Heart Transplantation for Patients with a Fontan Procedure

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History

- First human-to-human heart transplant in December, 1967
- First transplant for congenital heart disease also in December, 1967
- Increasing success with surgical management of single ventricle heart disease
- Seemingly increasing number of Fontan patients who will need heart transplantation
Risk Factors

- PVR calculation can be problematic
- Comorbidities (PLE, hepatic or renal dysfunction)
  - Cardiac cirrhosis, hepatitis C
- Elevated PRA due to prior blood product exposure
- Technically challenging operation
- Postop issues (bleeding, AP collaterals, debilitation, abnormal pulmonary vasculature)
The Effect of Age, Diagnosis, and Previous Surgery in Children and Adults Undergoing Heart Transplantation for Congenital Heart Disease

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Maryanne R. Chrisant, MD,§ William R. Morrow, MD,‖ Barry S. Clemson, MD,¶
James K. Kirklin, MD,‡ on behalf of the CTRD (Cardiac Transplant Registry Database) and the PHTS (Pediatric Heart Transplant Study)

New York, New York; Atlanta, Georgia; Birmingham, Alabama; Philadelphia, Pennsylvania; Little Rock, Arkansas; and Peoria, Illinois
Combined CTRD & PHTS Study (1990-2002)

- 7,345 tx from Cardiac Transplant Registry Database (CTRD) >18 yo at listing
- 121 (1.6%) with congenital heart disease
- 923 tx from Pediatric Heart Transplant Study (PHTS) >6 mos and <18 yo at listing
- 367 (40%) with congenital heart disease
- Total of 488 patients transplanted with congenital heart disease
Age at Transplantation

Mean: 14.8 yrs
Median: 12.4
Min: 0.5
Max: 61.8

Lamour et al, JACC, 2009
Last Major Operation

10% Mustard

7% unoperated

11% Bands/shunts

5% Norwood

16% Glenn

22% Fontan

29% 4-chamber repair

Lamour et al, JACC, 2009
Overall Survival

- Age < 18 yrs: ischemic or Idiopathic (n=372)
- All Ages Congenital (n=488)
- Age > 18 yrs: Ischemic or Idiopathic (n=6,498)

\[ p(\text{overall}) < 0.01 \]
\[ p(\text{congenital vs age < 18 yrs}) < .01 \]
\[ p(\text{congenital vs age > 18 yrs}) = .07 \]
## Multivariable Risk Factors

<table>
<thead>
<tr>
<th>Variable</th>
<th>Relative Risk</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Early phase</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Older recipient age</td>
<td>1.5</td>
<td>0.02</td>
</tr>
<tr>
<td>Previous Fontan operation</td>
<td>8.6</td>
<td>0.003</td>
</tr>
<tr>
<td>Longer ischemic time</td>
<td>1.6</td>
<td>0.002</td>
</tr>
<tr>
<td>Interaction of donor age and ischemic time</td>
<td>1.4</td>
<td>0.0007</td>
</tr>
<tr>
<td>Higher pre-Tx mean RAP (only in patients without previous Fontan)</td>
<td>2.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Constant phase</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Younger recipient age</td>
<td>1.8</td>
<td>0.0001</td>
</tr>
<tr>
<td>Higher systolic transpulmonary gradient</td>
<td>2.0</td>
<td>0.01</td>
</tr>
<tr>
<td>CMV+ donor, CMV – recipient</td>
<td>2.8</td>
<td>0.001</td>
</tr>
<tr>
<td>Previous classical Glenn operation</td>
<td>3.1</td>
<td>0.01</td>
</tr>
</tbody>
</table>

CMV = cytomegalovirus; RAP = right atrial pressure; Tx = transplant.
Effect of Prior Fontan on Survival

- Non-Fontan (n=381)
- Fontan (n=107)

Percent Survival vs Years After Transplant

p = .006

Lamour et al, JACC, 2009
Type of Fontan Failure Affects Results

Evaluating Failing Fontans for Heart Transplantation: Predictors of Death

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Background. Late complications of the Fontan operation represent a significant management challenge. Failing Fontan patients have two modes of presentation: impaired ventricular function (IVF) and those with preserved ventricular function (PVF) but with failing Fontan physiology (protein-losing enteropathy [PLE] and plastic bronchitis [PB]). This study evaluated whether failing Fontan patients referred for heart transplantation had a different outcome based on the mode of presentation.

