Circulatory Assistance With a Permanent Implantable IABP: Initial Human Experience

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Purpose—The Kantrowitz CardioVAD™ (KCV) is an electrically powered, pneumatically driven circulatory assist device which provides diastolic augmentation and systolic unloading to the failing heart. It consists of a 60cc-pumping chamber, a percutaneous access device (PAD), and an external controller. The pumping chamber, is surgically implanted in the descending thoracic aorta with the patient on cardiopulmonary bypass. Its physiologic function is analogous to that of the intra-aortic balloon pump (IABP).

Methods—Between 1997 and 2000, 5 men (age 59 to 73) with end-stage cardiomyopathy refractory to maximal drug treatment and with documented hemodynamic improvement on an IABP were enrolled in a feasibility study.

Results—Mean bypass time was 157 minute (range 120 to 196 minute); mean cross-clamp time was 101 minute (range 69 to 144). Patient 1 died intra-operatively. Compared with preoperative values, at 1 month, cardiac index increased (1.7 to 2.6 L/min/m²) and there were significant decreases in creatinine (2.6 to 1.5 mg/dL), pulmonary capillary wedge pressure (PCWP) (32 to 14 mm Hg), and right atrial pressure (RA) (19 to 9 mm Hg). NYHA class improved (IV to II). The mean increase in cardiac index with the KCV OFF to ON was 0.53 L/min/m² (36%). Two patients were discharged home. The device was used intermittently without thromboembolic complications. The only device related complications were attributed to PAD design and have been corrected.

Conclusion—Our initial human trial demonstrates successful implantation of the KCV in end-stage patients, the ability of the device to be used intermittently without anticoagulation, and documents hemodynamic and functional improvement in the status of these patients. (Circulation. 2002;106[suppl I]:I-183-I-188.)

Key Words: heart-assist device  heart failure  cardiomyopathy  inotropic agents

Congestive heart failure (CHF) is an increasing cause of morbidity and mortality in the industrialized world. Medical therapy has advanced significantly over the last decade. Treatment with ACE inhibitors, β-blockers, and spironolactone is associated with improved survival inpatients with NYHA Class II-IV heart failure.1-4 Inotropic therapy is more controversial as there is an immediate improvement in hemodynamics but a potential negative impact on long-term survival. Although many patients can be managed successfully as NYHA II and III, for some, the progression to end stage heart failure is inexorable. Heart transplantation has evolved into frontline therapy for these patients but its use is restricted by a donor shortage. Furthermore, immunosuppressive medications have significant side effects and the long-term survival is decreased by transplant arteriopathy. Therefore, an effective therapy, which can improve functional capacity, quality of life, and survival of these patients, remains elusive. Permanent mechanical circulatory assist devices are being developed to address these needs.

Mechanical assist devices use 1 of 3 principles: (1) direct systolic augmentation of the heart, (2) mechanical pumping to divert blood from the left atrium/ventricle directly into the aorta with sufficient force to maintain normal arterial pressure, or (3) diastolic augmentation.5 Intra-aortic balloon pumps (IABP) are the most commonly used mechanical assist devices and work by the principle of diastolic augmentation. The Kantrowitz CardioVAD™ (KCV) (L.VAD Technology, Detroit, MI) is an implantable IABP designed to provide permanent mechanical assistance that can be activated intermittently, require no anticoagulation, allow for treatment of CHF and potential myocardial recovery, and not pose an increased risk of cerebrovascular accidents (CVA). This study details the surgical implantation techniques for the KCV and short term results (30-day endpoint) inpatients enrolled in this FDA phase 1 feasibility trial.
Components of the Kantrowitz CardioVAD (KCV): a) blood pump, b) percutaneous access device (PAD), c) mobile drive console.

