Initial Clinical Experience With the Jarvik 2000 Implantable Axial-Flow Left Ventricular Assist System

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Background—Implantable left ventricular assist systems (LVASs) are used for bridging to transplantation, bridging to myocardial improvement, and for permanent circulatory support. Conventional implantable systems have inherent limitations that increase morbidity during support. In contrast, small, efficient, axial-flow pumps, which have been under development for the past decade, have the potential to improve the length and quality of life in patients with severe heart failure.

Methods and Results—To assess the safety and clinical utility of the Jarvik 2000, we implanted this device in 10 transplant candidates (mean age 51.3 years) in New York Heart Association (NYHA) class IV. Implantation was achieved through a left thoracotomy during partial cardiopulmonary bypass. The mean support period was 84 days. Within 48 hours postoperatively, the cardiac index increased 43%, pulmonary capillary wedge pressure decreased 52%, systemic vascular resistance decreased significantly, and inotropic support became unnecessary. Eight patients underwent physical rehabilitation and returned to NYHA class I. Their left ventricular dimensions, cardiothoracic ratios, and pressure-volume loop analyses showed good left ventricular unloading. Seven patients underwent transplantation and 3 died during support. No device thrombosis was observed at explantation.

Conclusions—The Jarvik 2000 functions as a true assist device by partially unloading the left ventricle, thereby optimizing the patient’s hemodynamics. Our preliminary results indicate that this LVAS may safely provide circulatory assistance for heart transplant candidates. (Circulation. 2002;105:2855-2860.)

Key Words: ventricles ■ heart-assist device ■ heart failure ■ transplantation

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n the basis of extensive clinical experience gained over the past 2 decades, implantable ventricular assist systems (VASs) are being applied to an increasingly broader heart failure population.2,3 So far, they have been used mainly for bridging to heart transplantation, but they may be equally useful for bridging to myocardial recovery4 and for permanent circulatory support.5

Although implantable VASs are safe and effective in heart transplant candidates, conventional systems exemplify concepts established by the National Institutes of Health (NIH) in the 1970s. These concepts called for the VAS to capture the entire cardiac output and to produce blood flows up to 12 L/min. To achieve these goals, pulsatile pumps of adequate size were needed. The size required to meet the goals of the NIH program made a body surface area of at least 2 m² desirable for complication-free placement. Smaller adults and children were denied the benefit of this therapy.6,7

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The Jarvik 2000 Heart (Jarvik Heart Inc)8 is a new type of implantable left ventricular assist system (LVAS) that produces axial flow by means of a single, rotating, vaned impeller. This system represents an innovative approach to implantable LVAS technology and has a number of advantages over conventional pulsatile systems. We became interested in continuous-flow pumps because they potentially could function without breaking the skin. In addition, these small pumps should be suitable for smaller adults and even children. The implantation operation is less extensive, so bleeding, infection, and other operative complications may decrease. The continuous flow and lack of stasis should minimize thrombus formation and bacterial adhesion. With only a single movable component, axial-flow pumps should be highly reliable for prolonged periods. Furthermore, these pumps can be used as true assist devices. In contrast, conventional VASs, which necessitate a fairly extensive implantation operation, are designed to capture the entire left ventricular output and to act physiologically as left ventricular replacement devices.

In April 2000, the Texas Heart Institute initiated the first clinical trials of the Jarvik 2000. We present the results of the first 10 cases in which this system was used.
This initial clinical study was undertaken to evaluate the safety and usefulness of the Jarvik 2000 LVAS. In this ongoing feasibility study, patients with New York Heart Association (NYHA) functional class IV heart failure and a small body surface area (<2 m²) who are on the transplant waiting list may be considered for enrollment. Eligible patients must be confined to the intensive care unit and facing imminent death related to heart failure. They must lack significant comorbidities such as sepsis, cancer, and irreversible end-organ failure. The criteria for this study are similar to other VAS bridge-to-heart-transplant protocols that have been conducted in the United States. Patients with previous median sternotomies and a body habitus that would make a conventional LVAS unfeasible (ie, tall and thin or short and stout) are also eligible for this therapy.

Physiological and quality-of-life data are recorded before, during, and after circulatory support. Once the pump has been implanted, speed-change and pump-off testing are performed periodically. Clinical data are analyzed for any adverse response related to the implanted device. An independent data and safety monitoring board evaluates the safety of the LVAS by monitoring the frequency and duration of adverse events. A secondary objective of the present study is to refine the clinical protocol to allow eventual expansion to a multicenter trial.

