SURGICAL INTERVENTIONS FOR TREATMENT OF END-STAGE HEART FAILURE: THE CLEVELAND CLINIC FOUNDATION EXPERIENCE

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End-stage heart failure poses a difficult challenge for medical treatment. Several surgical options have been tried to treat end-stage congestive heart failure. We retrospectively analyzed all patients who underwent surgical procedures for treatment of end-stage heart failure at the Cleveland Clinic Foundation. Included are 501 heart transplant (HTx) recipients and from the pool of patients waiting for heart transplant, 42 individuals undergoing ventricular remodeling procedure during the past 6 months. Additionally, 100 patients received the HeartMate left ventricular assist device (LV AD) as a bridge to transplant. Underlying etiologies for the LV AD group were ischemic heart disease and dilated cardiomyopathy, idiopathic dilated cardiomyopathy for the ventricular remodeling group, and for the HTx group dilated cardiomyopathy (ischemic or valvular heart disease). All three groups showed survival improvement and New York Heart Association (NYHA) functional class improvement compared to published data (cohorts of consensus and solvd trials). In the HTx group, there was an 88.2% 1-year actuarial survival estimate and 85% 2-year survival. In the ventricular remodeling group (from July to December 1996), most patients have been deactivated from the transplant list. In the early follow-up (few months), 72% had improved to functional class I or II (preoperatively 65% were NYHA functional class IV). The third group (LV AD) has shown improved survival rate awaiting transplant and improved quality of life; 80% pre-transplant survival and 92.3% 1-year post-LV AD-to transplant survival. Complications noted for LV AD included thromboemboli, bleeding, hemolysis, and infection (50% had positive blood cultures at some point). HTx complications were acute/chronic rejection, bleeding, infection, hypertension, and graft atherosclerosis. Ventricular remodeling complications are being monitored (still in its early stages). In addition to cardiac transplantation, promising new surgical techniques, such as ventricular remodeling and implantable left ventricular assist devices, are improving survival rate and quality of life for patients with end-stage heart failure.

IT HAS BEEN ESTIMATED that 3 million patients are suffering from congestive heart failure in the United States with 400,000 new cases every year.1-3 End-stage heart failure carries a high mortality and poor quality of life in spite of medical treatment with digitalis, diuretics, positive inotropic agents, and ACE inhibitors. Surgical interventions have emerged as alternative therapies for end-stage refractory cardiac disease. The Cleveland Clinic has developed and advanced a variety of options. Among these interventions are: implantable left ventricular assist devices (LV AD) which proved useful as bridge procedure in end-stage heart failure awaiting cardiac transplantation,4 heart transplantation and, most recently, ventricular remodeling.5

Cardiac transplantation at the Cleveland Clinic Foundation began on August 14, 1984.6 Since then, 501 patients have undergone this procedure.
Shortage of donors continues to be a major limiting factor for cardiac transplantation. Alternative therapies are being investigated, including xenotransplantation, cardiomyoplasty, axial-flow pumps, artificial hearts, implantable LV AD, and left ventricular remodeling. In the United States, the implantable LV AD appears to be the most likely first alternative to transplantation at present. At the Cleveland Clinic 100 devices were implanted since December 1991. A new surgical operation, ventricular remodeling, was recently introduced in the United States.

This novel procedure developed by the Brazilian surgeon, Rondas J.V. Batista, is showing compelling, although unpublished data. The Cleveland Clinic currently offers this operation to patients with nonischemic dilated cardiomyopathy who have a left ventricular (LV) end-diastolic dimension greater than 7 cm and are candidates for heart transplantation. The purpose of this presentation is to review the Cleveland Clinic Foundation experience with these promising surgical options and to compare patients' demographics, survival data, and complications.

Methods

Operative Technique

LV AD Implantation: The device most frequently used (Thermo Cardiosystems, Inc., Woburn, MA, USA) is implanted in a pocket in the left upper abdominal wall. Pump inflow is through a cannula inserted into the left ventricular apex, and the outflow conduit is anastomosed to the ascending aorta. Inflow and outflow tissue valves are used to control directional flow.

Ventricular Remodeling "The Batista Procedure": This procedure involves removal of a wedge from the left ventricle lateral wall (between the anterior and posterior papillary muscles). This causes a reduction in the left ventricular radius. By Laplace Law, this reduction seemingly produces a more efficient left ventricular contraction because of a reduction in wall stress.

Cardiac Transplantation: Myocardial preservation with cold crystalloid cardioplegia in the donor heart is followed by cold-blood cardioplegia when the heart arrives. A second dose of cardioplegia is given via a retrograde coronary sinus catheter followed by a 2-minute infusion of cardioplegia into the aortic root. This is repeated after 15 minutes. Prior to removing the aortic cross-clamp, warm blood at 50 mm Hg of pressure is infused into the coronary sinus until myocardial contraction is restored. Since 1992, the majority of transplants has been performed using direct caval anastomoses.