Methods. The medical records of all Fontan patients evaluated for heart transplantation at a single institution from 1994 to 2008 were retrospectively reviewed. Demographic, hemodynamic, and laboratory data were collected. Patients were stratified into an IVF or PVF group by echocardiographic criteria. Descriptive statistics and Kaplan-Meier analysis were used for hypothesis testing.

Results. Thirty-four Fontan patients were evaluated for heart transplantation. According to echo description of systolic function, 18 were categorized as IVF and 16 as PVF. The IVF group had a significantly lower cardiac index and venous oxygen saturation, and significantly higher systemic vascular resistance vs the PVF group (p < 0.05). PLE or PB was present in 13 PVF patients and none in the IVF group. Twenty patients underwent transplantation, with similar rates amongst the IVF and PVF groups. Within 1 year from evaluation, 2 IVF patients and 7 PVF patients had died (p = 0.052).

Conclusions. Failing Fontan patients with PVF have decreased overall survival independent of whether they underwent transplantation. This trend indicates a need to improve the management and timing for transplantation amongst this population.

Type of Fontan Failure Affects Results

- 34 patients with failing Fontan from Boston
  - 18 with impaired ventricular function, 16 with preserved ventricular function
  - All deaths in the 20 transplanted Fontan pts had preserved ventricular function

Table 3. Comparison of Mortality

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Impaired (n = 18)</th>
<th>Preserved (n = 16)</th>
<th>p Value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transplanted</td>
<td>11 (61.1)</td>
<td>9 (56.3)</td>
<td>0.774</td>
</tr>
<tr>
<td>Deaths, n (%)</td>
<td>2 (11.1)</td>
<td>7 (43.8)</td>
<td>0.052&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Transplanted</td>
<td>0/11</td>
<td>3/9 (33.3)</td>
<td>0.074&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Non-transplanted</td>
<td>2/7 (28.6)</td>
<td>4/8 (50)</td>
<td>0.473</td>
</tr>
</tbody>
</table>

<sup>a</sup>p ≤ 0.05 considered significant.
Conclusions

- Congenital heart disease is a risk factor with cardiac transplantation
- Most of the risk is early
  - Maybe better long-term survival (younger patients?)
- Prior Fontan is a definite risk
- Older age at transplant also an early risk factor
  - Should we transplant sooner?
Emory Pediatric Fontan Transplants

- 311 heart transplants from 1988 to April, 2015

Exclude:

- 34 retransplants
- 4 patients >18 years old
- 273 primary pediatric heart transplants
- 33 (12.1%) children with previous Fontan
Patient Age

Age at Fontan 4.5±3.3 yrs
Interval from Fontan to Tx:
3.7±4.3 years
9 <1 year interval
6 <6 months

13 of 33 Fontan pts (39%) had PLE
Patient Characteristics

- Fontan (n=33)
- Non-Fontan (n=240)

<table>
<thead>
<tr>
<th>Category</th>
<th>Fontan (%)</th>
<th>Non-Fontan (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRA &gt; 10%</td>
<td>21.2</td>
<td>18.9</td>
<td>P=NS</td>
</tr>
<tr>
<td>UNOS Status I</td>
<td>72.7</td>
<td>81.7</td>
<td>P=NS</td>
</tr>
<tr>
<td>Ventilated</td>
<td>18.7</td>
<td>18.2</td>
<td>P=NS</td>
</tr>
<tr>
<td>Prior Ops</td>
<td>100</td>
<td>50.3</td>
<td>P&lt;.0001</td>
</tr>
</tbody>
</table>
Operative Variables

