CARDIOPULMONARY SUPPORT AND PHYSIOLOGY

ONE HUNDRED PATIENTS WITH THE HEARTMATE LEFT VENTRICULAR ASSIST DEVICE: EVOLVING CONCEPTS AND TECHNOLOGY

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Background: Implantable left ventricular assist devices are common as a bridge to transplantation but are just reaching their goal as an alternative to transplantation. **Methods:** From December 1991 until December 1996, 97 left ventricular assist devices were implanted as a bridge to transplantation, one as an alternative to transplantation, and two as a bridge to recovery. Included were 64 pneumatic devices and 36 electric devices. Most patients (69%) had ischemic cardiomyopathy and most (53%) had had previous cardiac surgery. Preoperative circulatory support (extracorporeal membrane oxygenation) was used in 25. **Results:** Perioperative insertion of a right ventricular assist device was unusual (11%). The mean duration of support with a left ventricular assist device (bridge to transplantation) was 70 ± 41 days (up to 206 days). Survival to transplantation was 76%. Cause of death included multiple organ failure ($n = 13$), perioperative stroke ($n = 5$), device failure ($n = 5$), and controller disconnect ($n = 1$). Significant risk factors for death included (1) preoperative need for ventilator or extracorporeal membrane oxygenation, (2) elevated blood urea nitrogen, creatinine, or bilirubin, and (3) low pulmonary artery pressures. Risks after insertion of the left ventricular assist device were reoperation for bleeding, support with a right ventricular assist device, dialysis, or device failure. Catastrophic failure of the device occurred 14 times in 12 patients and was treated by emergency pump exchange in six instances. Only two device-related thromboembolic episodes were detected. Positive blood cultures were found in 59% of patients, driveline infection in 28%, and pump infection in 11%. **Conclusions:** The HeartMate device provided excellent hemodynamic support with low device-related thromboembolic events. Infection and reliability of the device contributed to the high cost of therapy. These areas need to be improved for the left ventricular assist device to attain its goal as a viable alternative to transplantation. (J Thorac Cardiovasc Surg 1998;115:904-12)

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Read at the Twenty-third Annual Meeting of The Western Thoracic Surgical Association, Napa, Calif., June 25-28, 1997.

Received for publication August 25, 1997; revisions requested Oct. 10, 1997; revisions received Dec. 1, 1997; accepted for publication Dec. 5, 1997.

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0022-5223/98 \$5.00 + 0 12/688016

Mechanical circulatory support technology has undergone a rapidly accelerating pace of maturation. In the 1970s the use of external left ventricular assist devices (LVADs) for postcardiotomy support were remarkable for the occasional survivor. In the 1980s permanent implants of the total artificial heart were introduced, only to be abandoned in favor of temporary support as a bridge to transplantation. The 1990s have seen a much faster rate of clinical and technologic development, with the introduction of portable battery-powered LVADs for bridge to transplantation, permanent LVADs as an alternative to transplantation or medical therapy, or long-term LVAD support until

Fig. 1. A, Patients supported by the pneumatic HeartMate LVAD were inpatients while awaiting transplantation but were ambulating and exercising. **B,** Patients supported by the vented-electric HeartMate LVAD could be discharged and resumed near-normal activities. This patient remodeled a garage during LVAD support. Note the portable batteries powering the LVAD on his waist.

sufficient cardiac recovery has occurred to allow LVAD weaning and removal (bridge to recovery).¹⁻⁴

Our experience with the HeartMate LVAD (Thermo Cardiosystems, Inc., Woburn, Mass.) began in December 1991 with the pneumatic system used for inpatient bridge to transplantation. By 1996 all Cleveland Clinic implants had been converted to the portable electric LVAD system for use as outpatient bridge to transplantation, as a bridge to recovery, or for permanent implantation as part of the REMATCH protocol (*Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure*).^{5,6} The purpose of this report is twofold: to review the rapid changes in technology and concepts and, more important, to objectively analyze the results in light of use of the LVAD for extended support as a bridge to recovery or permanent implant.