Materials and Methods

Patients

Between 1997 and 2000, after obtaining informed consent, 5 men with end-stage cardiomyopathy refractory to medical treatment and who were not transplant candidates, were enrolled in the study. This trial was approved by the University of Chicago Institutional Review Board. Patients were followed prospectively and inclusion criteria are detailed in Figure 1. After initial screening, patients underwent noninvasive and invasive testing and exclusion criteria based on those tests are described (Tables 2, 3). One patient deteriorated after all tests were complete and required mechanical ventilation and an IABP. All patients other were on chronic inotropic therapy and were minimally ambulatory. All patients had implantable cardiac defibrillators (ICD) placed for previous tachyarrhythmias, but had stable rhythms before KCV implantation. Effectiveness of the device was measured by a 6-minute walk test, resolution of the CHF syndrome and a Minnesota Living with Heart Failure Quality of life assessment (QOL; range 0 to 105 from none to disabling symptoms).

Surgical Technique

After the patient was deemed a good candidate for KCV, a 1 x 5 cm full thickness segment of skin was obtained from the forearm, under local anesthesia at the bedside. Autologous fibroblasts were cultured from the biopsy specimen for 10 to 14 days and used to coat the percutaneous access device (PAD). Once this procedure was completed, patients were admitted for KCV implantation.

Under general anesthesia, a left thoracotomy was performed through the 5th interspace. The aorta was encircled 1, 8, and 16 cm distal to the subclavian (points A, B, C, respectively). Patients were completely heparinized and placed on warm, heart beating cardiopulmonary bypass (CPB) using femoral arterial and venous cannulae. Another arterial cannula was placed at the aortic arch for cerebral perfusion. The aorta was crossclamped at points A and B and incised longitudinally. Removed from the edges were 3-mm strips of the aorta. The superior portion of the KCV was sutured in place with a single layer of 2 to 0 polypropylene running mattress suture. A felt strip was used on the aortic side as a buttress. The crossclamp at B was released and reapplied at point C. Intercostals were controlled with Fogarty catheters. The distal portion of the KCV was sewn to the aorta in a similar technique to the proximal end. The point C clamp was removed and a second layer of sutures used to further secure the KCV. After obtaining hemostasis, 3 epicardial screw-in electrodes (St. Jude Pacesetter, St. Paul, MN) were placed in a triangular pattern 1 cm apart on to the lateral portion of the heart. The device (bladder integrity and electrode sensing) was tested as mechanical support was initiated. This assisted in weaning from CPB. The thoracotomy incision was closed and the patient placed in the supine position. The PAD was then inserted into a subcutaneous pocket in the right upper quadrant and the device connected. Patients were extubated, weaned from inotropes and ambulated as soon as possible. All patients were run with maximum diastolic augmentation with the device set to inflate immediately after the dicrotic notch. Anti-coagulation was not used for the device—1 patient received coumadin for a mechanical prosthetic aortic valve.

Statistical Analysis

The SAS program (Statistical Analysis System; SAS Institute Inc, Cary, NC) was used for statistical analysis. Continuous data were expressed as mean ± SD and were evaluated for differences between groups with a two-tailed t test or analysis of variance. Significance was assumed if P < 0.05.

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TABLE 1. General Inclusion Criteria

1) 18 to 80 years of age
2) Dilated cardiomyopathy (idiopathic, ischemic, or because of other irreversible cause) not amenable to other invasive/surgical correction
3) Limiting CHF symptoms (NYHA class III or IV) refractory to maximal tolerated doses of diuretics, digoxin, ACE inhibitors, β blockers, or IV inotropes
4) Absence of obstructive valvular disease or aortic regurgitation
5) No history of recent myocardial infarction (within 2 weeks)
6) No irreversible and debilitating renal (chronic dialysis), pulmonary, or hepatic dysfunction

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TABLE 2. Exclusion Criteria from Noninvasive Testing

1) Leukocytosis indicating an infectious process
2) Renal insufficiency not due to CHF (creatinine > 2.5 mg/dL)
3) More than 3 x elevation in liver enzymes and bilirubin level
4) Uncorrectable abnormal coagulation parameters
5) Uncontrolled atrial or ventricular arrhythmias (heart rate > 120 bpm)
6) Ejection fraction > 35%
7) Sever pulmonary disease (FEV1 < 1.0 L, FVC < 1.5 L, FEV1/FVC < 35%, MVV < 50% predicted)
8) Significant carotid occlusive disease
9) Abnormalities of the aorta that would preclude surgery including aneurysms, coarctation, extreme tortuosity, inadequate length (< 19 cm)

