Heart Transplantation After Cardioverter-Defibrillator Implantation

A Case Control Study


A case control study was performed to determine whether previous implantable cardioverter-defibrillator (ICD) insertion adversely affects outcome after heart transplantation. Six male heart transplant recipients who had undergone ICD insertion 12±5 months before heart transplantation were compared to a cohort of six heart transplant recipients who were matched according to age, preoperative status and hemodynamics, date of transplantation, graft ischemic time, history of a previous cardiac operation, and duration of follow-up. There were no significant differences in operating room time, chest tube drainage, time to extubation, and the duration of intensive care unit or hospital stay between the two groups. Furthermore, there were no significant differences in the number of units of packed cells, fresh frozen plasma, platelets and cryoprecipitate transfused. The number of treated rejection episodes and the number of patients requiring intravenous antibiotics for infection in the first 90 days was identical between groups.

It was concluded that heart transplantation after ICD implantation did not appear to carry more risk than heart transplantation after a previous cardiac operation. Our limited experience supports the potential use of the ICD in patients with life-threatening ventricular dysrhythmias who are awaiting transplantation.  

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In recent years, the waiting time for heart transplant candidates has increased significantly, due to an increasing number of transplant centers without a corresponding increase in the donor heart supply. A significant minority of heart transplant candidates die suddenly, presumably due to ventricular dysrhythmias. The implantable cardioverter-defibrillator (ICD) has proved highly effective in decreasing the incidence of sudden death in selected patients with life-threatening ventricular dysrhythmias. Recent reports have emphasized the potential role of the ICD as a "bridge" to heart transplantation. However, no study has examined the relative risks of heart transplantation in the months and years following insertion of the ICD. We, therefore, conducted a case control study, comparing patients undergoing heart transplantation after previous ICD implantation with a matched group of patients undergoing transplantation after a previous cardiac operation.

PATIENTS AND METHODS

Our center has performed 304 heart transplant operations since 1981, as well as 75 ICD implantations since 1984. The ICD device was implanted intrapericardially by either a median sternotomy or left subcostal approach, according to previously-specified indications.

Usually, two or three epicardial patch electrodes and two pace-sense electrodes were positioned on the heart, and the ICD was implanted after three successful defibrillations at stored energies of less than or equal to 18 J. Heart transplantation was considered in these patients if symptoms of intractable heart failure developed despite appropriate medical management with digoxin, diuretics, and angiotensin-converting enzyme inhibitors. In addition, patients were listed for heart transplantation if the ICD discharged on multiple occasions despite maximal antarrhythmia therapy, and the device could therefore no longer be tolerated by the patient. In our experience, six patients were listed for transplantation following ICD implantation: three for the former, and three for the latter indication.

The six patients undergoing heart transplantation following ICD insertion were compared to a cohort of patients who had undergone a previous cardiac operation before transplantation, and who had undergone transplantation within the same 3-month interval. The ICD was routinely deactivated immediately prior to skin incision. In both groups of patients, median sternotomy was performed with the oscillating or reciprocating saw after all sternal wires were removed. Initially, tissues adherent to the ascending aorta and right atrium were cleared, and cardiopulmonary bypass was established using an ascending aortic and two vena caval cannulae. In one ICD patient, recurrent ventricular fibrillation prompted urgent femoral arterial and venous cannulation prior to pericardial dissection. The ascending aorta was routinely clamped before dissection of the heart from the pericardial wall. In the ICD group, patch electrodes placed on the left ventricular epicardium were left in situ if adhesions were extremely dense and there was a risk of injuring the phrenic nerve. In all cases, the generator was completely removed via a separate left subcostal incision during the reperfusion phase after donor heart implantation. Packed cells were transfused intraoperatively and postoperatively to maintain a hemoglobin value of...

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In addition, fresh frozen plasma, and on occasion, cryoprecipitate were transfused if pericardial bleeding was problematic and the prothrombin and partial thromboplastin times were prolonged. Likewise, platelets were transfused for a similar indication if the platelet count was less than 50,000/mm³. No patient in the ICD or cohort group received aprotinin perioperatively.

All patients undergoing heart transplantation were treated with a similar immunosuppressive regimen.11 Methylprednisolone, 500 mg, was administered intraoperatively, followed by methylprednisolone or prednisone in an initial dose of 1 mg/kg/day, with a taper to 0.2 mg/kg/day by 3 months postoperatively. All patients received a 1-week course of Minnesota antilymphocyte globulin, in an initial dose of 15 mg/kg/day, with subsequent titration to keep the absolute lymphocyte count less than 300/mm³. Cyclosporine was begun orally on postoperative day 3, and the dose was titrated to achieve a whole blood radioimmunoassay trough level of 300 to 500 ng/ml. This level of cyclosporine was maintained for the first year, and then allowed to decrease to 200 ng/ml by 2 years, and then to 100 ng/dl by 3 years, provided that rejection was not present. Azathioprine was used selectively, for previously-specified indications.11 Endomyocardial biopsies were performed at 1, 2, 3, 4, 6, 8, 10, and 12 weeks postoperatively, then at 3-month intervals until the first anniversary of transplantation, and at yearly intervals thereafter. Only moderate (grade IIa or greater) rejection was treated, usually with a boost of oral prednisone at a dose of 1 mg/kg for 3 days, followed by a taper to maintenance levels.