Patients and methods

The mean age of the patients was 53 ± 9 years (range 27 to 70 years), and 86% were male. Ischemic cardiomyopathy predominated (70%), and only 25% had idiopathic

dilated cardiomyopathy. Most patients (53%) had had previous cardiac surgery. Although we endorse the concept of early implantation of LVADs before the onset of irreversible other organ failure, in reality this was rarely possible. This may reflect a large number of outside referrals or admissions with near moribund heart failure. Circulatory support consisting of intraaortic balloon pumps (IABPs) was present before the operation in 84%, heparin-coated extracorporeal membrane oxygenation (ECMO) in 25%, and one patient was transferred while being supported with the Abiomed biventricular assist device (Abiomed, Inc., Danvers, Mass.). Sixty-two patients were supported with ventilators because of pulmonary edema or recent cardiac arrest. The mean cardiac index was 1.64 ± 0.30 L/min per square meter, with a left atrial pressure of 25 ± 7 mm Hg, pulmonary artery diastolic pressure of 29 ± 9 mm Hg, right atrial pressure of 20 ± 7 mm Hg, and pulmonary vascular resistance of 4.4 ± 2.6 Wood units. Preoperative information used to create a screening scale as reported by Oz and associates⁷ (and including 23 of our earliest patients) was collected and analyzed.

All operations were performed on cardiopulmonary bypass with the use of antegrade and retrograde cold blood cardioplegia. The inflow cannula was inserted into the left ventricular apex and secured with interrupted pledget-supported sutures. The outflow graft was anasto-

Table 1. *Thirty variables analyzed for risk factors for death while on LVAD support*

Preimplantation risk factors
Age
Sex
Diagnosis
Body surface area
Era (first 50 vs second 50 implants)
Ventilator
ECMO
IABP
Cardiac index
Pulmonary artery pressures (systolic/mean/diastolic)
Transpulmonary gradient
Pulmonary vascular resistance
Left atrial pressure
Right atrial pressure
Right ventricular ejection fraction
Total bilirubin
Creatinine
Blood urea nitrogen
Aspartate aminotransferase
Hematocrit
Operative and postoperative risk factors
Type of device (pneumatic vs electric)
RVAD
Reoperation for bleeding
Dialysis
Device infection
Device failure
Duration of support

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mposed to the right side of the aorta at an oblique angle that directed the graft under the right side of the sternum. This was also performed during the single crossclamp period. Care was taken to preserve patent coronary artery bypass grafts. The LVAD was placed in the abdomen in our first patient but preferentially in the abdominal wall pocket in successive patients, as described.⁸ More recently, we modified that technique so that the pump was placed under the posterior rectus sheath (and just above the peritoneum) to minimize contact of the pump with the raw surface of the posterior part of the rectus muscle and thereby decrease bleeding from the muscle. In additional efforts to decrease perioperative bleeding, aprotinin was administered to the last 93 consecutive patients, 2 units of fresh frozen plasma was used to prime the cardiopulmonary bypass circuit, and vitamin K was given before the operation and for 3 days after the operation because an earlier study documented that before LVAD insertion patients have reduced levels of vitamin K-dependent coagulation factors.⁹ A hemoconcentrator was used during cardiopulmonary bypass to reduce fluid overload.

Our surgical techniques frequently had to be adapted to the disease that we encountered and to the previous cardiac operation. For patients with implantable cardioverter-defibrillator (ICD) patches and leads outside the heart, we removed the foreign materials and ICD generator. For three patients with transvenous ICD systems, we left the ICD and placed the LVAD pump within the

abdomen so that the LVAD pump and ICD generator would not both be in the abdominal wall.

For patients with previous mechanical aortic ($n = 3$) or mitral ($n = 2$) valve prostheses, the valve was rereplaced with a tissue valve. The logic was that the tissue valve was less likely to cause thrombosis. Left ventricular aneurysms ($n = 4$) were partially decalcified, excised, and thrombus was carefully removed. The large ventriculectomy was plicated around the inflow cannula with multiple interrupted sutures. Patients with any angina underwent coronary artery bypass to nonoccluded vessels with greater than 50% stenosis, especially if the right coronary artery was involved.