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TABLE 3. Exclusion Criteria from Invasive Testing

1) Cardiac index without assistance should be < 2.2 L/min/m² with a PCWP > 15 mm Hg
2) During insertion of an IABP, there must be a 15% increase in cardiac output or stroke volume and a 15% reduction in PCWP
3) Coagulation and platelet parameters studied before and after use of the IABP must be within normal limits
4) Irreversible pulmonary hypertension on IABP (transpulmonary gradient > 14 mm Hg or pulmonary vascular resistance > 4 woods units)

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The 5 male patients averaged 69 years of age (range 53 to 74). Of the patients screened, none were excluded because of failure of IABP testing. Because of internal defibrillators, MRI and CT scan imaging of the descending aorta to determine appropriateness of KCV placement was ineffective. Transesophageal echocardiography (TEE) was then used to assess the descending aorta and proved to be the best imaging modality. Three patients had significant plaquing of the aorta (2 moderate and 1 severe), but the KCV could be implanted after crossclamping and debridement without difficulty. Four patients had ischemic cardiomyopathy, and 3 had previous CABG surgery. One patient had valvular aortic valve (St. Jude Medical, St. Paul, MN). All patients were NYHA class IV, and dependent on intravenous inotropic therapy. The ejection fraction (mean ± SD) was 16 ± 5% (range 9% to 24%). The mean weight loss during the year prior to KCV implantation was 31 ± 12 lbs. The first patient expired in the operating room from technical problems arising from left atrial to femoral bypass. After changing the technique to partial CPB, all subsequent 4 patients have survived to the first endpoint (30 days). The mean CPB time was 157 minutes (range 120 to 196). A crossclamp was applied proximally (position A) for a mean of 101 minute (range 69 to 144). The distal crossclamp was at position B for a mean of 55 minute (range 39 to 77) and at position C for a mean of 46 minute (range 30 to 67). The total crossclamp time decreased by half from the first to the last patient. For the 4 patients surviving the operative procedure, there were no re-operations for bleeding and mean chest tube blood loss was only 450cc (range 250 to 900). All patients were extubated within 48 hours. One patients who was ventilator dependent before implantation because of pneumonia required re-intubation 4 days later and received a tracheostomy. The other 3 patients were ambulatory and dischargeable. One patient stayed in the hospital because of lack of a FDA approved discharge protocol. All patients were on aspirin and only 1 required anti-coagulation for his prosthetic aortic valve. Hemodynamic and laboratory data before implantation and at 30 days are summarized in Table 4. The reductions in serum creatinine, RA and PCWP, as well as increase in CI, were statistically significant when compared with baseline values. Although, QOL parameters and 6-minute walk improved, the differences were not significant. 

**Results**

The 5 male patients averaged 69 years of age (range 53 to 74). Of the patients screened, none were excluded because of failure of IABP testing. Because of internal defibrillators, MRI and CT scan imaging of the descending aorta to determine appropriateness of KCV placement was ineffective. Transesophageal echocardiography (TEE) was then used to assess the descending aorta and proved to be the best imaging modality. Three patients had significant plaquing of the aorta (2 moderate and 1 severe), but the KCV could be implanted after crossclamping and debridement without difficulty. Four patients had ischemic cardiomyopathy, and 3 had previous CABG surgery. One patient had valvular aortic valve (St. Jude Medical, St. Paul, MN). All patients were NYHA class IV, and dependent on intravenous inotropic therapy. The ejection fraction (mean ± SD) was 16 ± 5% (range 9% to 24%). The mean weight loss during the year prior to KCV implantation was 31 ± 12 lbs. The first patient expired in the operating room from technical problems arising from left atrial to femoral bypass. After changing the technique to partial CPB, all subsequent 4 patients have survived to the first endpoint (30 days). The mean CPB time was 157 minutes (range 120 to 196). A crossclamp was applied proximally (position A) for a mean of 101 minute (range 69 to 144). The distal crossclamp was at position B for a mean of 55 minute (range 39 to 77) and at position C for a mean of 46 minute (range 30 to 67). The total crossclamp time decreased by half from the first to the last patient. For the 4 patients surviving the operative procedure, there were no re-operations for bleeding and mean chest tube blood loss was only 450cc (range 250 to 900). All patients were extubated within 48 hours. One patients who was ventilator dependent before implantation because of pneumonia required re-intubation 4 days later and received a tracheostomy. The other 3 patients were ambulatory and dischargeable. One patient stayed in the hospital because of lack of a FDA approved discharge protocol. All patients were on aspirin and only 1 required anti-coagulation for his prosthetic aortic valve. Hemodynamic and laboratory data before implantation and at 30 days are summarized in Table 4. The reductions in serum creatinine, RA and PCWP, as well as increase in CI, were statistically significant when compared with baseline values. Although, QOL parameters and 6-minute walk improved, the differences were not significant.