All data were obtained by retrospective chart review. Numeric data were expressed as means ± standard error of the mean. Values between groups were compared using the two-tailed Student's t-test. A p value < 0.05 was deemed significant.

RESULTS

All six patients in the ICD group were men and had undergone insertion of the device at a mean age of 48 ± 2 years. Two patients had received an early-model ICD (CPI AID-B), whereas in four patients, a PCD unit (Medtronic models 7215 or 7216A) was implanted. The mean interval between ICD implant and heart transplantation was 12 ± 5 months. The matched cohort group consisted of four men and two women who had undergone a redo sternotomy and heart transplantation within the same 3-month interval as the individual study patients. The mean duration between the first cardiac operation and heart transplantation in the cohort group was 46 ± 15 months. The two groups of patients had an identical preoperative clinical status, according to the grading system employed by the Multiple Organ Retrieval and Exchange system in the province of Ontario. At the time of transplantation, patients in the ICD group had a mean age of 49 ± 2 years, compared to 46 ± 5 years in the cohort

Table 1—Comparison of Intraoperative Variables Between Groups

<table>
<thead>
<tr>
<th></th>
<th>Matched Group</th>
<th>Matched Group</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operating room time, min</td>
<td>525 ± 89</td>
<td>465 ± 57</td>
<td>0.58</td>
</tr>
<tr>
<td>Cardiopulmonary bypass time, min</td>
<td>178 ± 26</td>
<td>144 ± 7</td>
<td>0.23</td>
</tr>
<tr>
<td>Total graft ischemic time, min</td>
<td>186 ± 32</td>
<td>231 ± 39</td>
<td>0.39</td>
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</table>

*Values are expressed as mean ± standard error.
Table 2—Comparison of Blood Loss and Transfusion Requirements Between Groups*  

<table>
<thead>
<tr>
<th></th>
<th>ICD Group</th>
<th>Matched Cohort Group</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest tube drainage at 24 h, ml</td>
<td>2,347 ± 1,819</td>
<td>1,185 ± 263</td>
<td>0.50</td>
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<tr>
<td>Chest tube drainage at 48 h, ml</td>
<td>2,844 ± 2,166</td>
<td>1,993 ± 472</td>
<td>0.68</td>
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<tr>
<td>Packed cells transfused, units/hospital stay</td>
<td>20 ± 11</td>
<td>10 ± 3</td>
<td>0.41</td>
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<tr>
<td>Fresh frozen plasma transfused, units/hospital stay</td>
<td>16 ± 9</td>
<td>9 ± 2</td>
<td>0.46</td>
</tr>
<tr>
<td>Platelets transfused, units/hospital stay</td>
<td>21 ± 12</td>
<td>9 ± 3</td>
<td>0.34</td>
</tr>
<tr>
<td>Cryoprecipitate transfused, units/hospital stay</td>
<td>8 ± 5</td>
<td>4 ± 3</td>
<td>0.52</td>
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</tbody>
</table>

*Values are expressed as mean ± standard error.

shown in Table 1. The “operating room time” includes the duration from patient arrival in the operating room until his departure for the intensive care unit. There were no significant differences in operating room time, duration of cardiopulmonary bypass, or total ischemic time of the heart graft between groups. In two patients in the ICD group, all of the leads and patch electrodes were removed without phrenic nerve injury or further bleeding. In four patients in the ICD group, some hardware was left in situ, including posterolateral wall patch electrodes and lead remnants in two patients (Fig 1 and 2) and subcostal lead remnants only in two other patients.

The chest tube drainage and requirement for packed cells and blood factor components in the two groups is depicted in Table 2. One patient in each group required reoperation because of coagulopathic bleeding postoperatively. There were no significant differences between groups in the total chest tube drainage at 24 and 48 h postoperatively, and in the requirement for packed cells, fresh frozen plasma, platelets, and cryoprecipitate.