Patient Selection

LV AD: Heart transplant (HTx) candidates who are deteriorating, despite maximum medical therapy with positive inotropic agents and often intra-aortic balloon pump counterpulsation, receive LV AD support. The LV AD is used to stabilize the patient hemodynamically prior to heart transplantation. More recently, select patients have received LV ADs as a permanent implant if they fail to qualify for transplantation because of age, other co-morbidities, or inability to tolerate immunosuppression.

Ventricular Remodeling: The Cleveland Clinic offers this operation to patients with nonischemic dilated cardiomyopathy who have a LV end-diastolic dimension greater than 7 cm and who are candidates for heart transplantation.

Patients are still eligible for a HTx if not improved and can be "bridged" to a transplant with a mechanical left ventricular assist device if needed.

Cardiac Transplantation: This is the treatment-of-choice for patients with progressive incapacitating congestive heart failure in spite of adequate medical therapy. Currently, no age limit exists. Each patient is judged individually. Exclusion criteria are active infection, untreated malignancies (recently treated malignancies), irreversible end-organ dysfunction (significant renal or hepatic dysfunction, for example), drug dependence, a history of noncompliance, obesity, smoking, or diabetes mellitus with complications. Pulmonary vascular resistance is calculated as: PVR = (PA mean-wedge)/cardiac output. If higher than 5 "units" while receiving sodium nitroprusside, patients are excluded from heart transplantation because of "fixed" pulmonary hypertension.

Patient Demographics

LV AD (Figure I): Since December 1991, 100 patients have undergone this procedure as a "bridge" to transplantation. Before implantation, all patients were in severe cardiogenic shock, despite inotropes and an intra-aortic balloon pump. The average age...
of the patients was 52 ± 9 y and 86% were males. Seventy percent had ischemic heart disease, 25% had dilated cardiomyopathy, 2% had valvular cardiomyopathy, and 3% myocarditis.

**Ventricular Remodeling:** Since July 1996, 42 patients with class IV heart failure have undergone ventricular remodeling at the Cleveland Clinic Foundation. The average age was 52 ± 14 y and 76% were males. All patients had idiopathic dilated cardiomyopathy. Ischemic cardiomyopathy and active myocarditis were considered contraindications.

**Cardiac Transplantation** (Figure 2): There have been 501 patients undergoing heart transplantation at the Cleveland Clinic between August 1984 and December 1996. One patient underwent a combined heart/kidney transplant, and one patient received a liver transplant 18 mo after his HTx. The average age at transplant was 48 ± 13 Y and 76% were males. The average time on the waiting list was 111 ± 156 d (but with a range of 884 d). Duration of LV AD support was 77 ± 32 d. Average follow-up time has been 39 ± 33 mo (Table 1). Primary diagnosis was cardiomyopathy in 45% of cases, ischemic heart disease in 47.2%, valvular abnormality in 4.4%, and miscellaneous diseases in 3.4%. Previous thoracic surgery had been performed in 43% of patients.

**Statistical Analysis**

Group data are presented as the mean plus or minus the standard deviation. Survival estimates were made using the Kaplan-Meier method.

**Results**

**Survival Data**

All three groups showed survival improvement and New York Heart Association (NYHA) functional class improvement compared to cohorts of consensus and solvd trials.

**LV AD:** This group has shown improved survival rate awaiting transplant and improved quality of life; 80% pre-transplant survival and 92.3% 1-year post-transplant survival. The suitability for LV AD implantation was studied at the Cleveland Clinic.9 A scoring system based on criteria obtainable at the time of evaluation was developed. Oliguria, ventilator dependence, elevated central venous pressure, elevated prothrombin time, and reoperation status were found to increase risk of LV AD failure and mortality.

**Ventricular Remodeling:** In an early 6-month follow-up period, 72% of patients improved to functional class I or II (preoperatively, 65% were NYHA functional class IV and 35% class III). One patient died suddenly 3 months postoperation after dramatic functional improvement. Another
Since 1984, 120 patients died. The most common cause of mortality was graft rejection (50%) and infection (13%). Tables 2 and 3 describe select characteristics for the 120 nonsurvivors. At later stages cardiac output deteriorates and systemic vascular resistance rises, leading to hypoperfusion of organs and ultimately shock. Mechanical support with intra-aortic balloon pump counterpulsation may be necessary before surgical intervention. Cardiac transplantation is considered for patients with intractable end-stage heart failure in spite of all other medical or surgical treatments.

15-month-old child died one month postoperation. The average postoperative hospital stay was 10 d.