**Discussion**

The treatment of CHF because of left ventricular dysfunction has evolved dramatically in the last decade. Advances in pharmacological treatment have helped patients in all stages of systolic dysfunction, even those with NYHA IV symptoms. However, for an expanding group of patients, cardiac

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**TABLE 4. Hemodynamic and Laboratory Results Compared Before and 30 Days After Implantation**

<table>
<thead>
<tr>
<th></th>
<th>Before KCV Implantation</th>
<th>30 Days after KCV Implantation</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IABP Off</td>
<td>IABP On</td>
<td>KCV Off</td>
</tr>
<tr>
<td>Hgb</td>
<td>10.8 ± 1.9</td>
<td>10.8 ± 1.9</td>
<td>9.9 ± 1.8</td>
</tr>
<tr>
<td>Platelets</td>
<td>203 ± 43</td>
<td>203 ± 43</td>
<td>187 ± 78</td>
</tr>
<tr>
<td>WBC</td>
<td>6.9 ± 1.7</td>
<td>6.9 ± 1.7</td>
<td>9.7 ± 3.2</td>
</tr>
<tr>
<td>Creatinine</td>
<td>2.6 ± 0.5</td>
<td>2.6 ± 0.5</td>
<td>1.5 ± 0.1</td>
</tr>
<tr>
<td>BUN</td>
<td>58 ± 25</td>
<td>58 ± 25</td>
<td>34 ± 4</td>
</tr>
<tr>
<td>LDH</td>
<td>310</td>
<td>310</td>
<td>220</td>
</tr>
<tr>
<td>AST</td>
<td>22 ± 8</td>
<td>22 ± 8</td>
<td>32 ± 18</td>
</tr>
<tr>
<td>ALT</td>
<td>20 ± 6</td>
<td>20 ± 6</td>
<td>18 ± 3</td>
</tr>
<tr>
<td>Albumin</td>
<td>3.9 ± 0.3</td>
<td>3.9 ± 0.3</td>
<td>4.1 ± 0.1</td>
</tr>
<tr>
<td>Tot protein</td>
<td>7.2 ± 0.3</td>
<td>7.2 ± 0.3</td>
<td>7.1 ± 0.2</td>
</tr>
<tr>
<td>PT (INR)</td>
<td>1.8 ± 0.3</td>
<td>1.8 ± 0.3</td>
<td>1.3 ± 0.1</td>
</tr>
<tr>
<td>APTT (sec)</td>
<td>36 ± 11</td>
<td>36 ± 11</td>
<td>29 ± 0.5</td>
</tr>
<tr>
<td>HR (beats per min)</td>
<td>67</td>
<td>65</td>
<td>68</td>
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<tr>
<td>BP systolic (mm Hg)</td>
<td>84 ± 5</td>
<td>100 ± 12</td>
<td>110 ± 13</td>
</tr>
<tr>
<td>BP diastolic (mm Hg)</td>
<td>65 ± 5</td>
<td>55 ± 10</td>
<td>65 ± 5</td>
</tr>
<tr>
<td>RA (mm Hg)</td>
<td>19 ± 1*</td>
<td>15 ± 3</td>
<td>17 ± 3</td>
</tr>
<tr>
<td>PCWP (mm Hg)</td>
<td>32 ± 3*</td>
<td>23 ± 7</td>
<td>31 ± 6</td>
</tr>
<tr>
<td>CI (L/min/m2)</td>
<td>1.7 ± 0.7*</td>
<td>2.2 ± 1.0</td>
<td>1.8 ± 0.5</td>
</tr>
<tr>
<td>MVO2</td>
<td>45</td>
<td>55</td>
<td>60</td>
</tr>
<tr>
<td>6 min. walk (feet)</td>
<td>375</td>
<td>550</td>
<td>550</td>
</tr>
</tbody>
</table>