Ideally, the transplant operation began 2 hours before anticipated return of the donor heart. Initially, we exposed a femoral artery before sternotomy because the dense adhesions encountered (many patients were undergoing their third cardiac operation or more) made reentry dangerous. We rarely do this now (the femoral incision heals poorly after transplant operations); instead we expose the outflow graft in the pocket for emergency cannulation before resternotomy. Because the outflow graft was placed under the right side of the sternum, it was never entered during resternotomy.

After LVAD implantation, patients were given inotropic agents as needed for right ventricular function. Nitric oxide was never used because it was not available in our institution. Alprostadil (prostaglandin E_1) was given occasionally early in our experience but was abandoned because of limited effectiveness on pulmonary pressures and the side effect of decreased systemic blood pressure. Amrinone became routine for patients with right ventricular dysfunction. Also, we adjusted LVAD flow down to approximately 4 L to decrease blood return (and workload) to the right side of the heart. Care was taken to avoid overdistention of the right ventricle (excessive volume transfusion) and to avoid hypoxemia and acidosis. Pressure-controlled ventilation was standard.

Only aspirin (325 mg/day) was used for LVAD anticoagulation. In patients with gastritis or other bleeding disorders, aspirin was withheld or stopped. Vancomycin was given during the operation, and other antibiotics were given as directed by the infectious disease consulting service.

Evolution of HeartMate LVAD. The HeartMate LVAD has been described extensively in previous reports.^{1, 6} In brief, pump inflow was from a cannula inserted into the left ventricular apex, the pump was in the patient's left upper quadrant (in the abdominal wall, or intraperitoneal), and pump outflow returned blood to the ascending aorta approximately 3 cm distal to the aortic valve. Blood-contacting surfaces are textured to promote the formation of a pseudo-neointima, which contributes to the low device-related thromboembolic event rates with this device.¹⁰

Our initial experience (64 patients) was with the pneumatic air-driven system (1000 IP). Patients were tethered to the portable air-driven console but were mobile and could wander through the hospital and the hospital grounds and exercise on a treadmill (Fig. 1, A). Logistics of transporting the console, however, required that the patient be maintained in the hospital until transplanta-

tion. A newer, smaller, portable driver for the pneumatic system exists, but we have very limited clinical experience with this system.

In 1993 we began to use the vented-electric HeartMate LVAD, which contained the same blood-contacting surfaces and connections to the heart but was actuated differently and was powered by portable batteries. The initial vented-electric implants had a "two-lead" system with separate percutaneous lines for power and external venting. After further experience this became a "single-lead" system with a single percutaneous driveline that contained both the power cable and vent. Eventually the single-lead system was moved so that it arose from the left side of the pump, which allowed the surgeon to make a long subcutaneous tunnel with the driveline, which could exit from the patient's right flank, and frequently leave 10 inches or greater of driveline within the subcutaneous tissue. The hope is that the long tunnel will help resist pocket infections. There have been many continuous ongoing refinements of both the pneumatic and electric systems to facilitate implantation and patient care and to respond to device failures.

In 1995 we made the transition from pneumatic (1000 IP) implants to exclusively vented-electric implants. In our opinion, the goal of permanent implants, or prolonged implants allowing for bridge to recovery, will best be accomplished using the portable electric systems. Through a graduated series of steps, the Food and Drug Administration (FDA) now allows patients supported by the vented-electric device to be discharged before transplantation (Fig. 1, B). The net effect of all of these evolutions in device design was that we progressed from inpatient bridge to transplantation with air-driven systems to outpatient support with portable, battery-powered devices for a variety of destinations other than just bridge to transplantation.

Statistical analysis. Results are reported as percentages or means $\pm$ standard deviation as appropriate. Univariately, a χ^2 test or Fisher's exact test was used to compare the incidence of death in various groups. A Wilcoxon rank sum test was used to compare the value of continuous factors by death. The factors that were at least marginally significant ($p < 0.20$) by univariate analysis were included in a stepwise multivariable logistic regression model. The first model tested all these factors after adjusting for the duration of support (forcing and keeping duration of support in the model). The second model included only the variables known at the time of implantation (still adjusting for duration of support).

