary artery diastolic pressure decreased from 30.2 ± 8.2 mm Hg before LVAD insertion to 21.2 ± 7.2 mm Hg after LVAD insertion, 22.5 ± 9.3 mm

Hg at 24 hours, and 15.0 ± 6.7 mm Hg at LVAD explantation. The transpulmonary gradient showed an interesting transient increase that has been inferred⁷ but not documented. The transpulmonary gradient increased ($p = 0.046$) after LVAD insertion (Fig. 3), most likely because of a combination of the effects of cardiopulmonary bypass and blood product administration on the pulmonary bed and a delay as the lungs clear the pulmonary edema present before LVAD insertion. By 24 hours the transpulmonary gradient had returned to baseline

and was lower, but not significantly so ($p = 0.29$), at explantation.

Pulmonary vascular resistance was elevated before LVAD insertion (4.4 ± 2.7 Wood units) and decreased with LVAD pumping (Table II), despite the early increase in transpulmonary gradient, because of a much higher cardiac output. Pulmonary vascular resistance gradually decreased (3.5 ± 2.2 Wood units after LVAD insertion, 3.0 ± 2.5 Wood units at 24 hours) and reached a typical level for heart transplant recipients (2.2 ± 1.1 Wood units) at the time of LVAD explantation.

Changes in the right side of the heart mirrored the changes in pulmonary artery pressures and pulmonary vascular resistance, further supporting the conclusion of most investigators that right heart function during LVAD support is primarily determined by right ventricular afterload.⁷⁻⁹ The right ventricle was markedly dilated in most patients and decreased in volume (both end-systolic and end-diastolic volume) during LVAD pumping (Fig. 4). The right ventricular ejection fraction also steadily increased (see Table II) and correlated well with right ventricular acoustic quantification (obtained independently by transesophageal echocardiography during the operation and at LVAD explantation). Studies are ongoing with right ventricular Millar catheters (Millar Instruments, Inc., Houston, Tex.) to determine right ventricular pressure-volume loops. However, our only other measure of right ventricular contractility, right ventricular stroke work index, showed no intrinsic change in right ventricular function. Right ventricular stroke work index was low and stayed low (Table II) in the early period and before explantation (all $p > 0.05$). Finally, right atrial pressure, which was elevated at baseline (20.1 ± 6.4 mm Hg), gradually decreased (see Fig. 1) to near normal before LVAD explantation (12.3 ± 6.2 mm Hg).

We could not identify any preoperative factors in the four patients who required RVAD support that would indicate that they were at particularly high risk to need RVAD support. Pre-LVAD transpulmonary gradients were 17, 8, 7, and 16 mm Hg for these four patients. The pulmonary vascular resistances were 3.5, 3.6, 7.0, and 5.2 Wood units, and right ventricular ejection fractions were 17%, 9%, and 18% (one not available).

Because most deaths eventually were related to multiple organ failure, we analyzed renal and hepatic function at baseline and during support. Liver dysfunction was common before LVAD insertion,

Fig. 2. Pulmonary artery (PA) pressures were elevated in these patients with severe congestive heart failure. The pressures dropped immediately after the start of LVAD pumping and showed a further decrease by the time of device explantation.

with a mean total bilirubin value of 2.9 ± 2.8 mg/dl, most likely related to liver hypoperfusion, and elevated right atrial pressure (20.1 ± 6.4 mm Hg). At baseline, no difference was apparent between patients who survived and those who died during LVAD support (Fig. 5). During support, however, the bilirubin value returned to normal in survivors and rose in those who had hepatorenal dysfunction and died. Also, the aspartate aminotransferase level was elevated at baseline (in part because of recent myocardial infarction in some patients) and returned to normal in survivors (Fig. 5).

Renal dysfunction was also common before and after LVAD insertion. A statistically significant difference ($p = 0.01$) was noted at baseline in blood urea nitrogen values between survivors and those who died (Fig. 6). Also, serum creatinine concentration was significantly higher ($p = 0.02$) in the patients who died (Fig. 6). Three patients who survived became anuric in the early post-LVAD period and were treated with hemodialysis. Urine output returned from 3 to 6 weeks after LVAD insertion and the patients were withdrawn from dialysis. Mild elevations in blood urea nitrogen and creatinine values after dialysis was stopped in these patients are reflected in the late increases seen in Fig. 6. All three patients continued with stable renal function, without dialysis, after heart transplantation. Although a significant difference in blood urea nitrogen and creatinine levels at baseline was noted between survivors and nonsurvivors, the difference was not specific. Three patients survived who had a blood urea nitrogen value greater than 50 mg/dl, similar to the nonsurvivor group.

Fig. 3. The transpulmonary gradient (mean PA pressure minus mean LA pressure) rose after insertion of the device ($p = 0.046$). This was thought to be due to the effects of cardiopulmonary bypass and blood product administration. The transpulmonary gradient gradually decreased after this as the patient recovered from the operation (24 hours) and was not significantly different from baseline at the time of device explantation. TPG, Transpulmonary gradient; PA, pulmonary artery; LA, left atrium; N.S., Not significant.

