Single Ventricle Palliation Using a Ventricular Assist Device: A Quite Different Perspective

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October 6, 2010
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HYPOPLASTIC LEFT VENTRICLE

• Hypoplastic Left Heart Syndrome (HLHS) accounts for ~9% of congenital heart defects
  • responsible for as many as 25% of cardiac deaths in the newborn period
  • 95% fatal by 1 month of life before the era of effective surgical palliation
  • Mean survival 4-23 days
  • Very rare case reports of survival into 20’s
HYPOPLASTIC LEFT VENTRICLE

• Anatomy
  – Hypoplasia or absence of left ventricle
  – Severe hypoplasia of ascending aorta
    • Ascending aorta 1-8mm (3.8 mm mean)
      – 55% <3mm
      – Serves only as conduit for retrograde blood flow to coronary arteries
  – Systemic circulation dependent on right ventricle via PDA
  – Dilated and hypertrophied RV is dominant ventricle and forms apex
  – Obligatory mixing of pulmonary and systemic venous blood in right atrium

• Clinical Features/Diagnosis
  – Diagnosis can be made in prenatal period
  – Tachypnea and cyanosis within 24 to 48 hours of birth
  – Diminished systemic perfusion rapidly occurs when ductus begins to close
    • Pallor, lethargy, and diminished pulses
    • Metabolic acidosis and renal failure

• Medical Support
  – PGE-1 (0.05mcg/kg/min) for ductal patency
  – Maintain hematocrit at 45 - 50%
  – Balance pulmonary blood flow
  – O$_2$ saturation 70 -75% (FIO$_2$ 0.18 - 0.21) prevents the pulmonary vasodilation associated with high O$_2$ concentrations (↑ pulm blood flow → ↓ systemic blood flow → acidosis)
  – Maintain PCO$_2$ 40 – 50 (↑ ventilation → ↓PVR and ↓ systemic blood flow)
  – Acidosis reversed rapidly with sodium bicarb
  – Inotropic support if patients with depressed RV function
HLHS Treatment Options

- Do Nothing
- Staged Norwood Palliation
- Transplantation

HYPOPLASTIC LEFT VENTRICLE

- Staged Surgical Therapy
  - Norwood procedure as neonate
    - Atrial septectomy
    - Systemic - pulmonary shunt
    - Aortic reconstruction
  - Bi-directional Glenn
    - 4 - 8 months
    - Fontan procedure
      - 24 - 36 months

NORWOOD PROCEDURE

- Reconstruct Aorta
- Atrial Septectomy
- Provide pulmonary blood flow with a shunt

Postoperative Care:
“The Fun Has Just Begun”

- Parallel Circulation
- Delicate balance between SVR/PVR
- Pulmonary steal
  - Low diastolic BP, coronary insufficiency, myocardial dysfunction
- Long circulatory arrest times-myocardial dysfunction
HYPOPLASTIC LEFT VENTRICLE

- Sano Modification
  - RV to PA conduit
  - Theoretically eliminates the aortic diastolic runoff and coronary steal that occurs during BT shunts
  - Improved immediate postop cardiac function
  - Less complex postop course
  - Improved growth of the PAs
  - Improved survival?
  - Improved neurologic function?

SANO MODIFICATION

HYPOPLASTIC LEFT VENTRICLE

- Bidirectional Glenn (“Stage 2”)
  - 4 - 8 months
  - Increases effective pulmonary flow which improves the systemic arterial oxygen saturation
  - Removes the obligatory volume load on the ventricle which allows time for resolution of excessive ventricular hypertrophy prior to the Fontan procedure
  - Alters the ventricular geometry
    - Right ventricular end-diastolic volume decreased by 33%
    - Right ventricular anterior wall increased in thickness by only 13%

Fontan Procedure (“Stage 3”)

Lateral Tunnel

Extracardiac
**Fontan Procedure**

Lateral Tunnel

Extracardiac

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**CHOP Experience by Era -Survival-**

<table>
<thead>
<tr>
<th>Era</th>
<th>Norwood</th>
<th>Glenn</th>
<th>Fontan</th>
</tr>
</thead>
<tbody>
<tr>
<td>1984–1988 (n=269)</td>
<td>56.2%</td>
<td>96.3%</td>
<td>76.0%</td>
</tr>
<tr>
<td>1989–1991 (n=255)</td>
<td>64.7%</td>
<td>80.0%</td>
<td>87.5%</td>
</tr>
<tr>
<td>1992–1994 (n=173)</td>
<td>67.6%</td>
<td>93.6%</td>
<td>93.1%</td>
</tr>
<tr>
<td>1995–1998 (n=143)</td>
<td>71.3%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

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**Why can’t we perform all 3 operations at the time of the original operation?**

- Increased pulmonary vascular resistance (PVR) in the neonate
  - Need for systemic to PA shunt
- Gradual relief of the obligatory volume load on ventricle imposed by a systemic to PA shunt
  - allows time for resolution of excessive ventricular hypertrophy

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**Transitional Circulation at Birth**

- Pulmonary blood flow increases 8-10 fold
- PA pressures are ½ systemic at 24 hours of life and reach adult levels at 2-6 weeks after birth
- Similar pattern in both humans and animals
Physiologic Problems Following Norwood/Stage 1 Palliation