- % w/ PA Reconstruction: Fontan (n=33) 100, Non-Fontan (n=240) 21.2
- Donor Ischemia (min): Fontan (n=33) 213, Non-Fontan (n=240) 176
- CPB Time (min): Fontan (n=33) 199, Non-Fontan (n=240) 124

Significance:
- P<.0001
- P<.001
Post-Operative Variables

- Fontan (n=33)
- Non-Fontan (n=240)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Fontan</th>
<th>Non-Fontan</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilation</td>
<td>4.4</td>
<td>2.5</td>
<td>.03</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>18.6</td>
<td>14.7</td>
<td>.13</td>
</tr>
</tbody>
</table>
Early Results

- One 30-day mortality in the Fontan group
  - 30-day survival 97.7% vs. 94.6%
- One early retransplant for graft failure in the Fontan group
- All eleven patients with PLE who survived 6 months had complete resolution
Early Rejection

- Rejection Episodes per Patient
- 30 Days: Fontan 0.70, Non-Fontan 0.36
- One Year: Fontan 2.00, Non-Fontan 1.70

Statistical Significance:
- P = 0.3972
- P = 0.0218
Patient Survival

PATIENTS AT RISK

<table>
<thead>
<tr>
<th>Year</th>
<th>0</th>
<th>1</th>
<th>3</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fontan</td>
<td>33</td>
<td>27</td>
<td>20</td>
<td>18</td>
</tr>
<tr>
<td>Non-Fontan</td>
<td>240</td>
<td>195</td>
<td>156</td>
<td>118</td>
</tr>
</tbody>
</table>

P = .2622
ReTransplantation

- 5/33 (15.1%) of Fontan pts were retransplanted 4.9±3.6 yrs post-tx
  - Range 2d-9.4 yrs
- 26/240 (10.8%) of non-Fontan pts were retransplanted 5.2±3.6 yrs post-tx
  - Range 34d-11.7 yrs
Observations

- Children with a Fontan procedure undergoing heart tx have more complicated operations and longer hospitalizations
- Very early rejection is more common
- Early and intermediate survival is similar
- Ongoing risk of death and retransplantation
Technical Considerations

- Obtain adequate donor tissue (arteries, veins)
- Match donor to recipient
  - Avoid marginal donor
  - Consider ischemic time
  - ?Oversize donor?
- Protect RV (collaterals, venting, PVR calculations)
- Beware of pre-sensitization
- Meticulous technique (abnormal coags, collaterals)
Technical Considerations

- Allow adequate time for careful recipient dissection
- Avoid RV distension
  - May need 2 LA vents or additional PA vent
- Can use extracardiac Fontan remnant for IVC anastomosis
- Usually can patch Glenn and Fontan insertions on RPA with donor PA; can use donor descending aorta or pericardium
- Do not routinely use iNO
Adequate Donor Vessels for Complex Reconstruction

Can Be a Challenge with Multivisceral Donors
Can Use Donor PA to Patch Fontan Site

Often Need Add’l LA or PA Vent
Situs Inversus, Interrupted IVC with Azygos Continuation to LSVC

Use right atrial cuff to form IVC channel
IVC Channel

Donor aorta for SVC extension

Separate pulmonary vein anastomoses

Open Left Pericardium

Completed Transplant
Conclusions

- Heart transplantation in children after the Fontan procedure can be performed with comparable results to non-Fontan patients.

- Be careful—there are a lot of Fontan patients out there!!

- Concomitant hepatic failure problematic.
Future Directions

• Improved surgical strategies

• Improved medical therapy

• Minimize transplant risk
  - Patient selection
  - Timing of transplant

• Mechanical circulatory support
Mechanical Support of the Failing Fontan

- Case reports of VAD use
- Total artificial heart promising
Mechanical Support of the Failing Fontan

Mechanical Support of the Failing Fontan

Rodefeld et al, JTCVS, 2010