Results

Seventy-four of the 97 patients undergoing bridge to transplantation (76%) survived until transplantation. Mean length of support was 70 ± 41 days (up to 206 days). Thirty preoperative or perioperative variables were studied (Table I) to determine risk factors for death. As expected, the duration of support was less for the patients who died before transplantation (35 vs 81 days; $p < 0.001$). Many patients died early of progressive multiple organ

Table II. Significant or borderline univariate risk factors for death

Risk factor	Risk	p Value
Preoperative		
Ventilator use (% deaths)	33% versus 8%	$p = 0.006$
ECMO use (% deaths)	48% versus 16%	$p = 0.003$
Total bilirubin (mg/dl) (median)	2.20 versus 1.4	$p = 0.01$
Blood urea nitrogen (mg/dl) (median)	46.0 versus 28.0	$p = 0.03$
Creatinine (mg/dl) (median)	1.8 versus 1.4	$p = 0.04$
Pulmonary artery pressure, mean (mm Hg) (median)	31.5 versus 38.0	$p = 0.04$
Pulmonary artery pressure, systolic (mm Hg) (median)	41.5 versus 50.0	$p = 0.06$
Pulmonary artery pressure, diastolic (mm Hg) (median)	24.5 versus 29.0	$p = 0.08$
Operative and postoperative		
RVAD use (% deaths)	73% versus 18%	$p = 0.0004$
Need for dialysis (% deaths)	63% versus 14%	$p = 0.0004$
Device failure (% deaths)	50% versus 20%	$p = 0.03$
Duration of support (days) (median)	15 versus 78	$p = 0.0001$

failure. Univariate risk factors for death before transplantation (Table II) included preoperative ECMO, ventilator requirement, low pulmonary artery pressures, and elevation of bilirubin (4.5 vs 2.6 mg/dl), blood urea nitrogen (49 vs 34 mg/dl), and creatinine (2.0 vs 1.5 mg/dl) concentrations. Postoperative risks included need for support with a right ventricular assist device (RVAD), reoperation for bleeding, dialysis, and device failure. Important univariate factors that were not found to be risk factors for death included device type, diagnosis, era (first 50 implants vs second 50 implants), need for preoperative IABP, infection while on LVAD support, age, cardiac index, transpulmonary gradient, pulmonary vascular resistance, right ventricular ejection fraction, and right atrial pressure. By multivariable logistic regression (Table III), after adjusting for duration of support, risk factors for death included postoperative dialysis ($p = 0.02$, odds ratio 8.1), device failure ($p = 0.0006$, odds ratio 29.1), and requirement for an RVAD ($p = 0.09$, odds ratio 6.2). When we analyzed only the variables that were known before implantation, preoperative ECMO ($p = 0.08$, odds ratio 3.6) and creatinine ($p = 0.05$, odds ratio 2.4) were at least marginally significant.

We then analyzed our patients according to the

Table III. Results of multivariable logistic regression

Factor	Odds ratio	95% CI	p Value
<i>Considering preoperative and postoperative factors (adjusted for duration of support)</i>			
Postop. dialysis	8.1	1.3-50	0.02
Device failure	29.1	4.2-200	0.0006
Creatinine	2.7	0.95-2.0	0.06
RVAD requirement	6.2	0.75-50.6	0.09
<i>Considering only baseline factors (adjusted for duration of support)</i>			
ECMO	3.6	0.85-14.8	0.08
Creatinine	2.4	0.98-5.65	0.05

CI, Confidence interval.

screening scale created to identify patients at high risk for death before discharge from the intensive care unit (ICU) after HeartMate LVAD implantation.⁷ Failure in this article was defined as death after LVAD implantation but before discharge from the ICU, and the series included our initial 23 patients. This definition of failure applied in 16 of our 97 patients (16.5%). In our 97 patients mechanical ventilation was a risk factor for failure (22% vs 5.6%; $p = 0.03$), urine output less than 30 ml per hour was a borderline risk factor (36% vs 13%; $p = 0.07$), and a total score greater than 5 was significant (24% vs 6%; $p = 0.02$). However, when analyzing the 64 patients operated on since the initial group were used to create the scale, we no longer can identify any significant, or borderline significant, risk factors (mechanical ventilation 16% vs 4%; $p = 0.22$; low urine output 17% vs 10%; $p = 0.52$; score greater than 5, 13% vs 3%; $p = 0.29$).

