Cardiac Transplantation After the Fontan or Glenn Procedure

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OBJECTIVES
The purpose of this study was to review the clinical course and outcome of cardiac transplantation after a failed Glenn or Fontan procedure.

BACKGROUND
Late complications of the Glenn or Fontan procedure, including ventricular failure, cyanosis, protein-losing enteropathy, thromboembolism, and dysrhythmias often lead to significant morbidity and mortality. If other therapies are ineffective, cardiac transplantation is the only therapeutic recourse. Transplantation in this unique population presents significant challenges in the operative and perioperative periods.

METHODS
The anatomic diagnoses, previous operations, clinical status, and indications for transplantation were characterized in patients transplanted after a Glenn or Fontan procedure. Outcomes after transplantation, including postoperative complications and mortality, were reviewed. Comparisons were made between survivors and nonsurvivors.

RESULTS
Primary orthotopic cardiac transplantation was performed in 35 patients (mean age 15.7 ± 8.5 years) with a mean follow-up of 54 ± 46 months. A total of 11 patients had undergone a Glenn shunt and 24 patients a Fontan procedure. Indications for transplantation were a combination of causes including ventricular dysfunction, failed Fontan physiology, and/or cyanosis. Ten patients died ≤2 months after transplantation; nine of the deaths occurred in the Fontan patients. Overall, one-year survival was 71.5%, and five-year survival was 67.5%. Survival was not significantly different between patients transplanted after a Glenn or Fontan procedure and patients transplanted for other etiologies.

CONCLUSIONS
Cardiac transplantation can be performed successfully in patients with end-stage congenital heart disease after a Glenn or Fontan procedure, with outcomes similar to transplantation for end-stage heart failure secondary to other etiologies. (J Am Coll Cardiol 2004;44:2065–72) © 2004 by the American College of Cardiology Foundation

Although the results of palliative surgery for patients with single ventricle have improved markedly over the past 20 years (1–15), these patients remain at risk for late morbidity and mortality (16–20). Survival rates after a “perfect” Fontan operation have been reported to be between 70% to 93% at five years and 60% to 81% at 10 years (2–5,10). Late complications contributing to morbidity and mortality include progressive ventricular failure, atrioventricular valve regurgitation, protein-losing enteropathy (PLE), progressive cyanosis, evidence of poor cardiac output (failed Fontan physiology), thromboembolism, pulmonary arteriovenous malformations (AVMs), atrial tachyarrhythmias, and Fontan pathway obstruction (21–24). If unresponsive to medical, surgical, and catheter-based intervention, cardiac transplantation may be the only therapeutic recourse available to these patients after a Fontan or Glenn procedure (8,25–34).

Orthotopic cardiac transplantation is now a standard option for end-stage congenital heart disease (30,31,35–42), and congenital heart disease is one of the leading indications for cardiac transplantation in the pediatric population (43). Patients with single-ventricle physiology comprise 70% to 80% of patients transplanted for congenital heart disease. Heart transplantation in patients with single-ventricle physiology who have undergone multiple palliative procedures poses unique challenges in the pre- and peritransplant period, given the complex anatomy, physiology, and chronically debilitated conditions that are often associated with these lesions (26,34,44–51). Limited data is currently available outlining the clinical outcome of cardiac transplantation in patients after a failed Fontan or Glenn procedure (34,51).

The purpose of this study was to review the clinical course and outcome after orthotopic cardiac transplantation in all patients with end-stage congenital heart disease after a Glenn or Fontan procedure.

METHODS

Patients. All patients who underwent orthotopic cardiac transplantation after either the Glenn or the Fontan procedure between June 1984 and August 2001 were included for study. Patients were characterized by anatomic diagnosis, number and type of previous cardiac surgeries, indications...
for transplantation, and clinical status before transplantation (including the need for inotrop support, mechanical ventilation, or ventricular mechanical assistance).

Patients were classified with regard to the presence or absence of growth failure, chronic effusions, PLE, cyanosis, and intractable arrhythmias. Significant growth failure was defined as failure to thrive with height and/or weight persistently below the fifth percentile for age. Protein losing enteropathy was defined as persistent hypoalbuminemia with resulting edema, ascites, pleural effusion, or chronic diarrhea. Persistent cyanosis with systemic saturations below 80% after a Fontan operation or below 70% after a Glenn operation was considered significant, and was often associated with one or more other indications for transplant. Arrhythmias were regarded as being intractable if they persisted despite maximal medical therapy with antiarrhythmic medications and/or cardiac pacing.