Methods

Clinical Protocol

Figure 1. The Jarvik 2000 system consists of an intraventricular blood pump, a 16-mm outflow graft, a percutaneous power cable, a speed controller, and a battery. The controller and battery are worn on a belt or are carried in a bag.

The Jarvik 2000 LVAS provides continuous flow into the descending thoracic aorta. Because of its small size, this device can be placed within the left ventricle, and no inlet cannula is needed. The continuous blood flow eliminates the need for valves, an internal compliance chamber, or an externalized vent.

The system consists of a blood pump, 16-mm outflow graft, percutaneous power cable, pump-speed controller, and direct-current power supply (Figure 1). The blood pump is simple in design, its single movable component being an impeller located in the center of the titanium housing (Figure 2). A brushless direct-current motor contained within the housing creates the electromagnetic force necessary to rotate the impeller. The impeller consists of a neodymium–iron–boron magnet suspended by 2 ceramic bearings. On the impeller’s outer surface are 2 titanium hydrodynamic blades. All the blood-contacting surfaces within the pump are made of smooth titanium. Blood flow is directed through the outflow graft by stator blades located near the pump outlet. The motor receives power from the external controller through a series of wires that are contained in a silicone tube covered with Dacron. The motor speed is manually adjusted and is regulated by a pulse-width–modulated, speed-control circuit. Lead acid or lithium ion batteries provide the system’s 12-volt power supply. The pump’s operating range is 8000 to 12 000 rpm; under optimal physiological conditions, these speeds can generate flows of up to 6 L/min. The normal power consumption is 3 to 7 watts. The pump’s speed is adjusted in 1000-rpm increments until minimal flow is ejected through the aortic valve. In case of a system malfunction, the controller provides both an aural and visual alert. Ambulatory patients can maintain the system’s external equipment and change the batteries as needed.

Implantation Operation

The pump is implanted through a thoracotomy incision with the aid of partial cardiopulmonary bypass (CPB). The femoral artery and vein are exposed for CPB cannulation. A left thoracotomy is then made in the fifth or sixth intercostal space, and the heart and descending thoracic aorta are exposed. The aorta is partially occluded while the outflow graft is anastomosed to the aorta. The femoral vessels are then cannulated and CPB is begun. Ventricular fibrillation is induced, and a circular knife is used to create an opening in the left ventricle. A silicone/polyester sewing cuff is sewn to the apex of the heart with pledgeted sutures. The power cable is tunneled subcutaneously across the abdomen from left to right just below the diaphragm and exits the skin at the right anterior portion of the abdomen. The pump is inserted into the left ventricle and is secured with cotton tape around the cuff and pump housing. The pump’s outflow graft is anastomosed to the graft previously placed on the aorta. The heart is then defibrillated, and air is removed from the left ventricle, pump, and graft. As CPB is gradually discontinued, the pump is turned on. Pulmonary vasodilators and inotropic agents are used as necessary to support right-sided cardiac function.

Intraoperatively, hemodynamic assessment is performed with transesophageal echocardiography, a pulmonary artery catheter, an arterial pressure line, a pressure line to the left ventricle, and an ultrasonic flow probe on the pump’s outflow graft. Hemodynamic values are recorded at each pump speed, and the optimal speed is determined. Flow through the pump can be calculated accurately against varying mean pressures.5 The ultrasonic flow probe is removed before the thoracotomy incision is closed. In the early postoperative period, hemodynamic function is assessed with an arterial pressure line, a pulmonary artery catheter, and transesophageal echocardiography. Once all the monitoring lines have been removed, hemodynamic assessment is based on echocardiography and routine evaluation of vital signs.