The causes of death before transplantation were multiple organ failure with sepsis ($n = 13$), perioperative intracranial bleeding and stroke ($n = 5$), complications from device failure ($n = 5$), and disconnection of the electric controller, which occurred in one patient who was found dead at home (by later analysis the device and controller appeared to function well). The reason the patient disconnected the controller (and stopped pump function) is unknown. Two patients had bridge to recovery. One patient had dilated cardiomyopathy and had been on device support for 3 months with persistent positive blood cultures and a pump infection. He underwent removal of the LVAD along with partial left ventriculectomy (Batista procedure).⁵ The patient returned to New York Heart Association functional class II but died at an outside hospital from the rapid return of heart failure 7 months after device removal. The other patient had had partial

left ventriculectomy and received the HeartMate LVAD days later because of fever, hypotension, and borderline cardiac function. The patient's cardiac function improved during HeartMate support and he underwent device removal after 86 days. The patient is alive (functional class II) 14 months after device removal. The one patient with a permanent implant did well initially but died of device failure after 8 months, as has been reported.⁴

Perioperative morbidity was not uncommon in these seriously ill patients. Perioperative reoperation for bleeding was required in 21%. The need for perioperative RVAD support was low, only 11%. Three patients had severe right ventricular dysfunction with low flow, but this was thought to be due to the effects of hypoxemia on the pulmonary vascular resistance. These patients were treated with venovenous ECMO (returning oxygenated blood to the right atrium), and all showed an immediate improvement in right ventricular function and were easily weaned from venovenous ECMO after diuresis improved their pulmonary edema.

Device-related thromboemboli were remarkably uncommon despite minimal or no anticoagulation. Only two patients had transient ischemic attacks. Other neurologic events were seen in the immediate postoperative period and were thought to be related to preoperative or intraoperative events (prolonged cardiac arrest, intracranial bleeding from heparin, embolus from intraventricular thrombus). There were no air emboli during device insertion. At the time of device explantation, while waiting for the donor heart, one patient had an air embolus originating from the LVAD inflow, and she died from cerebral anoxia after transplantation.

Positive blood cultures were common and were detected in 59% of patients during support. All patients had been in ICUs before LVAD insertion, and all had multiple deep lines that were frequently the source of infection. Clinical driveline infection occurred in 28% of patients and clinical pump infection in 11% of patients (fever, positive blood cultures, tenderness over the device, and positive cultures from the device). We never denied transplantation to patients solely because of device infection or clinical driveline infection. In fact, that was considered an indication for urgent transplantation, sometimes with a marginal donor or a donor who was positive for hepatitis C virus. At the time of transplantation, the LVAD pocket was opened first, the infected area was copiously irrigated with saline and antibiotic solution, and then the remainder of

the transplant operation was completed. Only one patient had a low-grade wound infection in the pump pocket necessitating debridement after transplantation. There were no posttransplantation deaths related to infection.