The presence of signs and symptoms of poor cardiac output in the absence of ventricular dysfunction was defined as “failed Fontan physiology.” Cardiac function was evaluated by two-dimensional echocardiography and cardiac catheterization. Ventricular dysfunction was defined quantitatively as a shortening fraction below 29% in single left ventricles (LV) and defined qualitatively as greater than or equal to mild dysfunction for single right ventricles (RV). Atrioventricular valve regurgitation was graded by echocardiography as mild, moderate, or severe based on the width of the Doppler color flow jet and the extent of the regurgitation into the atrium.

The operative course was characterized, including the need for reconstructive surgery, the duration of bypass, the need for groin bypass, cross-clamp, and donor ischemic times. The post-transplant course was reviewed for length of hospital stay, perioperative morbidity (including duration of PLÉ, cyanosis, infection, residual cardiac defects), rejection history, the need for re-transplantation, and mortality. The cause of death was identified in each patient. Patients were followed until December 2001. Comparisons were made between the survivors and the nonsurvivors to identify differences in age; diagnosis; and pretransplant status, including hemodynamics, PLÉ, arrhythmias, cardiopulmonary bypass time, donor ischemic time, and the incidence of infections. Patient survival was compared between patients who underwent transplantation between two eras: 1984 to 1995 and 1996 to 2001. Survival of patients with failed Fontan and Glenn physiology after transplantation was also compared with survival in patients transplanted for other reasons.

### Abbreviations and Acronyms

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AVM</td>
<td>arteriovenous malformation</td>
</tr>
<tr>
<td>LV</td>
<td>left ventricle/ventricular</td>
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<tr>
<td>NYHA</td>
<td>New York Heart Association</td>
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<tr>
<td>PLE</td>
<td>protein-losing enteropathy</td>
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<tr>
<td>RV</td>
<td>right ventricle/ventricular</td>
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### Statistical Analysis

The Student t test was used to compare the following continuous variables: age at transplant; clinical status before transplantation; number of previous operations; duration between the last surgical procedure to transplantation; pretransplantation hemodynamics, including systemic oxygen saturation, mean pulmonary artery pressure, and pulmonary vascular resistance; intraoperative and postoperative variables such as cardiopulmonary bypass, cross-clamp, and ischemic times; days on inotropic support; number of days from transplantation to discharge; and infection rate.

Categorical variables including gender, ventricular morphology, LV versus RV or indeterminate ventricle, ventricular dysfunction, PLÉ, arrhythmias, and cyanosis were compared using chi-square analysis.

Kaplan-Meier survival was also determined. Differences in survival were compared using the log-rank (Mantel-Cox) test between patients transplanted after the Glenn procedure and those transplanted after the Fontan, between patients who were transplanted during the two eras, and between patients transplanted after the Glenn or Fontan procedure and those transplanted for other reasons during the study period.

### RESULTS

#### Patient Population

Of the 187 patients who underwent primary orthotopic cardiac transplantation during the study period, 35 patients had undergone a Glenn and/or Fontan procedure. The primary anatomic diagnoses of the 35 patients are shown in Table 1. The LV was dominant in 23 of the 35 patients (66%). Additional anatomic diagnoses among these patients included dextrocardia (n = 3), anomalous pulmonary venous return (n = 2), interrupted inferior vena cava withazygous continuation (n = 3), and discontinuous pulmonary arteries (n = 3). Mean age at the time of transplantation was 15.7 ± 8.5 years with a median of 15.3 years (range 1.1 to 39 years). The mean follow-up time from transplantation was 4.9 ± 3.1 years with a median of 4 years. The mean age at transplantation was 15.4 ± 7.2 years in the Fontan patients and 16.3 ± 7.23 years in the Glenn patients. The time from last surgery to transplantation was 4.94 ± 3.21 years in the Fontan patients and 9.1 ± 7.1 years in the Glenn patients. A total of 21 patients (60%) were male and 14 were female.