Hgb indicates hemoglobin; BUN, blood urea nitrogen; LDH, lactate dehydrogenase; AST, serum aspartate aminotransaminase; ALT, serum alanine aminotransaminase; PT, prothrombin time; APTT, activated partial thromboplastin time; RA, right atrial pressure; PCWP, pulmonary capillary wedge pressure; CI, cardiac index; MVO2, mixed venous oxygen saturation.
replacement therapy is the only option. Transplantation is limited by a shortage of donors, the complications of immunosuppression, and allograft vasculopathy. This has focused attention on mechanical circulatory assist devices for permanent use. Investigators have utilized mechanical energy in 3 ways to improve circulation. The first is direct augmentation of the heart, demonstrated by concepts such as dynamic cardiomyoplasty, the Abioboster (Abiomed Corp, Danvers, MA), and Direct Mechanical Ventricular Acutuation (DMVA). Cardiomyoplasty has not shown to be effective in advances stages of heart failure, because of operative mortality, the length of time needed to train the latissimus dorsi muscle, chronic muscle fatigue, and only marginal efficacy in improving myocardial function. The Abioboster and DMVA wrap around and squeeze the heart. These devices are still under development.

Another method of augmenting circulation is pumping blood from the left atria/ventricle, and to the aorta with enough force to maintain systemic blood pressure. The HeartMate/Thoratec,11-12 (Thoratec Inc, Pleasanton, CA) and Novacor11 (WorldHeart Corp., Ottawa, Canada), devices are currently FDA approved for ventricular assistance as bridges to transplantation. Current devices undergoing trial for permanent implantation include the HeartMate (REMATCH trial),12 Novacor (INTERMID trial), and the AbioCor total artificial heart (Abiomed Corp, Danvers, MA). These devices all have valves and deliver blood in a pulsatile fashion. Another group of devices pump blood in a nonpulsatile fashion using axial flow or centrifugal technology. All these devices are “obligatory.” That means that they cannot be stopped even for a short period of time without dire consequences for the patient such as thromboembolic events or VAD regurgitation.

The third method of mechanical assistance is to supply energy to portions of the vascular system to decrease the workload of the heart and increase cardiac output. This approach, referred to as diastolic augmentation, increases myocardial blood flow, increases diastolic blood pressure and decreases the systemic resistance applied to the heart during systole. The most common method to augment diastolic pressure is the IABP. It is the most frequently used mechanical assist device in the world (>100,000 uses annually, personal communication Datascope Corp). The most common use has been for treatment of cardiogenic shock, primarily ischemic but for other causes as well such as postcardiomyopathy, myocarditis, transplant rejection, and as a bridge to transplant.14 By increasing coronary blood flow and decreasing myocardial work, the heart is given an opportunity to recover.15,16 It is even used in chronic heart failure to recover patients from a decompensated state of CHF by decompressing the heart and bringing the myocytes to a better portion of the Starling Curve. Once the IABP is removed, the beneficial effects can be long-lasting.14

The dramatic results with the IABP led to attempts to create a permanent device. Named dynamic patch aortoplasty, the concept, was to replace portions of the descending aorta with a patch that could inflate and displace blood in the descending aorta.17 The initial system was made of layers of dacron, and although showed promise in hemodynamic super-
fixed to the optimal position in the descending aorta. There were no patients rejected from the study because of an inadequate response to the IABP. Other entry criteria were similar to that of the REMATCH trial\textsuperscript{12}—in fact, 4 of the patients had either refused entry into or were deemed too sick to be candidates for the REMATCH trial.