Twelve patients had catastrophic device-related events, and two patients had more than one event. Fracture of the internal tubing of the pneumatic driveline caused air leaks in three patients, resulting in low flow. One patient died, and two patients required emergency reoperation for pump replacement.¹¹ Blood leak from the inflow valved conduit (Fig. 2) caused major hemorrhage in six patients.^{12, 13} One patient had had previous pump replacement for internal pneumatic fracture. This patient died of sepsis and multisystem failure shortly after device replacement. Another patient required pump replacement for inflow bleeding, recovered, but had a second bleeding event. Only the inflow conduit was replaced during the second bleeding episode. The patient was in moribund condition hours after this operation, underwent a desperate heart transplant operation, and died the next day of multisystem failure. Inflow conduit leaks occurred in four other patients, and one patient required pump replacement. Two patients had intermittent bleeding from the percutaneous driveline site necessitating increasing blood transfusions. Urgent heart transplantations using marginal donors were performed in both, and erosions in the inflow conduit were noted at transplantation. The fourth patient had episodes of sepsis before the inflow valve hemorrhage and was thought to be too ill to undergo emergency pump replacement. This patient died of bleeding. Another patient was returned to the operating room to evaluate fluid accumulation in the pump pocket and bleeding from the driveline site. At surgery we found the outflow valved conduit was disconnected from the graft, and he required rapid cannulation for cardiopulmonary bypass and reconnection of the outflow valve site. This patient underwent transplantation within 24 hours and recovered. Another patient became hypotensive after being turned, and he was immediately returned to the operating room. The inflow cannula had pulled out of the sleeve securing it into the left ventricle, and the patient bled to death. In another patient electrical malfunction resulted in emergency reoperation because the pump stopped (the back-up pneumatic actuation failed also). We exchanged the vented-electric system for a pneumatic device and he underwent successful transplantation later. Pump

Fig. 2. A, Patient required an emergency operation for sudden massive bleeding months after LVAD insertion. An erosion of the inflow cannula (indicated by forceps) was identified and successfully managed by LVAD replacement.

failure of the electric system occurred in the patient on permanent support and the back-up system did not function. The patient died.⁴

In summary, 14 major device-related events occurred in 12 patients, and six of these patients died. Some of these mechanisms of device failures have already been reported in the literature.^{2, 4, 11-13} Most important, the major causes of device failure (inflow conduit bleeding, percutaneous driveline fracture, and failure of the electric system) had causes that were identified, analyzed, and corrected in newer versions of the device. The failures in our devices were with some of the very earliest implants of the systems, and new techniques may help predict problems before device failure.¹⁴⁻¹⁶

Hospital charges were available since 1993 in 67 patients (43 with pneumatic devices; 24 with vented-electric devices). The mean hospital charge ($\pm$ standard deviation) from the time of implantation until the time of transplantation or death was \$244,000 $\pm$ \$100,000 total: \$257,000 $\pm$ \$106,000 for the pneumatic device and \$220,000 $\pm$ \$87,000 for the electric device. There was no statistically significant difference in charges by type of device ($p = 0.20$).

Of the 35 patients undergoing bridge to transplantation with an electric device, 26 were on support for greater than 30 days and therefore met the earliest FDA criteria for potential hospital release. Twenty-three patients met echocardiographic criteria (aortic valve opened intermittently when the

Fig. 3. Actuarial survival on LVAD support demonstrates early mortality, usually from multiple organ failure or perioperative strokes. Later mortality was usually from device failure.

pump rate was decreased to a fixed rate of 50 beats/min), 22 patients had a companion available, and 20 patients were in medically stable condition. Eighteen patients entered into the protocol with day trips. Twelve of 18 took a 3-day pass, and 7 of the 18 were discharged to their homes. Failure to progress to discharge was related to development of blood-stream infections ($n = 6$), device malfunction ($n = 1$), ventricular fibrillation ($n = 1$), and insufficient rehabilitation ($n = 1$). Two patients were discharged but withdrew from the release protocol and were returned to the hospital to wait for transplantation because of frequent changes of the controller ($n = 1$) and perceived excessive burden on the companion ($n = 1$).

Actuarial survival during LVAD support is illustrated in Fig. 3. This figure shows that the risk of death is not just early failures in the ICU but continues because of the unpredictable occurrence of device failures. Actuarial survival of the 74 patients after transplantation showed a 1-year survival of $90\% \pm 3.5\%$ and a 4-year survival of $80\% \pm 7.2\%$ (mean $\pm$ standard error).

Discussion

The rapid evolution in LVAD technology points to a promising future. The devices are hemodynamically effective, with a low need for perioperative RVAD support and an extremely low risk of device-related thromboemboli with the HeartMate device. The portable electric system allows the patients greater mobility and the expectation for hospital discharge. There are still problems to be addressed and solved, but the LVADs are already effective and

much safer than the alternative (continued medical therapy), which in this end-stage patient population has a low chance of success.