### Table 1. Diagnoses (n = 35)

<table>
<thead>
<tr>
<th>Diagnoses</th>
<th>Patients (n)</th>
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<tbody>
<tr>
<td>Tricuspid atresia/stenosis</td>
<td>11</td>
</tr>
<tr>
<td>DILV</td>
<td>9</td>
</tr>
<tr>
<td>Unbalanced AV canal</td>
<td>6</td>
</tr>
<tr>
<td>Complex single ventricle</td>
<td>3</td>
</tr>
<tr>
<td>PA-IVS</td>
<td>2</td>
</tr>
<tr>
<td>Heterotaxy syndrome</td>
<td>3</td>
</tr>
<tr>
<td>TGA, VSD</td>
<td>1</td>
</tr>
</tbody>
</table>

AV = atrioventricular; DILV = double inlet left ventricle; PA-IVS = pulmonary atresia with intact ventricular septum; TGA = transposition of the great arteries; VSD = ventricular septal defect.
Prior surgical intervention. The average number of previous operations per patient was 2.6 ± 1.6, ranging from 1 to 8. The mean interval from the last surgery to transplantation was 6.1 ± 5.2 years, with a range of 0 to 24 years. Three patients required transplantation within a month after the Glenn or Fontan operation due to acute hemodynamic compromise. The types of previous operations are summarized in Table 2. A total of 11 of 35 patients (31%) had undergone a Glenn shunt alone (8 bidirectional and 3 classic Glenn shunts). A total of 24 patients had undergone a modification of the Fontan procedure (69%). A total of 23 patients had prior closed-heart procedures, including aortopulmonary shunts (n = 16), coarctation or interrupted aortic arch repair (n = 2), pulmonary artery banding (n = 6), pulmonary artery reconstruction (n = 5), ligation of a ductus arteriosus (n = 2), thoracic duct ligation (n = 1), and pleurodesis (n = 1). Nine patients had undergone prior open-heart operations, including Fontan re-do (n = 4), Mustard operation (n = 1), atrial septectomy (n = 2), and 1 patient each had undergone a tricuspid or mitral valve replacement. There were 23 patients (66%) who had more than one procedure in addition to the Glenn or Fontan before transplantation.

Catheter therapy. Twenty-one patients (60%) underwent catheterization interventions before transplant in an effort to improve their hemodynamic state. Three patients had more than one procedure performed. Five patients with PLE had coil embolization of aortopulmonary collaterals, three had coil embolization of aortopulmonary collaterals because of ventricular failure, two had coil embolization of venous collaterals because of a history of cyanosis, one patient with ventricular failure had a Blalock-Taussig shunt coiled, and another three had pulmonary AVMs coil occluded. Pulmonary artery angioplasty and stents were placed in three patients with evidence of Fontan failure, two in the pulmonary vein and the other in an obstructed baffle. Balloon angioplasty for superior vena cava syndrome after the Glenn procedure was performed in one patient, and clamshell devices were placed across a baffle leak in two patients with cyanosis.

Hemodynamics. The pretransplant hemodynamics at the time of transplant evaluation in the Glenn and Fontan patients are listed in Table 3. The mean pulmonary artery pressure was 17.7 ± 11.7 mm Hg in the Glenn patients and 17.1 ± 8.2 mm Hg in the Fontan patients. In the 14 patients who had normal ventricular function and evidence of a failed Fontan physiology, the mean pretransplant pulmonary artery pressures and pulmonary capillary wedge pressures were 19.35 ± 10.7 mm Hg and 16.2 ± 7.3 mm Hg, respectively. The mean pulmonary vascular resistance was 3.8 ± 1.5 U. Cardiac index and systemic saturations were similar in the failed Fontan patients compared with the Fontan group as a whole.