Despite the severity of illness in these patients, the study has demonstrated low surgical morbidity and mortality. The first patient done with left atrial to left femoral bypass expired since that amount of support was inadequate for the failing heart. With the use of CPB, all patients have survived and been able to be extubated within 48 hours. One patient who had preexisting pneumonia and was intubated before implantation, required reintubation 5 days after surgery and received a tracheostomy for controlled respiratory weaning. Bleeding has been minimal and subsequently, right heart failure has not been a problem. Injury to the spinal arteries and potential for paraplegia could be a potential concern. However, compared with aneurysm repair with a graft, the intercostals arteries are not disrupted and are allowed to perfuse normally. Additionally, the initial crossclamp is at the subclavian and 8 cm distal to this area. This arrangement allows sewing the proximal portion of the KCV without disrupting distal aortic perfusion. The 8 cm clamp is then moved to distally another 8 cm (16 cm from the subclavian) to allow complete implantation of the KCV. This technique limits distal cord ischemia to less than 20 minutes. This combined with distal arterial perfusion insures adequate cord perfusion.

This study has demonstrated the ability to implant the KCV safely. In addition, there is reversal of the heart failure syndrome with improved hemodynamics. All patients could be weaned off inotropic support while maintaining improved end-organ perfusion. At 1 month, there was reduction in PCWP, and RA pressures with an increase in cardiac index. There also was a significant improvement in renal function with normalization of serum creatinine levels. There was no deleterious effect of the KCV on red blood cells, platelet number, liver function or coagulation parameters. None of the patients received anti-coagulation for the KCV (1 patient was placed on coumadin for a prosthetic mechanical aortic valve) and there were no strokes or thromboembolic events. The KCV has also shown the ability to be used intermittently without any adverse events. Although, the patients required KCV assistance for the majority of the time, the device could be disconnected to allow for increased patient comfort. This allows them to shower or perform other activities of daily life without being tethered to any device. This nonobligatory feature simplifies outpatient management and reduces the impact of device failure in the field. The device is also very easy to use and has only a patient controlled on/off switch.

There were 2 device related problems that required KCV modifications. The driveline in the earlier patients showed accumulation of small brownish particles, which was discovered to arise from edema fluid that seeped into the PAD and became desiccated by the shunting of compressed air. This problem was corrected by making the PAD connection watertight. The fifth patient had an early leak form the PAD because of a manufacturing defect of the silastic/polycarbonate interface. The connection has been re-engineered to prevent this problem in the future.(personal communication, L.VAD Technology)

There are several limitations to this study. This initial trial was designed to test feasibility in surgical implantation and to test the concept of chronic diastolic augmentation. The number of patients enrolled was small, and although there were trends in many parameters, statistical significance was not obtained. Longer-term follow-up will be reported later as the data are obtained. This is a nonrandomized single arm trial and will be followed with a pivotal trial comparing the device to medical management.

In summary, this initial clinical experience with the KCV has demonstrated that it can be implanted with very low peri-operative morbidity and mortality. It is a novel nonobligatory device that has several advantages over other existing devices. There is no need for anti-coagulation, and no valves or internal electronics that could fail and force VAD replacement. The control algorithm is simple, as the device is triggered “on-demand” by the electrical activity of the native heart. Furthermore, it is nonobligatory so it can be turned on/off at will by the patient without increasing the risk of thromboembolic events. The disadvantages are that it provides only “partial” support. It increases cardiac output by approximately 40\% depending on the afterload condition of the patient. It depends on native heart activity to function and cannot be placed inpatients with severe biventricular function, uncontrolled tachyarrhythmias, or with native valvular disease. The degree of support obtained seems sufficient to reverse the heart failure syndrome, improve end-organ dysfunction and remove inotrope dependency. The KCV can be considered equivalent to a mechanical, permanent, and non-energy depleting inotrope. The Phase II pivotal trial will test the KCV in patients with compensated heart failure who are on intermittent or continuous inotropic therapy. Patients who are decompensated despite inotropes will require higher levels of circulatory support. Perhaps by treating advanced CHF early, the KCV may reduce the number of patients progressing toward cardiac replacement therapy with transplantation or a total artificial heart.

References