The proper timing for LVAD insertion is still controversial. It is intuitively obvious that early LVAD implants will yield a higher chance of successful bridge to transplantation than when the patient is moribund. Nevertheless, the cost of bridge to transplantation is high (average hospital charge \$244,000), and it does expose patients to complications unique to mechanical circulatory support (infection, device failure, air emboli). Therefore we have waited until decompensation begins before proceeding to LVAD implant. We may carefully watch a patient without LVAD implantation while waiting for a "marginal" donor (e.g., hepatitis C virus positive, older donor with normal coronary angiography). Several patients who have been scheduled for LVAD implantation underwent transplantation the night before with marginal donor organs.

The dilemma is what to do with patients who are already in severe shock, frequently with impending multiple organ failure. These patients may be admitted after acute myocardial infarction (e.g., left main occlusion), may be transferred from outside institutions, or their condition may have deteriorated after recent cardiac surgery. This was more typical of our patient population, such that 83% were on IABP support and 25% were in such severe shock that they required ECMO for circulatory support before LVAD insertion. The screening scale originally proposed would indicate that these patients are at very high risk for early failure after LVAD insertion.⁷ The decision then can be made to not insert an LVAD; however, the outcome will almost invariably be fatal for these patients. Alternatively, we have proceeded with LVAD insertion, understanding that the chances of success may be reduced. For some patients ECMO support was used to stabilize other organs that were failing (e.g., renal and hepatic function, which were predictors of mortality in our experience) and to determine that the patient was a transplant candidate (for patients who have not previously been assessed). With increased experience we became more aggressive, using ECMO before LVAD implantation for these moribund patients, and this may explain why the screening scale was not able to accurately predict failures after LVAD insertion in our more recent experience.^{17, 18} Survival to transplantation

for our 25 patients supported by ECMO before LVAD insertion was 68%.

Although most of our experience has been bridge to transplantation, there are evolving new uses for implantable LVADs: permanent implants or long-term bridge to recovery.²⁻⁵ Experiences with these new uses are still early and anecdotal but indicate the rapid introduction of concepts in this field. Also, in the past year we have aggressively used LVAD "back-up" for high-risk conventional operations (coronary artery bypass, valve surgery, aneurysmectomy, or partial left ventriculectomy) as alternatives to transplantation. If the conventional operation fails, then the patient has already been approved as a transplant candidate and can be expeditiously placed on LVAD support as a bridge to transplantation.

The ultimate goal of LVAD technology must be for long-term use, either as a bridge to recovery or for permanent implants. Bridge to transplantation is an expensive way to rearrange which patients receive the scarce number of donors, and it does not solve the huge deficit in donor organs. The evolution in device technology has eliminated many obstacles to permanent implants. However, to successfully achieve this goal, in a cost-effective manner, we must focus our efforts on solving the remaining problems. Device durability and reliability may become major issues as patients have extended support. Fortunately, the complications that we had with device failure can be addressed and corrected. However, just like the first pacemaker implants and heart valve implants, this technology is still a "work in progress." Further refinements will be necessary. Infection, either systemic via indwelling catheters or ascending via the driveline, are another potential threat to success of permanent implants. The true magnitude of the problem will not be apparent from the bridge-to-transplantation experience because infections can be suppressed until a donor becomes available, or urgent transplantation can be performed in the face of device infection. However, for permanent implants, chronic infection will decrease quality of life, increase cost of therapy, and may require pump replacement(s) or device explantation if cardiac improvement has occurred.

Finally, we need to do all that we can to expedite approval of these devices. The epidemiology suggests that every day, hundreds of patients die of end-stage heart disease who may otherwise be candidates for mechanical circulatory support.¹⁹ Al-

though the devices are not yet perfected, they are better than the alternative. In addition, only through extensive clinical experience are we able to learn about the shortcomings of mechanical circulatory support and then make modifications and improvements as needed. Delays in the process only cost more patients their lives.

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Discussion

Dr. Walter P. Dembitsky (*San Diego, Calif.*). When you compared the vented-electric devices and those with pneumatic devices, you noted no significant changes in the Nottingham quality of life profile. In our own experience, discharge to home has had the most profound effect on the quality of life profile. Were any of your patients with the vented-electric device discharged to their homes?