Postoperative Management

Postoperatively, the goal is to maintain pump flow at the lowest level compatible with a normal cardiac index and NYHA class I status. Hemodynamic and echocardiographic studies are performed routinely to determine the proper pump-speed setting. During these tests, the pump speed is increased in 1000-rpm increments over the

Figure 2. A cutaway view of the Jarvik 2000 blood pump. The vaned impeller rotates in response to the electromagnetic force created by the motor, which is contained within the pump housing. The impeller is suspended by ceramic bearings (not shown). Outflow stator blades (not shown) direct blood flow through the pump’s outflow conduit.
Mean Hemodynamic Values at Baseline and Up to 48 Hours After Device Implantation

<table>
<thead>
<tr>
<th>Variable</th>
<th>At Baseline</th>
<th>At 12 h</th>
<th>At 24 h</th>
<th>At 48 h</th>
</tr>
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<td>Cardiac index, L/min per m²</td>
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<td>Heart rate, bpm</td>
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<td>3.26</td>
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<td>21.7</td>
<td>13.3*</td>
<td>12.2*</td>
<td>10.3*</td>
</tr>
</tbody>
</table>

*Significant compared to baseline values (P<0.05 by paired t test).

Results

Patients

Between April 2000 and March 2001, we implanted the Jarvik 2000 LVAS in 7 men and 3 women with an average age of 51.3 years (range: 30 to 60 years) and a mean heart failure duration of 7.9 years (range: 0.5 to 24 years). All 10 patients were approved for heart transplantation. They had cardiomegaly (Table) and deteriorating cardiovascular hemodynamic function, with a cardiac index below 2, decreased blood pressure, and increased wedge pressure. Their hemodynamics were all sustained by intravenous pharmacological agents.

Seven patients have undergone heart transplantation and been discharged from the hospital, and 3 died during support. The 7 transplant recipients had an average follow-up period of 13.5 months (range: 8.6 to 19 months), and all remain in NYHA class I. For the series as a whole, the average duration of support has been 84 days (range: 13 to 214 days), and the total duration of support has been 812 days. Two of the deaths were from ventricular ectopia, and one death was due to adult respiratory distress syndrome secondary to coagulopathy and significant blood transfusion.

Hemodynamic Assessment

Compared with preoperative values, the hemodynamic function of all the patients improved considerably with LVAS support (Table). Forty-eight hours after device implantation, the average cardiac index increased by 43% and the pulmonary capillary wedge pressure decreased by 52%. The mean arterial blood pressure was stable, and the need for inotropic support was greatly reduced.

Although the average cardiac index was normal at all pump speeds, it decreased by 33.5% when the pump was turned off. However, 48 hours after implantation, the average cardiac index (2.31 L/min per m²) was 22% greater than the preimplantation value even with the pump off. The average pulse pressure was 13 mm Hg at 12 000 rpm and 42 mm Hg with the pump off. This finding reflected the increased flow from the left ventricle through the pump throughout the cardiac cycle. Interestingly, as the flow through the pump was decreased by lowering the rpm, the native ventricular function improved (a normalization of Starling’s law in these advanced heart failure patients) so that cardiac output (pump and native heart) remained relatively constant (Figure 3).

To avoid stasis in the aortic root, an effort was made to allow the aortic valve to open. The point at which the aortic valve opens was verified echocardiographically. The pump speed that maintained pulsatility seemed to be the optimal one for cardiac function. In most cases, the chosen speed was 9000 rpm to 10 000 rpm.

Echocardiographic data confirmed the pump’s left ventricular unloading effect. Doppler-flow imaging showed that flow was continuous throughout the entire cardiac cycle but increased during systolic augmentation (when the increasing left ventricular pressure augmented the preload to the pump, thereby causing flow to increase). As the pump speed increased, diastolic blood flow increased (Figure 4). Flow through the aortic outflow tract decreased progressively as the pump speed increased, correlating inversely with right-sided flow (Figure 5). In brief, (5-minute off-pump studies) cardiac output was maintained at a reduced level by the native
ventricular ejection. The mean regurgitant flow was 0.35 L/min per m², and the average regurgitant fraction for the 4 patients studied was 11%. As the pump speed increased, the cardiac output also increased, but not linearly. At 11,000 and 12,000 rpm, flow through the left ventricular outflow tract was minimal, indicating that the pump captured nearly all of the cardiac output.

The left ventricular dimensions decreased as the level of support increased. Compared with values obtained during pump-off periods, the left ventricular diastolic dimension (LVDD) decreased by 16% during LVAS support. The average LVDD was 7.1 cm before device implantation and 5.9 cm 48 hours after implantation. The left ventricular unloading effect was also noted on anteroposterior chest roentgenograms. The average cardiothoracic ratio was 0.71 before implantation and 0.62 at 48 hours after implantation.