Ventricular function and atroventricular valve regurgitation. Moderate-to-severe right or LV dysfunction was present in 20 patients; 10 of 11 of the Glenn patients and 10 of 24 of the Fontan patients. The mean shortening fraction was 23 ± 3.9% in the 14 patients with single LVs, and 6 patients with a dominant RV had moderate-to-severe dysfunction. In the 20 patients with ventricular dysfunction, the mean age at Fontan or Glenn procedure was 11.8 ± 7.3 years, and 55% had a dominant single LV. Ventricular function was normal by echocardiography in 15 patients (43%); 1 patient with a Glenn shunt had normal LV function in the context of severe, debilitating cyanosis, and 14 of 24 patients (58%) transplanted after the Fontan procedure had a fractional shortening between 29% to 35% (mean 30 ± 2.1%). The patients with relatively preserved ventricular function after the Fontan procedure all had features of a failed Fontan physiology. Atrioventricular valve regurgitation was present in 10 patients including 3 with mild, 5 with moderate, and 2 with severe insufficiency.

Indications for transplant. The indications for heart transplantation in the 35 patients are summarized in Table 4. Twenty-two patients had more than one indication for transplantation. The majority of patients (57%) had significant heart failure with systolic ventricular dysfunction. Significant cyanosis limiting exercise capacity was present in 13 patients; 12 of these had associated findings of ventic-
ular dysfunction and/or failed Fontan physiology that, in combination with cyanosis, led to transplantation. Exercise intolerance secondary to severe cyanosis (resting oxygen saturation <68%) was the primary indication for transplant in one patient with pulmonary atresia and intact ventricular septum who had a classic Glenn shunt and severe pulmonary hypertension of the left lung.

A total of 16 of the 24 patients who had undergone a Fontan had one or more findings of a failed Fontan physiology (summarized in Table 5). Two of these patients had associated ventricular dysfunction, and 14 patients had failed Fontan physiology with preserved systolic function.

**Protein-losing enteropathy.** A total of 15 patients (42%) had signs of PLE, with ascites noted in 10 patients and pleural effusions in 12 patients. Before transplantation, the mean serum albumin level for the PLE group was 2.73 ± 0.65 g/dl, and ranged from 1.3 to 3.6 g/dl. Six patients required frequent albumin infusions to maintain a normal serum albumin. Patients with PLE were treated pretransplant with various combinations of a low fat/high protein diet, digoxin, diuretics, afterload reducing agents, and subcutaneous heparin. After transplantation, the mean serum albumin in the surviving PLE patients was 4.0 ± 0.3 g/dl and ranged between 3.5 to 4.5 g/dl.

**Arrhythmias.** Significant arrhythmias occurred in 13 patients (37%). Nine had atrial flutter and/or atrial fibrillation (26%), and therapy included digoxin, beta-blockers, rapid atrial pacing, and/or cardioversion. Three of nine patients required frequent hospitalizations for recurrent atrial flutter despite maximal medical therapy. Five patients were treated with combinations of lidocaine, amiodarone, beta-blockers, mexiletine, and/or magnesium sulfate for either ventricular tachycardia (three patients) or frequent ventricular ectopy (two patients). Five patients required cardiac pacing for bradycardia: three patients with sick sinus syndrome and two patients with second-degree heart block.

**Pretransplant clinical status.** Sixteen patients (46%) required inotropic support while awaiting transplantation, including dobutamine, dopamine, epinephrine, milrinone and/or vasopressin. Mechanical ventilation was needed in six patients (18%). Ventricular assist devices were utilized in three patients while awaiting transplant: extracorporeal membrane oxygenation in two patients and an implantable LV assist device in one patient. Hemodialysis was necessary in one patient before transplantation.

**Table 5. Failed Fontan Physiology (n = 16 Patients)**

<table>
<thead>
<tr>
<th>Findings</th>
<th>Patients (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe growth retardation</td>
<td>16</td>
</tr>
<tr>
<td>Normal systolic function with signs of low cardiac output</td>
<td>14</td>
</tr>
<tr>
<td>Protein-losing enteropathy</td>
<td>15</td>
</tr>
<tr>
<td>Chronic pleural effusions</td>
<td>12</td>
</tr>
<tr>
<td>Ascites</td>
<td>10</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>13</td>
</tr>
</tbody>
</table>