The postoperative course of the two groups of patients is compared in Table 3. There were no significant differences in the time to extubation or the duration of inotropic support between groups. One patient in the ICD group developed staphylococcal pneumonia and a right lower lobe lung abscess, necessitating a prolonged stay in the intensive care unit. Nevertheless, the mean durations of intensive care unit stay were not statistically different between groups; if the ICD patient with the lung abscess is excluded, the intensive care unit stays were markedly similar. The average duration of hospital stay prior to discharge was identical in the two groups, as was the number of rejection episodes requiring increased immunosuppression during the first 90 postoperative days. Furthermore, three patients in each group required reinstitution of intravenous antibiotics for infection postoperatively. One patient in the ICD group developed staphylococcal mediastinitis, necessitating debridement and the institution of a close irrigation system for 2 weeks; no hardware had been left in this patient at the time of the transplantation. The most common infectious complication was pneumonia, which occurred in three patients in the ICD group and two patients in the cohort group. One ICD patient died of rejection at 31 days and one in the cohort group died of cytomegalovirus and Pneumocystis carinii pneumonia at 5 months postoperatively.

The mean duration of follow-up to date is 41 ± 7 months in the ICD group and 47 ± 8 months in the cohort group. All ten survivors are in functional class I. In no case has retained ICD patch electrodes or lead remnants caused morbidity.

Comment

In recent years, the ICD has been implanted in several thousand patients world-wide for recurrent, life-threatening ventricular dysrhythmias. The operative mortality rate in large series has ranged from 1.5 to 5.5 percent,3,5 and compared to historic control subjects, the actuarial incidence of sudden cardiac death has been reduced dramatically.3,5 Most of the patients receiving an ICD have poor ventricular function, often due to one or more myocardial infarctions as a result of extensive coronary artery disease. Indeed, a large study with almost complete long-term follow-up reported a 20 percent actuarial incidence of nonsudden cardiac death at 5 years in patients receiving an ICD.3

Despite the large number of patients who have undergone ICD implantation world-wide, there are only a few published reports of heart transplantation after ICD insertion, and the number of patients in each study has been small. Bolling and associates6 reported five patients who underwent heart transplanta-
transplantation after ICD implantation; these patients had been listed as candidates for cardiac transplantation and had received an ICD as a "bridge" to transplantation. Very few data were presented concerning the postoperative course of these patients, except that four of them were alive and well 1 to 25 months after transplantation. A recent abstract by Siegel and associates referred to ten patients undergoing heart transplantation after previous insertion of an ICD. No perioperative or postoperative data were reported, and the main focus of this study was on the "bridging" of heart transplant candidates to transplantation with the ICD.

In our experience, no patient underwent ICD implantation initially for the purpose of sustaining them until transplantation. Patients who were found to have recurrent malignant ventricular dysrhythmias in the setting of uncontrolled heart failure were referred for heart transplantation rather than ICD insertion at the outset. All six patients in whom the ICD was implanted experienced significant initial benefit from the device. Three patients subsequently developed severe heart failure, with functional class 4 disability, that could not be reversed by optimal medical management. An additional three patients experienced repeated shocks despite treatment with antiarrhythmic agents including amiodarone. They were disabled by the profound psychological impact of repeated shocks and were therefore referred for transplantation even though their heart failure status was functional class 3.

There is no clear consensus in the literature as to which patients awaiting heart transplantation should receive an ICD, or whether this device should, in fact, be used as a "bridge" to heart transplantation. A recent multicenter retrospective analysis of 309 patients with coronary artery disease awaiting heart transplantation revealed a 1 year actuarial risk for sudden cardiac death of 20 percent. Sudden cardiac death accounted for a greater proportion of mortality among patients in functional class 3 as opposed to functional class 4, although a larger proportion of class 4 patients received a transplant during the follow-up interval. The authors concluded that a bridge-to-transplant trial using an ICD would be most efficient if performed in heart transplant candidates with functional class 3 symptoms. A recent report by Lindsay and colleagues demonstrated that signal-averaged electrocardiographic analysis and the response to programmed ventricular stimulation improve risk stratification for sudden cardiac death in heart transplant candidates. Clearly, if a prospective, randomized bridge-to-transplant trial was to be carried out using the ICD, only patients with the highest risk for dysrhythmic death and the maximum potential for benefit should be included.

The results of this study demonstrate that patients with an ICD may undergo heart transplantation with a similar expectation of risk as other patients who have had a previous cardiac operation. Although the chest tube drainage and perioperative transfusion requirements were not statistically different between the ICD and cohort groups, the perioperative blood loss was greater than in patients undergoing a first-time sternotomy and heart transplant. Although extrapericardial patch placement may have resulted in less pericardial hemorrhage perioperatively than intrapericardial patch insertion, the risk of pulmonary and pleural bleeding would undoubtedly have been greater during patch explantation. We have been impressed at the ability of intraoperative aprotinin therapy to markedly reduce perioperative blood loss during redo operations, and now use it routinely in patients undergoing heart transplantation after a previous cardiac procedure. Moreover, we have been encouraged by new developments in transvenous defibrillation lead technology that may obviate the need for epicardial patch electrode placement in some patients. Further experience with ICD patients undergoing heart transplantation will lead to additional strategies to reduce postoperative morbidity and lessen transfusion requirements in this subset of transplant recipients.

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