Cardiac Transplantation (Figure 3): (KaplanMeier survival estimates from first transplant) There has been an 88.2% one-year, 85% two-year, 70% five-year, and 50% ten-year survival rate. Post-transplant hospital stay has decreased to 15.5 d.

Complications

LVAD: Infection in implantable LV AD patients is common.IO This includes driveline infection, septic embolus, and device infection. Pathogens isolated from the bloodstream during LV AD support were Candida species, Staphylococcus aureus, Staphylococcus epidermidis, Enterococcus species, Pseudomonas aeruginosa, and Enterobacter species. Early bleeding which required reoperation was a problem in a small group of patients who had low factor VII and XI and hepatic dysfunction. 11 Thromboembolic risk from cardiac and pump source is still to be studied.4

Ventricular Remodeling: This procedure is still in the early stages and data are still to be analyzed in the near future. So far, recurrence of congestive heart failure is the prominent complication requiring LV AD and/or transplant.

Cardiac Transplantation: Rejection is treated with corticosteroids and with OKT3 if steroid resistant. Table 4 describes rejection information.
for the 375 survivors based on their biopsy results (within 6 months post-transplant). Infection prophylaxis includes administration of ganciclovir postoperatively for patients at risk for cytomegalovirus. Hypertension and hyperlipidemia associated with cyclosporine has an enhancing effect on the accelerated graft atherosclerosis. In a recent study done at the Cleveland Clinic on 50 recipients, during the first few weeks after transplantation, intravascular ultrasound imaging detected coronary atherosclerosis in 56%.12

Table 4. Survivors: describing rejections. *

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<thead>
<tr>
<th>Biopsy degree</th>
<th>Percent</th>
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<tbody>
<tr>
<td>Mild accelerated</td>
<td>11.7</td>
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<tr>
<td>Mild acute</td>
<td>41.9</td>
</tr>
<tr>
<td>Minimal</td>
<td>10.8</td>
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<tr>
<td>Moderate</td>
<td>17.7</td>
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<tr>
<td>Resolving</td>
<td>16.5</td>
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<tr>
<td>Severe</td>
<td>1.5</td>
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*From the Cleveland Clinic Foundation, Cleveland, Ohio, USA.

End-stage heart failure is a complex phenomenon. It becomes more frequent with our aging population and with the new drug therapies that improved survival in acute myocardial infarction. It is usually due to diseases, such as hypertension, coronary artery disease, valvular heart disease, and cardiomyopathies (dilated or ischemic). Decreased cardiac output and poor oxygenation impair regular activity and disrupt quality of life. Current treatments include dietary sodium and fluid restriction and administration of specific pharmacological agents (diuretics, digitalis, vasodilators, inotropic agents, ACE inhibitors).

At later stages cardiac output deteriorates and systemic vascular resistance rises, leading to hypoperfusion of organs and ultimately shock. Mechanical support with intra-aortic balloon pump counterpulsation may be necessary before surgical intervention. Cardiac transplantation is considered for patients with intractable end-stage heart failure in spite of all other medical or surgical treatments.
The 1-year survival rate of transplantation improved from 50% in the mid-1970s to 85% to 90% today. At present, it is superior to all other forms of treatment (Figure 4). The number of HTx is increasing steadily at the Cleveland Clinic Foundation (Figure 5) as well as the volume of transplantation reported to the Registry of the International Society for Heart and Lung Transplantation (ISHLT). Still, it is a relatively small number compared to the large number of patients awaiting HTx. The limited availability of donor hearts and the cost of the procedure are the main limiting factors. For these reasons, alternative therapies are considered as bridges to transplantation while patients are waiting for a donor heart.

In select patients, LV AD appears to be an acceptable bridge to HTx. The Cleveland Clinic Foundation experience with 100 cases has shown definite improvement in quality of life and improved survival while awaiting for HTx. The improvement in technology has made the device portable with less morbidity. At present, the Cleveland Clinic Foundation and the National Institutes of Health have begun a trial to consider LV AD insertion as a permanent form of therapy for end-stage congestive heart failure. Ventricular remodeling is reserved for patients with idiopathic dilated cardiomyopathy. All patients undergo a battery of sequential studies to detail pre- and postoperative cardiac performance. These studies include hemodynamic measurements, echocardiography, magnetic resonance imaging, measurement of cytokine and neurohormone levels, metabolic stress tests, and quality-of-life analyses. With time, data will accumulate about these new procedures and will help in selecting the patients who would benefit from them as a final therapy for end-stage heart failure.

In conclusion, it appears that LV AD and ventricular remodeling are viable options as bridges...
to cardiac transplantation in an era of limited donor hearts. Although we do not have extended follow-up data yet on the long-term efficacy and safety of these two options, they seem to be promising alternatives to HTx in select patients. HTx, despite its limitations, remains the best option for select patients with end-stage intractable congestive heart failure. More research and time are needed to investigate the new alternatives.

References