Heart Transplantation and the Batista Operation for Children With Refractory Heart Failure

Medically refractory heart failure may be present in children with cardiomyopathy (CMP) or complex congenital heart disease (CHD). In adults, the surgical management of this condition is either heart transplantation or the Batista operation. From March 1995 to January 2000, a total of 6 children, aged from 1 to 16 years, with medically refractory heart failure associated with CMP or complex CHD underwent cardiac transplantation and one of them also had the Batista operation as a bridge to transplantation. One of the 6 patients died of intractable sepsis 17 days after the operation, but the other 5 were discharged with satisfactory hemodynamics. Immunosuppressive agents, including azathioprine, cyclosporin or FK-506, were given. One patient experienced moderate acute rejection, but it was controlled by FK-506, OKT-3 and solumedrol. However, another suffered from lymphoproliferative disease 8 months after transplant, but it was controlled by intravenous immunoglobulin, interleukin-7, interferon and acyclovir. Cardiac function during serial follow-up (range, 1 month to 5 years) revealed normal systolic and diastolic function and none received any anticongestive medications. Almost all patients received an oversized donor heart. The left ventricle (LV) mass was remodeled, initially as an increase and later as a decrease. The patient who underwent the Batista operation was discharged 1 month after the operation with an increased LV ejection fraction (from 10% to 22%). She was successfully bridged to heart transplantation 7 months after the Batista operation. The results of cardiac transplantation in growing children are satisfactory and the Batista operation may be adopted as a bridge to heart transplant with a fair response.

Key Words: Batista operation; Cardiomyopathy; Complex congenital heart disease; Heart transplant

Before the era of cardiac transplantation, medical treatment was the only way of managing patients with dilated cardiomyopathy (DCMP), so for those with medically refractory heart failure, the outcome was dismal. For patients with complex congenital heart disease (CHD), many delicate surgical procedures were advocated, and they indeed improved the survival of these patients. For example, total cavopulmonary circulation, the so-called Fontan procedure, for single ventricle disease. However, despite improved short-term and even long-term survival, the patients’ quality of life and their exercise tolerance was different from the normal population. In addition, complications such as arrhythmia, thromboembolic episodes, late heart failure, central nervous system dysfunction, liver function impairment and protein-losing enteropathy further limited its success.

After cardiac transplantation was successfully performed in 1967, it was soon being performed in pediatric patients and with advances in surgical technique, its long term outcome is now satisfactory. Cardiac transplant has now become the mainstay of treatment for medically refractory heart failure, but the shortage of donor hearts is still the major concern. The Batista operation was introduced in 1994 for medically refractory heart failure with DCMP and other types of congestive heart failure associated with dilated ventricles. The preliminary reports in adult patients are that cardiac function improves after the operation, and it has been suggested as a bridging operation to heart transplantation. As shown in previous reports, while patients are on transplantation waiting list, the 1-year mortality is 60% in children and 76% in infants if transplantation is not performed, which highlights the importance of early surgical management of medically refractory heart failure. Here we present our experience of surgical treatment of children with medically refractory congestive heart failure.

Methods

Study Population
From March 1995 to January 2000, 6 pediatric patients (age at operation less than 18 years; Table 1) had surgical management for medically refractory heart failure: cardiac transplantation in 6 patients, one of whom also had the Batista operation. The underlying disease was idiopathic DCMP in 3 patients, restrictive CMP in 1, and complex CHD in 2. All patients were New York Heart Association (NYHA) functional class IV before operation.

Surgical Technique
In the 2 patients with complex CHD, surgical palliation had been performed before transplant (Table 2): patient No.
received a Blalock-Taussig shunt for palliation at 1 and 2 years of age, respectively, and a bi-directional Glenn shunt at 6 years; patient No. 5 underwent pulmonary artery banding with patent ductus arteriosus ligation at 1 year old, B-T shunt at 3 years, and total cavopulmonary connection (Fontan operation) at 9 years. All 6 patients received a cardiac transplant; patient No. 6 underwent a preliminary Batista operation because of a lack of a donor heart and cardiac transplant was then done 7 months later. Total ischemia time ranged from 57 min to 330 min. All patients received an oversized donor heart and the donor – recipient bodyweight (BW) ratio was up to 3.6, as in patient No. 2. Despite this significant BW discrepancy, however, the heart size ratio measured during operation showed no significant difference.

The immunosuppressant protocol was: antithymocyte globulin and solumedrol for induction, and triple therapy with azathioprine, prednisolone and cyclosporin as maintenance therapy. Endomyocardial biopsy was performed weekly during the 1st week, biweekly in the 2nd month, monthly for 6 months, and yearly thereafter. FK-506 and mycophenolate mofetil were used if severe rejection or adverse reaction occurred after using the standard immunosuppressants.