Fig. 4. The right heart was markedly dilated in these patients, decreased with the initiation of LVAD support, and decreased further by the time of device explantation. Changes were seen in both the right ventricular end-diastolic volume (RVEDV) and end-systolic volume (RVESV), and the difference between the two represents right ventricular stroke volume.

Along with hemodynamic and physiologic improvements, all patients were actively motivated to regain muscle strength and physical conditioning. All patients were in New York Heart Association functional class I or II before transplantation. Patients were temporarily inactivated on the transplant waiting list until they were out of the intensive care unit, physically active, and had regained near normal renal and hepatic function. Daily exercise on a

treadmill was recorded and reflects the steadily improving condition of these patients (Fig. 7).

No thromboembolic events occurred in these patients despite a conservative anticoagulation regimen consisting of (at most) antiplatelet agents. The total number of patient-days of LVAD support was 1583 days. No device failures occurred. Among the 76% of patients undergoing transplantation overall, there was 100% survival after transplantation, and

Fig. 5. Measures of liver function such as total bilirubin and aspartate aminotransferase (AST) levels were elevated at baseline. Both bilirubin and aspartate aminotransferase returned to normal levels in patients who were survivors and were underwent transplantation. There was an increase, especially notable in the total bilirubin levels, in patients who died. There was no significant difference at baseline between patients who were survivors and those who were nonsurvivors.

Fig. 6. Measures of renal function, blood urea nitrogen (BUN) and serum creatinine (Scr), were generally elevated before device insertion. The levels for the patients who died were significantly higher for both blood urea nitrogen ($p = 0.01$) and serum creatinine ($p = 0.02$). For patients who survived and underwent transplantation, blood urea nitrogen and creatinine generally returned to normal. Inasmuch as three survivors were removed from long-term dialysis with the recovery of renal function, a slight increase in blood urea nitrogen and serum creatinine were seen late.

all patients are in New York Heart Association functional class I.

Discussion

Developments in mechanical circulatory support over the past decade bode well for the future application of such devices for patients with end-stage heart disease. Univentricular support with an LVAD was shown to be feasible for most patients awaiting heart transplantation,^{7,8} with generally better results than those obtained with a total artificial heart.^{4,10} Occasional patients supported with an implantable LVAD, however, need at least temporary right ventricular mechanical support (16% in our series), and we have been unable preoperatively to predict which patients are at risk for early right heart failure.^{2,4,8} Preoperative measurements of right ventricular contractility and afterload are not good predictors because of poor specificity. Only

one of our five patients with a right ventricular ejection fraction less than 10% (range 3% to 9%) and one of our five patients with a pre-LVAD pulmonary vascular resistance greater than 7 Wood units (range 7 to 10 Wood units) required an RVAD.

Although most investigators agree that increased right ventricular afterload is the most important determinant of right heart failure, many other factors also contribute. The Fontan operation physiology was observed in several patients during periods of ventricular tachycardia. With loss of right ventricular contractility, LVAD flow decreased to 3.5 to 4.0 L/min. This is the same flow obtained by our patient with chronic right heart failure during attempts to wean the patient from the inotropic drugs supporting right ventricular contractility. Therefore, right ventricular afterload and contractility are important to obtain optimal LVAD flow and patient rehabili-

Fig. 7. Treadmill distance during daily exercise indicated the steadily improving physical condition of patients receiving long-term support. Shortly after patients left the intensive care unit, levels of activity were low, but they steadily increased as the patients returned to better physical condition before transplantation.

tation. Until we develop consistent criteria to preoperatively predict post-LVAD need for right ventricular mechanical support, we will continue to apply just LVAD support despite apparently high pulmonary vascular resistance and low right ventricular contractility.

Preoperative blood urea nitrogen and creatinine levels were significantly higher in the nonsurvivor group by univariate analysis (the number of deaths was too small for multivariate analysis). Preoperative blood urea nitrogen elevation (but not creatinine) was also identified by the Thoratec investigators as a risk factor for death.¹¹ The FDA criteria for insertion of a HeartMate device allow use of the device if the blood urea nitrogen level is 100 mg/dl or less. We agree with others^{11,12} that rising blood urea nitrogen levels should be considered a relative contraindication to LVAD insertion. However, such elevations are not a certain predictor of failure, inasmuch as three of our 19 survivors had a blood urea nitrogen level of 50 mg/dl or more before LVAD insertion. Therefore, we do not hesitate to proceed if blood urea nitrogen elevation is the only contraindication to LVAD insertion. Also, to help preserve renal and other organ function in patients with acute profound heart failure, we have used a heparin-coated ECMO system while transplantation evaluation is started. Although survival with ECMO as a "bridge-to-bridge" has been satisfactory (71%), the patients are a high-risk group. Two of the five survivors of ECMO to LVAD to transplantation were anuric while receiving temporary hemodialysis.