**Table 6. Surgical Procedures at the Time of Transplantation (n = 31 Patients)**

<table>
<thead>
<tr>
<th>Operation</th>
<th>Patients (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary artery reconstruction</td>
<td>18</td>
</tr>
<tr>
<td>SVC reconstruction</td>
<td>3</td>
</tr>
<tr>
<td>Excision of PA aneurysm</td>
<td>2</td>
</tr>
<tr>
<td>Transection of apical aortic conduit</td>
<td>1</td>
</tr>
<tr>
<td>Shunt takedown</td>
<td>2</td>
</tr>
<tr>
<td>Reconstruction of systemic venous atrium</td>
<td>1</td>
</tr>
<tr>
<td>Innominate vein reconstruction</td>
<td>2</td>
</tr>
<tr>
<td>Baffling of LSVC to right atrium</td>
<td>1</td>
</tr>
<tr>
<td>Flap repair of common atrium</td>
<td>1</td>
</tr>
<tr>
<td>Aortic aneurysm resection</td>
<td>1</td>
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</tbody>
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**Operative course.** Groin bypass was necessary in 18 patients (51%) at the time of transplantation. Mean cardiopulmonary bypass time was 4.8 ± 1.4 h, and ranged between 2.2 and 8.1 h. The mean aortic cross-clamp time was 3.0 ± 1.0 h, with a range of 1.1 to 4.2 h. Ischemic time ranged between 1.8 and 7.4 h, with a mean of 4.7 ± 1.5 h. Additional surgical procedures at the time of transplant were performed in 91% of patients and are summarized in Table 6. In addition to reconstruction of the venous connections, extensive pulmonary artery reconstruction was performed in 18 patients.

**Postoperative course.** The duration of mechanical ventilation ranged between 1 and 123 days with a median of 3 days. Inotropic support was required for a median of 6 days, ranging from 2 to 20 days. Cardiac catheterization with coil occlusion of aortopulmonary collateral vessels was performed in five patients with high-output heart failure and persistent pleural effusions, including two with a history of PLE. The median length of hospital stay after transplant was 21 days, with a range of 9 to 159 days.

**Perioperative morbidity.** Early infection occurred in 8 of 35 patients (22%). The infectious agents included herpes zoster, herpes simplex, cytomegalovirus, candida, clostridium difficile, and enterobacter. *Staphylococcus aureus* pericarditis occurred in one patient. Transient renal dysfunction occurred in four patients, and hepatic failure in one patient. Unilateral phrenic nerve palsy occurred in one patient. Steroid-induced diabetes mellitus occurred in two patients.

Neurological events occurred after transplant in four patients. Three patients had evidence of embolic infarcts and presented with seizures, and one patient had left-sided arm and leg weakness. One of the patients with an embolic event had a documented right-to-left shunt through pulmonary AVMs after transplant. One patient had transient blindness that subsequently resolved.

**Protein-losing enteropathy.** Of the 15 patients who had signs of PLE before transplant, 6 (40%) died early after transplant (4 within 24 h after transplant). The causes of death included hemorrhage (n = 2), RV failure, multisystem organ failure, aspiration pneumonia, sepsis, and brain death. In the nine patients who survived, signs of PLE...
resolved, and serum albumin returned to normal (mean 3.9 ± 0.28 g/dl) at a mean of 4.0 ± 2.1 weeks after transplant.

**Perioperative mortality.** Ten patients died (28.5%) within six weeks after transplantation at a median of one day after transplant. A total of 6 of 10 deaths were within 24 h after transplantation, including 3 due to postoperative bleeding. Three patients died of infectious causes, with RV failure and graft failure being additional factors contributing to death in two of these patients. The causes of early death are listed in Table 7. One patient in the Glenn group died 34 days after transplant from sepsis. The remaining nine perioperative deaths occurred in the Fontan group. There was no significant difference in early deaths between the Glenn and the Fontan patients (p = 0.11).

Comparison of the pretransplantation clinical profiles of the patients who died early after transplant to those who survived indicated no significant difference between the groups with respect to age, gender, underlying anatomic diagnosis, clinical status before transplantation, number of previous operations, duration between the last surgical procedure to transplantation, hemodynamics including systemic oxygen saturation, mean pulmonary artery pressure or pulmonary vascular resistance, or the indications for transplantation. Similarly, no significant differences were noted between the two groups with respect to intraoperative and postoperative variables such as cardiopulmonary bypass time, cross-clamp time, ischemic time, days on pressor support, and number of days from transplantation to extubation.