Follow-up and End-Point
All patients had regular follow up, including echocardiography.

### Table 1 Clinical Characteristics of 6 Patients

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Underlying disease</th>
<th>Age at onset</th>
<th>Age at surgery</th>
<th>Indication for surgery</th>
<th>Complication prior to surgery</th>
<th>Prior surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14</td>
<td>F</td>
<td>DCMP</td>
<td>3 years</td>
<td>9 years 7 months</td>
<td>LVEF 8%</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>M</td>
<td>DCMP</td>
<td>4 months</td>
<td>14 months</td>
<td>LVEF 20%</td>
<td>LV thrombus</td>
<td>Nil</td>
</tr>
<tr>
<td>3</td>
<td>16</td>
<td>F</td>
<td>Double inlet left ventricle, right atrial isomerism</td>
<td>Birth</td>
<td>16 years</td>
<td>LVEF 13%</td>
<td>Protein-losing enteropathy</td>
<td>Nil</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>F</td>
<td>Dextrocardia Situs ambiguous RV dominance, TGA, PS</td>
<td>Birth</td>
<td>6 years 8 months</td>
<td>Hypotension Desaturation</td>
<td>Failed Glenn shunt</td>
<td>1,2Y: B-T shunt 9Y: Fontan op</td>
</tr>
<tr>
<td>5</td>
<td>16</td>
<td>F</td>
<td>Restrictive CMP r/o myocarditis</td>
<td>12 years 9 months</td>
<td>14 years 8 months</td>
<td>Diastolic dysfunction</td>
<td>Atrial fibrillation</td>
<td>Nil</td>
</tr>
<tr>
<td>6</td>
<td>4</td>
<td>F</td>
<td>DCMP</td>
<td>5 months</td>
<td>3 years 4 months (Batista op) 3 years 11 months (Transplant)</td>
<td>LVEF 10%</td>
<td>LVEF 28%</td>
<td></td>
</tr>
</tbody>
</table>

### Table 2 Surgical Data in 6 Patients

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Operation</th>
<th>Ischemia time (min)</th>
<th>Pre-op PAP (mmHg)</th>
<th>Donor/recipient BW (kg)</th>
<th>Donor/recipient age (years)</th>
<th>Heart size ratio</th>
<th>Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Transplant</td>
<td>57</td>
<td>58/38</td>
<td>53/22</td>
<td>16/9</td>
<td>45/50</td>
<td>Subendocardial fibrosis</td>
</tr>
<tr>
<td>2</td>
<td>Transplant</td>
<td>200</td>
<td>NA</td>
<td>20/5.5</td>
<td>6/1</td>
<td>1.2/1</td>
<td>RV endocardial fibroelastosis</td>
</tr>
<tr>
<td>3</td>
<td>Transplant</td>
<td>240</td>
<td>18</td>
<td>51/34</td>
<td>16/16</td>
<td>NA</td>
<td>Complex CHD</td>
</tr>
<tr>
<td>4</td>
<td>Transplant</td>
<td>330</td>
<td>22/8</td>
<td>26/16</td>
<td>7/6</td>
<td>NA</td>
<td>Complex CHD</td>
</tr>
<tr>
<td>5</td>
<td>Transplant</td>
<td>99</td>
<td>32/20</td>
<td>69/42</td>
<td>18/14</td>
<td>NA</td>
<td>Hypertrophic cardiomyopathy</td>
</tr>
<tr>
<td>6</td>
<td>Transplant</td>
<td>218</td>
<td>20/9</td>
<td>42/12</td>
<td>16/4</td>
<td>NA</td>
<td>Subendocardial fibrosis</td>
</tr>
</tbody>
</table>

NA, no analysis; PAP, pulmonary arterial pressure; BW, body weight; CHD, congenital heart disease.

4 received a Blalock-Taussig shunt for palliation at 1 and 2 years of age, respectively, and a bi-directional Glenn shunt at 6 years; patient No. 5 underwent pulmonary artery banding with patent ductus arteriosus ligation at 1 year old, B-T shunt at 3 years, and total cavopulmonary connection (Fontan operation) at 9 years. All 6 patients received a cardiac transplant; patient No. 6 underwent a preliminary Batista operation because of a lack of a donor heart and cardiac transplant was then done 7 months later. Total ischemia time ranged from 57 min to 330 min. All patients received an oversized donor heart and the donor – recipient bodyweight (BW) ratio was up to 3.6, as in patient No. 2. Despite this significant BW discrepancy, however, the heart size ratio measured during operation showed no significant difference.