Multiple organ failure, specifically the combination of renal and hepatic failure, has been the contributing cause of death for most of our patients. We do not yet have enough patient numbers to be able to predict which patients will have this frustrating complication, despite adequate LVAD flow. Perhaps more aggressive use of perioperative dialysis, ECMO, and even temporary extracorporeal hepatic support¹³ will allow us to save more of these patients.

The ultimate goal of the implantable LVAD program, however, is not to salvage moribund patients. The hemodynamic and physiologic findings in this report and others^{2,9,14,15} suggest that most stable patients with New York Heart Association class IV heart failure who receive these devices should have marked symptomatic improvement. With a remarkably low risk of thromboemboli (none in more than 4 patient-years of experience in this series), many of the previous impediments to chronic circulatory support have been addressed. Our studies already indicate that *hospitalized* patients with the HeartMate LVAD experience a quality of life similar to that of patients who have had heart transplantation.¹⁶ The portable vented electric HeartMate device designed by Poirier, and first used by Frazier,¹⁷ should further improve quality of life and allow patients to be discharged. As we embark on a new phase of outpatient mechanical support instead of heart transplantation, new issues, such as device durability, failure modes, and the risk of chronic device infection, will assume more importance. More extensive clinical studies with the portable outpatient LVAD is a necessary next step to address these issues and unmask other problems that cannot be identified with the bridge to transplantation experience. The hemodynamic and physiologic effectiveness of the implantable LVAD has been established in the bridge to heart transplantation experience.

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Discussion

Dr. Walter P. Dembitsky (*San Diego, Calif.*). We are interested in the exercise capacity of patients in whom the HeartMate LVAD was implanted. We thought that right ventricular function was the function defining the upper limit. Thus, using Swan-Ganz catheters (Baxter Healthcare Corp., Edwards Division, Santa Ana, Calif) and

echocardiograms, we studied (and reported on) four patients with implanted LVADs, encouraging them to exercise to anaerobic thresholds. We found that left ventricular performance actually determined exercise capacity. At high levels of exercise the recovered left ventricle began to eject in parallel with the pump. It contributed significantly to the cardiac output. We also measured oxygen consumptions in the range of 15 to 20 ml/min.

Have you noticed the degree of ventricular recovery on the left side with these implanted LVADs? Have you measured oxygen consumptions during exercise?

Dr. McCarthy. We studied left ventricular fractional shortening, which was only 7% at the time of LVAD implantation. It did not rise significantly, being only 10% and 11% after LVAD insertion and at LVAD explantation. We have noticed individual patients who appear to have more significant recovery. In general, however, we do not think that there will be significant recovery in most patients with ischemic cardiomyopathy.

I did not present the limited data that we have on oxygen consumption because the measurements were made early after the patients received the devices. We have measured maximum oxygen consumption in the range of 15 ml/min. However, I am aware of data from the Texas Heart Institute showing that patients undergoing a longer duration of support have a further increase in oxygen consumption; one patient in The Netherlands reached an oxygen consumption of more than 30 ml/min during support. One advantage of the LVAD over the total artificial heart is that the patients with an LVAD will be able to have some contribution to total cardiac output from the native heart, and therefore a higher oxygen consumption.

Dr. Nelson A. Burton (*Annandale, Va.*). We have had a similar experience at Fairfax Hospital over the past 4 years having implanted the TCI HeartMate LVAD in 15 heart transplant candidates who were moribund and near death. Fourteen of these patients received the pneumatic device and one the portable electric LVAD. Three patients were only 14 years of age. We have previously presented our hemodynamic data, which is nearly identical to yours, and have been very impressed with the hemodynamic capability of the HeartMate LVAD. We have also been impressed with the fact that no thromboembolic events have occurred in more than 1000 patient-days of support, an average of more than 60 days of support per patient, maintained on minimal anticoagulation. One patient who received the nonthethered electric device was supported for nearly 6 months. Twelve of the 15 had successful transplantation and all 12 are alive 3 months to 4 years after cardiac transplantation.

For anticoagulation with the electric device, we used warfarin sodium (Coumadin) instead of low-dose aspirin, which we use for pneumatic devices. Given the report at this meeting by Dr. Clark about microscopic emboli detected by transcranial Doppler studies during cardiopulmonary bypass, as well as a report from the group at Columbia showing increased transcranial Doppler signals in patients while supported by the TCI LVAD, should we use additional anticoagulation for long-term LVAD support? Should we consider using low-dose warfarin or some additional anticoagulation for patients in whom this de-

vice may be implanted for a period of years rather than months?

Dr. McCarthy. The only patient to whom I administered warfarin sodium was a patient with a large left ventricular aneurysm filled with thrombus who received a vented electric HeartMate LVAD last month. He had no emboli before successful transplantation after 30 days of support. The source of emboli is not just from within the device, but also from within the patient's own

heart, the aorta, or from prosthetic valves. In terms of the HeartMate device, whether it is used for short-term or long-term support, I do not think that the patients need to be given warfarin. Today, we give the patients only one aspirin a day. I think that it may be reasonable to administer warfarin to the unusual patient who is at risk for clot formation within the native heart, such as the patient with an aneurysm or a very large, dilated heart.

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