Figure 3. Arterial pressure waveform observed when the pump speed was increased by 1000-rpm increments over the entire operating range (8000 to 12,000 rpm). The dicrotic notch is present at 8000 and 9000 rpm but is absent at 10,000 rpm. In this case, the pump speed was set at 9000 rpm, so there was some aortic outflow. BP indicates blood pressure.

Hematologic Evaluation
The hematologic values for all patients remained within an acceptable range throughout the support period. Also, 1 patient had chronic bleeding from a gastric ulcer and arteriovenous malformation throughout the small intestine (INR ranged from 1.0 to 1.2). Cauterization of the ulcer and resection of the bowel were necessary to minimize the persistent bleeding. This patient was supported for 244 days without anticoagulation. Activation of bleeding from arteriovenous malformation has been reported previously in patients with aortic stenosis. Thus, this may be a future consideration for patients with a narrowed pulse pressure. Except for the usual elevations seen after surgery, no significant hemolysis was seen in any patient during the remaining support period. The average plasma free hemoglobin level was 14.1 mg/dL, compared with an average preimplantation value of 7.4 mg/dL.

Nine of the 10 patients received conservative anticoagulant therapy involving some combination of heparin, warfarin, aspirin, and dipyridamole. The average INR over the entire duration of support was 1.3, and the highest value achieved was 1.7. In the 7 explanted devices, no thrombus was observed within the device.

Jarvik 2000 System Operation
Operation of the Jarvik 2000 was uncomplicated, with only 3 minor technical problems occurring during the cumulative 812 days of support. The operator broke 2 power-cable connectors, and a patient bent a connector pin. These minor problems were resolved quickly and without adverse consequences to the patient.

The patients and their family members were taught to exchange batteries and to identify emergency situations.
recovering sufficiently from the implantation surgery, the patients participated in daily physical rehabilitation that consisted of walking on a graded treadmill and performing lightweight lifting exercises. The patients reported that increasing the pump speed during exercise augmented their exercise capacity; when the exercise was concluded, they returned the speed to its usual setting. They walked about the hospital at will, ate meals in the hospital cafeteria, and went outdoors for visits. The survivors achieved NYHA class I cardiac status within 2 weeks of implantation. Because of protocol restrictions, however, they were not allowed to leave the hospital property. Their medical and physical conditions would otherwise have been fully compatible with hospital discharge.

Discussion

The goal with the Jarvik 2000 is to augment left ventricular function by providing flow throughout the entire cardiac cycle. The primary variables that determine the amount of blood flow through the pump are the impeller speed and the mean arterial pressure (resistance). As the pressure within the left ventricle increases during systole, blood flow through the pump increases. End-organ flow is further augmented because the pump provides positive pressure flow throughout diastole, which normally has passive flow. In fact, under actual physiological conditions, blood flow is continuous from the left ventricle to the aorta throughout the entire cardiac cycle. The cyclical increase and decrease in flow through the pump is augmented by the pumping action of the native ventricle. As the pump speed increases, the pulse pressure decreases because of left ventricular unloading by the pump. Additionally, changes in left ventricular contractility lead to changes in the pulse pressure when the intravascular volume, pump speed, and vascular tone are relatively constant. Although blood flow through the pump is continuous, arterial blood flow ideally is pulsatile, reflecting the contribution of the augmented left ventricle. With the pump speed set to the usual submaximal flow rate, the aortic valve opens during systole. The pulse pressure is normally large enough to palpate a peripheral pulse and to measure blood pressure by noninvasive methods.

In 1 patient, high pulmonary vascular resistance and right heart failure developed secondary to adult respiratory distress syndrome. During a period when the pump speed was relatively high (11,000 rpm), an echocardiogram revealed that the intraventricular septum had shifted significantly to the left. The poor left ventricular filling and the continuous pump flow apparently resulted in some degree of negative pressure that caused a septal shift, contributing further to right ventricular dysfunction. In such cases, right ventricular support must be instituted to allow for filling of the left ventricle.

In the present study, the mean cardiac index at the usual speed setting (9000 rpm) was 3.2 L/min per m², and the average aortic valve-opening time was 150 ms. This level of circulatory assistance was sufficient to allow complete physical rehabilitation and recovery from the implantation surgery. The continuous flow throughout the cardiac cycle provided both systolic and diastolic unloading of the left ventricle. When the pump was on, the left ventricular systolic and diastolic dimensions consistently decreased by 13% to 16%.