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### Table 4 LV Parameters of Echocardiography in Patients Prior and Post Operation

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Pre-operative</th>
<th>1 week</th>
<th>1 month</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LVEF</td>
<td>LV mass (g)</td>
<td>LVEF</td>
</tr>
<tr>
<td>1</td>
<td>32.5%</td>
<td>5.13/4.5</td>
<td>65%</td>
</tr>
<tr>
<td>2</td>
<td>23%</td>
<td>3.78/3.39</td>
<td>79%</td>
</tr>
<tr>
<td>3</td>
<td>13%</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>4</td>
<td>NA</td>
<td>NA</td>
<td>77%</td>
</tr>
<tr>
<td>5</td>
<td>Diastolic dysfunction (71%)</td>
<td>3.71/2.14</td>
<td>66%</td>
</tr>
<tr>
<td>6</td>
<td>28%</td>
<td>6.07/5.25</td>
<td>68%</td>
</tr>
</tbody>
</table>

NA, no analysis; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic dimension; LVESD, left ventricular end-systolic dimension.
ography and endomyocardial biopsy, after transplant. The primary end point of the study was death.

**Results**

Of the 5 patients receiving cardiac transplantation only, 1 died 17 days after operation (patient No. 3) (Table 3). That patient’s postoperative course was complicated with cardiac tamponade, septic shock, repeated thrombosis of the superior vena cava, and right upper limb gangrene. Clinical and laboratory result indicated sepsis with disseminated intravascular coagulation, and powerful antibiotics were given. The endomyocardial biopsy taken 1 week after operation showed no evidence of rejection, but she died from the intractable sepsis. The transplantation success rate in this study was 83%.

The other 4 patients were all doing well during the follow-up that ranged from 1.5 years to nearly 5 year. All showed a dramatic improvement in left ventricular ejection function (LVEF) to greater than 60% after transplant (Table 4). No anticongestive medication was given, and all had a normal NYHA functional class I life. Patient No. 6 received a preliminary palliative Batista operation, after which her LVEF improved from 10% to 28% and she was then tapered off intravenous inotropic agents. However, she still needed anticongestive medication at home, and intravenous inotropic agents intermittently. Cardiac transplantation was performed smoothly 7 months later and she no longer needs anticongestive drugs and her LVEF improved to 68% after the transplant.

None of the 5 survivors experienced severe rejection. Moderate rejection was noted in patient No.1 and was controlled with FK506, OKT-3 and solumedrol. Acute humoral rejection was detected in patient No.5 and was controlled by FK-506 and mycophenolate mofetil. Patient No. 2 developed post-transplant lymphoproliferative disorder, presenting as neck lymphadenopathy 8 months after operation. Biopsy confirmed the diagnosis, and after reducing the cyclosporin dose and giving interferon, acyclovir and intravenous immunoglobulin (IVIG), it then regressed. A positive IgM study for Epstein-Barr virus (EBV) suggested the cause of the lymphoproliferative disease. Patient No. 1 also had the complication of subarachnoid hemorrhage postoperatively, which although it resolved without surgery, the patient had partial seizures that were controlled with carbamazepine.

As regards infection, patient No. 2 suffered from *Staphylococcus hominis* and *S. epidermidis* sepsis 2 months after operation, which was controlled with antibiotics. Serology detected cytomegalovirus (CMV) infection in patients No. 2 and 4, which was controlled with ganciclovir.

From the serial echocardiography follow-up of the left ventricular (LV) parameters after transplantation, we found that the oversize heart transplant was gradually remodeled,
with an initial decrease in heart size and a gradual increase thereafter (Table 4).

Discussion

Pediatric cardiac transplantation has blossomed since 1980, and the number of patients has been steadily increasing to 352 patients worldwide in 1997. Cardiac transplantation can be applied to almost all kinds of heart failure, but the most common underlying diseases for which pediatric patients receive heart transplantation are CMP and decompen-sated CHD, which together account for more than 90% of patients. It is often performed in patients with congestive heart failure unresponsive to aggressive medical control and conventional palliative surgery, and with a NYHA functional class III–IV, and a LVEF less than 20%. The contraindica-tions of cardiac transplantation are similar to those for other transplants; that is, untreated infection, severe irreversible liver or kidney disease (except when simultaneous liver or kidney transplant is considered), active ulcer, malignancy, and psychiatric disorder. However, the patient with pulmo-ny vascular resistance greater than 6–8 Wood units is not a candidate for transplant, and these patients often need a heart–lung transplant.

Generally, survival after heart transplantation is favorable; reported survival rates are 1-year 76%, 5-year 64% and 10-year 55%. The younger the age at operation, especially in a candidate for transplant, and these patients often need a heart–lung transplant.

After cardiac transplantation, infection, acute or chronic rejection, and graft failure accounts for most of the causes of failure in the world registry and an adult series in Taiwan. Infection is still one of the major causes of death after transplantation, with a reported incidence of 50–75% in the 1st to 2nd year of follow-up causing 16–25% of the deaths after transplantation. In the present patients also, the only death was related to uncontrollable sepsis.