**Patient survival.** Kaplan–Meier survival after cardiac transplantation after a failed Glenn or Fontan procedure was 71.5% at 1 year, 67.5% at 5 years, and 62% at 10 years after transplant (Fig. 1). Two patients died late after transplant. One patient who was medically noncompliant died suddenly at 4.2 years with acute rejection; another patient in whom immunosuppressive therapy had been minimized due to the presence of post-transplant lymphoproliferative disease died 6 years after transplant with graft vasculopathy and chronic renal failure. The 1-, 5-, and 10-year survival among those who survived to hospital discharge was 100%, 96%, and 92%, respectively.

Kaplan–Meier survival was compared between the patients transplanted from 1986 to 1995 and 1996 to 2001. Five-year survival was 64% in the earlier era and 77% in the later era: the difference was not statistically significant (p = 0.5). Survival of patients transplanted after a failed Glenn versus a failed Fontan procedure was also compared (Fig. 2). No significant difference in overall survival was seen between the two groups (p = 0.06). In addition, survival was compared between the patients who were transplanted after a Glenn or Fontan procedure and patients who were transplanted for other etiologies within the same time period. There was no significant difference (p = 0.8) in overall survival between the two groups (Fig. 3).

**Late morbidity.** Among the 23 late survivors, there have been nine different morbidities, summarized in Table 8. Hypertension is the most common late morbidity, occurring in 39% of patients. The mean number of rejection episodes per patient was 2.2 ± 2.0, with a range of 0 to 9 per patient. The incidence of rejection per patient month among the late survivors was 0.02 ± 0.01. Three patients have developed graft vasculopathy, and one was re-transplanted.

**Post-transplantation hemodynamics.** At latest follow-up, echocardiography demonstrated good LV function in all 23 patients. The mean pulmonary artery pressure was 18.7 ± 4.4 mm Hg, ranging from 11 to 24 mm Hg. The mean pulmonary capillary wedge pressure was 9.9 ± 3.2 mm Hg, with a range of 5 to 14 mm Hg. The mean pulmonary...
vascular resistance index was $2.74 \pm 1.2$ U. The mean cardiac index was $3.0 \pm 0.5$ l/min/m$^2$ and ranged between 1.5 and 5.2 l/min/m$^2$. The mixed venous saturations in the pulmonary artery ranged between 60 and 83 mm Hg. Cyanosis resolved in all patients, and the mean systemic arterial oxygen saturations were $97 \pm 1.7\%$.

**Functional capacity.** Among the 23 survivors, 22 are in New York Heart Association (NYHA) functional class I (96%), and all attend either school or are employed; 1 patient is in NYHA functional class II.

**DISCUSSION**

Previous reports of transplant after the Glenn or Fontan procedure have included small numbers of patients and largely focused on the surgical challenges of implanting the heart and repairing associated lesions (1–13). Vouhe et al. (14), Carey et al. (15), and Fullerton et al. (16) have reported on small numbers of patients transplanted after the Fontan or Glenn procedure with good early and intermediate-term survival. There are multiple other isolated reports of cardiac transplantation after the Glenn or Fontan procedure in published data (17,18). The present study of 35 patients transplanted after the Glenn or Fontan procedure represents the largest series to date.

The Glenn and Fontan procedures constitute standard forms of surgical palliation for patients with complex congenital heart disease (19–24). Among these patients, late failure with a poor functional outcome has been well recognized (25–37). The manifestations of late Fontan complications or failure include ventricular dysfunction, PLE, arrhythmias, cyanosis from AVMs or venous collaterals, atrioventricular valve regurgitation/stenosis, Fontan pathway obstruction including pulmonary artery distortion and pulmonary venous stenosis, and failed Fontan physiology with low cardiac output despite normal ventricular function (38–46). Functional capacity may be severely limited in patients who manifest one or more of these complications, and late survival after the Fontan operation is reported to be 70% to 93% at 5 years, 60% to 81% at 10 years, and 73% at 15 years. Within our study population, complications necessitating transplant occurred over a varied period extending up to 24 years after the initial Glenn or Fontan procedure.