Dr. Smedira. Our experience will mimic yours in that patients who can leave the hospital and are free to go home and return to their environment have a significant improvement in their quality of life. Their hospital discharge also improves the quality of life of their companions and families. The requirement for discharge to have a companion and to be tethered either to the hospital or to a facility close to the hospital is a significant strain for all members involved with support.

Dr. Dembitsky. The way these implanted LVADs integrate themselves into the patient is going to be increasingly important. We have seen the late development of aortic insufficiency in two patients. The cause, we believe, is that the valve is obliged to continuously carry both systolic and aortic pressure during LVAD ejection. Therefore, we think that aortic insufficiency is due to the dilatation at the sinotubular ridge. We now reinforce that area with felt when we implant the pumps. Have you seen any instances of late aortic insufficiency?

Dr. Smedira. We have not.

Dr. Dembitsky. The results of bridge to transplantation after VAD implantation are excellent around the world, but the results of bridge to recovery and the results of using these devices as an alternative to transplant are unknown. You are involved with the REMATCH trial. I know you do not have enough experience to do anything but speculate about bridge to recovery, but I would like to hear what you think the results will be. Also, can you tell us a little bit about the REMATCH trial?

Dr. Smedira. The REMATCH trial is currently involving three centers, the Cleveland Clinic, Texas Heart Institute, and Columbia University, and will involve the randomization of patients with end-stage congestive heart failure to either permanent device therapy or medical therapy. It appears that the criteria for inclusion will be patients who are older or who have comorbidities that

exclude them from transplantation. To date, nine patients have been randomized, five to the surgical arm and four to the medical arm.

It is too early in the bridge-to-recovery program to guess what the results will be. There are anecdotal experiences: we have two, which I mentioned, Texas Heart has a few, Columbia has a few, and there is a larger series from the Berlin Heart Institute. We know that reverse remodeling of the ventricle occurs with LVAD support. The difficulty as I see it will be selecting the patients with a dilated cardiomyopathy who will be best served with temporary LVAD support and then explantation. Also, issues of how long the patient can be supported with the hope of ventricular recovery are still unknown. And after removal of the LVAD, will the process return?

Dr. Vaughn A. Starnes (*Los Angeles, Calif.*). This is a very effective, reliable pump. One of the issues that will surface, however, is the biologic valve that is currently used in this pump. If we are evaluating this device as an alternative to transplantation, what are the considerations about these valves? Will we simply exchange them? Will we change the configuration of the pump, perhaps by using a mechanical valve? Of course, doing that raises the issue of anticoagulation. How are you addressing this problem?

Dr. Smedira. That is a valid concern. The stresses on the valves are quite high with the rate of pressure rise generated by the pump. The use of mechanical valves in the pump and the need for anticoagulation create a set of problems that we will have to deal with. We need to look at alternatives to the prosthetic valve, but right now we do not have anything on the drawing board.

Dr. Edward D. Verrier (*Seattle, Wash.*). One of the advantages of this device is that the biologic membrane that lines the inner bladder causes an endothelialization; the endothelialization also seems to dramatically increase the preformed reactive antibodies. Almost all of these patients have a marked increase in such reactive antibodies. Has that affected your ability to then match them for transplantation? Has your waiting time increased? What would be an effective therapy to avoid that sensitization?

Dr. Smedira. We evaluated our experience with preformed reactive antibodies and found no effect on our ability to perform transplantation in these patients. However, a few patients that had extremely high preformed reactive antibodies (90+%) have been difficult to manage. We found when we reviewed our experience that it is the number of blood products that were transfused during the support period, specifically platelets, that resulted in a higher preformed reactive antibody score than those that had fewer blood products. To avoid that, we have used aprotinin routinely in all but our first patients and tried to diminish the number of blood products that the patients are receiving, especially platelets. For the patients who have had elevated preformed reactive antibodies, we have used both plasmapheresis and immunoglobulins to try to reduce the antibodies. These methods have been generally successful.