Acute rejection is common and occurs in more than half the patients after cardiac transplantation. Most cases of rejection are mild, and only regular follow-up is necessary. In those with more than mild rejection, early treatment with strong immunosuppressants can lead to a good outcome. The clinical manifestations of acute rejection include hypoten-sion (blood pressure drop more than 20 mmHg), hyperther-mia, malaise, tachycardia, arrhythmia, and cardiomegaly. However, not all patients with rejection have typical symp-toms, so routine endomyocardial biopsy is advocated for early detection. In the present study, 1 patient had moderate rejection (ISHLT grade IV), 1 had acute humoral rejection, and 1 had mild rejection (ISHLT grade I–II), and all were confirmed by endomyocardial biopsy. The moderate rejec-tion and acute humoral rejection both manifested as unstable blood pressure and increased LV mass and LV dilatation on echocardiography. The case of mild rejection was detected by routine endomyocardial biopsy. Although the role of echocardiography in the detection of acute rejection is still controversial, it can be an adjunct to biopsy for early detec-tion. None of our patients had any clinical evidence of chronic rejection (post-transplant coronary artery disease). Coronary angiography was performed in 2 patients whose follow-up was longer than 2 years (patients No. 1 and 2), and no coronary artery disease was detected. In Chinese patients, the incidence of chronic rejection is low, which may be related to a low incidence of active CMV infection and acute rejection episodes, less racial disparity and less human leukocyte antigen mismatches.

Post-transplantation lymphoproliferative disease, which occurs in 2–6% of patients after transplantation, is thought to be caused by EBV-related B cell proliferation and may progress to lymphoma or Hodgkin disease. Patient No. 2 had neck lymphadenopathy 8 months after operation, and the pathology revealed post-transplantation lymphoproliferative disease. After aggressive treatment with IVIG, β-interferon and acyclovir, and a reduction in the cyclosporin dose, it regressed. The mortality rate in patients with post-transplant lymphoproliferative disease is reported to be as high as 36%, and can be up to 70% if disseminated; early detection and management are mandatory for this potentially lethal disorder.

As shown in the present study, the donor–recipient BW ratio does not correlate with heart size ratio during operation, because the heart size markedly increased in the recipients and the BW ratio between the donor and recipient was up to 3.6 without a heart size discrepancy. An oversize donor heart need not be a contraindication in pediatric cardiac transplant, and in the present study the oversized heart transplants did not influence post-transplantation heart or lung function, except in 2 patients who experienced hyper-tension immediately after operation (patients No. 2 and 6, who each had a large donor–recipient BW ratio). Hyper-tension can be controlled by antihypertensive drugs, such as angiotensin-converting enzyme inhibitors, diuretics, and β-blockers, and it usually regresses within 2–3 months. It can be partially explained by LV remodeling, which in the present patients we found to be an initial decrease in heart size and then a gradual increase thereafter. The remodeling may be related to the hemodynamic adjustment of cardiac muscle, but the mechanism remain unclear.

The Batista operation is also called partial left ventricu-lectomy or left ventricle reduction surgery and is primarily based on La Place law. After its proposal by Batista et al in 1994, it has been performed in many patients with intractable heart failure who are waiting for heart transplantation. Several studies suggest a good short-term outcome, with a 1-year survival rate 70–80% and a 2-year survival rate of 60%. Patient No. 6 is the first pediatric case of Batista operation in Taiwan. After the operation, she no longer needed continuous inotropic agents and her LVEF increased from 10% to 22–28%. However, intermittent intravenous inotropic agents were still required, so she underwent cardiac transplantation 7 months later.

The advantages of cardiac transplantation are its wide app-liability and established short-term and long-term results. However, the shortage of donor hearts and the necessity of long term immunosuppressant therapy are the major draw-backs. In contrast, the indication for the Batista operation is not as wide as for transplantation, and the long-term outcome is still not established. However, it is not restricted by donor source and simplicity make it suitable for most patients with refractory congestive heart failure. A controlled study showed that the 1-year survival rate is the same in patients undergoing the Batista operation or heart transplantation, but the heart failure rate and the rate of relisting for trans-plantation were much higher in the Batista group. Therefore, the Batista operation should be better viewed as a bridge to heart transplantation until further study establishes its long-
term outcome.

In conclusion, in children with medically refractory heart failure, whether it is caused by CHD or CMP, cardiac transplantation is safe and effective. When there is a shortage of donor hearts, the Batista operation can be performed as a bridge to cardiac transplantation with acceptable results. Whether it can be used as the definitive surgery still needs further study.

References