In this study, the most common indication for transplantation was single-ventricle dysfunction in 57% of patients. Ventricular function was normal in 43% of the patients, who all exhibited significant exercise intolerance secondary to a failed Fontan circulation. The presence of severely limited functional capacity despite normal ventricular function highlights the multifactorial causes of low cardiac output in these patients. In this series, transplantation was an effective therapy for the manifestations of a failed Fontan circulation. Perioperative survival after transplant was 60% in the patients who had PLE, indicating the severely debilitated state of these recipients. Protein-losing enteropathy resolved in all survivors, with no late mortality. Mertens et al. (47) reported five patients with PLE who underwent transplantation. Similarly, PLE resolved in all three survivors in the immediate postoperative period but recurred a few years later in one patient despite good hemodynamics. Successful resolution of PLE after transplant was also reported by Sierra et al. (48). Cyanosis resolved after transplant in all patients in this series, including three patients with significant pulmonary AVMs (49).

The surgical approach to patients undergoing transplantation after a Glenn or Fontan procedure offers a unique challenge (2,4,7,10,12,14,50). Partial groin bypass was utilized in 50% of the patients in order to maintain systemic perfusion during the period of instituting standard cardiopulmonary bypass. Similar to other studies (5,7,14,15,51), mean bypass and ischemic times were relatively long in this group of patients (4.8 ± 1.4 h and 4.6 ± 1.5 h), indicating the complexity of the surgical repair. Reconstructive surgery was required in 91% of patients, not only to restore normal systemic venous return, but also to correct multiple extra-cardiac lesions such as distorted pulmonary arteries (13,14,17,52).

The postoperative course of these patients was characterized by a 22% incidence of early infection, compared with a 7% to 35% overall incidence reported in patients undergoing heart transplantation for all causes (7,8,16,53–55). An important finding was that three of the seven early deaths were secondary to infection. A complication unique to this
group of patients was the occurrence of high-output congestive heart failure secondary to significant left-to-right shunting through residual aortopulmonary collaterals (56,57). The patients improved after coil occlusion, highlighting the importance of aggressive management of collateral vessels in this group of patients.

In this study, one-year survival after transplant was 72%, with one-third of the deaths occurring secondary to postoperative hemorrhage or multisystem organ failure within 36 h of transplantation; 70% of the deaths occurred within a week of transplant. These results are similar to that reported from the Registry of the International Society for Heart and Lung Transplantation, which reported that congenital heart disease of any kind was a significant risk factor for one-year survival (55). Survival in patients successfully discharged home was 92% at 10 years.

The majority of deaths occurred in the patients who underwent transplantation after the Fontan procedure with a 63% one-year and a 57% five-year survival. In patients who were transplanted after a Glenn procedure, the one- and five-year survival was 90%. Statistical analysis failed to detect a significant difference in survival between the Glenn and Fontan groups (p = 0.06); this may well be due to the small patient numbers and limited statistical power.

The Kaplan-Meier survival was 64% in the earlier transplant era compared with 77% in the later era. Although no significant difference was demonstrated, this study is underpowered for this comparison. There was no difference in 10-year survival between the patients who underwent transplantation for complex congenital heart disease and those transplanted for other reasons at our institution, and the 5-year survival of 68% in this study is comparable to the data reported from the registry for all pediatric patients regardless of diagnosis (53,54,57–59).

CONCLUSIONS

The present study demonstrates that, although their perioperative course may be more complicated, patients who have undergone a Glenn or Fontan procedure have long-term survival after heart transplantation comparable to patients transplanted for other causes. The early mortality seen in this study secondary to postoperative hemorrhage and infection and the high incidence of death in the patients with PLE highlights the challenges posed by transplantation in this group of debilitated patients with complex cardiac defects (60). In addition to routine post-transplant care, these patients must be monitored for complications that can occur related to their preoperative congenital heart disease.

Although successful palliation of patients with single ventricle has led to an increasing number of long-term survivors after the Fontan procedure, late complications continue to occur. The results of this study indicate that cardiac transplantation should be considered a standard option for the patient with a failed Glenn or Fontan procedure. Efforts should be made to optimize patient selection and the timing of transplantation in the hope of decreasing the significant early mortality and morbidity seen in this group.

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REFERENCES