The hemodynamic support provided by the Jarvik 2000 optimizes the ratio between myocardial oxygen consumption and delivery. The continuous pulsatile flow into the descending aorta, along with the aortic outflow, provides sufficient coronary perfusion. The increased diastolic flow and pressure, as well as the decreased aortic valve–opening time, also promote coronary perfusion. Animal studies have shown that continuous unloading of the left ventricle with an axial-flow pump decreases coronary perfusion to nons ischemic myocardium while increasing perfusion to ischemic myocardium. This decrease in coronary flow to the normal myocardium may be a concern in conditions of prolonged nonpulsatility.

The need for anticoagulant therapy in patients supported by the Jarvik 2000 has yet to be determined. The 10 patients described in this report had varying degrees of such therapy, and no significant thromboembolic events occurred. Likewise, anticoagulant therapy in numerous animals has resulted in an INR of less than the target level of 1.5, and no thrombotic events have been observed. The nonthrombogenic quality of the Jarvik 2000 probably is due to its ultrasmooth titanium surface, continuous blood flow, and minimal surface area, which reduce blood contact with foreign materials.

We believe there are definite advantages to an intraventricular pump. In our early experiments, an inlet cannula was shown to introduce abnormal rheology by generating negative pressure to fill the pump. This deformation of platelets contributes to their activation and may contribute to thrombosis and pannus formation in the inlet graft. Also, with a continuous flow pump, the ventricle is offloaded throughout the cardiac cycle. By having the pump inside the ventricle, the pump moves with the motion of the heart, thereby obviating any possibility of inlet obstruction on the septum or the lateral wall. If the pump were placed outside the ventricle, the inlet cannula might be obstructed as the heart moves, which would affect the filling either on the lateral or the septal side. In addition, if the pump stops or malfunctions, regurgitation back into the ventricle may occur. By having the pump inside the ventricle, there is a limitation to the amount of pressure that can build up, thus avoiding a problem with regurgitation.

During the 17 pump-off tests in our series, the amount of regurgitant flow through the pump was not excessive and therefore not life threatening. All the patients remained fully alert and conscious and maintained a systolic blood pressure of >80 mm Hg. The mild regurgitant fraction detected by echocardiography was similar to that seen in patients with mild aortic insufficiency. The resistance of the pump impeller apparently minimizes regurgitant flow during diastole. Forty-eight hours after support was initiated, all 4 patients had an improved cardiac index with the pump off. Should pump failure occur (not seen experimentally or clinically), the patient should remain sufficiently alert to initiate emergency measures. While the pump is turned off, blood flows through it in both directions, and this flow may help prevent thrombosis within the pump.

The Jarvik 2000 was designed to be reliable, easy to implant, and simple to operate. In our series of 10
of a cardiopulmonary bypass or with bypass times of <10 minutes. The less extensive implantation surgery has lessened surgical complications. The patients and hospital staff found the system quite easy to operate. Remarkably, there were few technical problems with system components, and no serious device-related adverse events occurred. Although 2 patients had superficial infections at the power cable’s exit site, these infections did not alter the clinical course. Continuation of both bridge-to-transplant and long-term destination studies now ongoing in Europe\textsuperscript{15} will allow assessment of the role of this technology in the treatment of heart failure.

In summary, initial clinical studies of the Jarvik 2000 LVAS have shown that it can safely and satisfactorily support patients with severe heart failure who are awaiting transplantation. Because the Jarvik 2000 acts in concert with the native pulsatility of the heart, it functions as a true left ventricular assist device. Its optimal application is one where native heart function is augmented by the continuing unloading of the pump, with pulsatility being supplied by the assisted native heart. This function contrasts with the more commonly designated implantable LVADs, ie, the HeartMate and the Novacor, which are really better termed left ventricular replacement devices. Once these devices are implanted, ejection by the native heart seldom occurs. Thus, axial-flow pumps offer important advantages, but the superiority of these pumps can be demonstrated only through further clinical trials. Nevertheless, axial-flow technology continues to advance, and these pumps may eventually provide an alternative to heart transplantation in selected patients. The lower operative risk associated with implantation of the Jarvik heart will allow it to be placed safely in class IV heart failure patients maintained on outpatient medical therapy, therefore broadening considerably the role of circulatory support devices as a treatment option for this complicated patient population.

References

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