- Parallel systemic and pulmonary circulations
- Ventricular volume overload
- Increased ventricular workload
- Increased myocardial wall tension
- Excessive or inadequate pulmonary blood flow

Physiologic Problems Following Stage 1 Palliation

- Coronary artery, brain, etc., oxygen saturations are 60-75%
- Coronary perfusion becomes inadequate secondary to diastolic shunt runoff
- Sano-fails to alleviate:
  - issues of hypoxemia
  - parallel circulations
  - volume loading of the single ventricle

Stage 2 (Bi-directional Glenn) and Stage 3 (Fontan)

- Survival and hemodynamic stability of Stage 2 and Stage 3 palliation improves dramatically
- Direct consequence of taking down the systemic shunt and establishing cavopulmonary blood flow

Can the Deleterious Effects Associated with Stage 1 Physiology be Eliminated?
### Theoretical Advantages of a Cavopulmonary Assist Device

- Change a univentricular circulation to 2-ventricular physiology
  - pulmonary and systemic circulations in series rather than parallel
- Single ventricle pumps only 1 systemic ventricular output while the cavopulmonary assist device supports the equivalent of the right ventricular output
  - can overcome high PVR
- Single ventricle NOT subjected to volume overload
- Early reduction of volume work benefits long-term myocardial function

### Theoretical Advantages of a Cavopulmonary Assist Device

- Coronary perfusion pressure, which is dependant on diastolic blood pressure may be improved
- Normal arterial oxygenation ranges
  - improve myocardial performance
  - prevent end-organ ischemia
  - protect neurologic development
  - minimize PVR
- Minimize (or eliminate) pathologic pulmonary vascular remodeling

### Hypothesis

- Pump-assisted cavopulmonary diversion using a ventricular assist device would yield stable pulmonary and systemic hemodynamics and maintain pulmonary gas exchange without altering cardiac output in a neonatal lamb model
  - Can this acute study support an indication for a longer-term device using a similar, portable model of pump-assisted cavopulmonary diversion?

### Methods

- 8 Newborn lambs anesthetized and mechanically ventilated
- Total cavopulmonary diversion using Levitronix PediVAS
- Hemodynamic Data measured every hour (8 hours)
  - Systemic arterial blood pressure
  - Central venous pressure
  - Pulmonary arterial pressure
  - Left atrial pressure
  - Continuous cardiac output
- Arterial blood gases
- Lactate levels
- ACT levels
Animal Model of Single Ventricle Palliation

Results

• 8 Newborn lambs
  – 100% survival
  – Mean age 5.25 days (range 2-10 days)
  – Mean weight 4 kg (range 2-6 kg)
  – Mean BSA 0.21m² (range 0.14-.28 m²)
• No evidence of thrombus (ACT 250-300)
• No evidence of excessive bleeding
Levitronix UltraMag VAD

- Smaller, portable, magnetically levitated ventricular assist device

UltraMag VAD

UltraMag Features

- Small and portable features make long term chronic studies more feasible.
- Only one moving part and a low priming volume (7.5 cc).
- No valves, bearings, seals or other sources of friction, which may reduce the level of hemolysis.
- No regions of stasis, heat generation, wear, or mechanical malfunction, which may make it less prone to thrombus formation.
- Does not have a limited life span which makes it a more practical consideration for long term survival models of cavopulmonary support, which has never been studied.
- Has the possibility, like the PediVAD VAD, of being available for clinical use in the near future.
### Table 3: Hemodynamic and Pulmonary Vascular Reactivity Indicators

| Indicator                              | Mean ± SD | Mean ± SD | p Value ND vs Mean T
|----------------------------------------|-----------|-----------|---------------------|
| Mean Arterial Pressure                | 128.6 ± 7.6 | 128.4 ± 10.2 | 0.2205
| Mean Pulmonary Arterial Pressure      | 29.8 ± 6.6  | 29.8 ± 5.7 | 0.6710
| Cardiac Output (liters/min)           | 5.2 ± 1.5   | 5.1 ± 1.5 | 0.7110
| Pulmonary Capillary Wedge Pressure    | 10.5 ± 2.5  | 10.8 ± 2.2 | 0.2792
| LVED Pressure (mmHg)                  | 95 ± 15     | 74 ± 22  | 0.2300
| Stroke Work (dyne.sec/cm²)            | 7.7 ± 1.8   | 7.4 ± 2.4 | 0.5340
| Pulmonary Vascular Resistance         | 2.2 ± 0.7   | 2.1 ± 1.0 | 0.4680
| Cardiac Index (liters/min/m²)         | 3.2 ± 0.8    | 3.3 ± 1.2 | 0.8590
| Pulmonary Vascular Resistance (mmHg)  | 14.5 ± 4.2   | 14.4 ± 5.0 | 0.6907
| Hematocrit (%)                        | 39.4 ± 1.5  | 39.8 ± 1.5 | 0.1380

**Experimental Group Cardiac Index**

- Cardiac Index (liters/min/m²)

**Experimental Group Pulmonary Vascular Resistance**

- Pulmonary Vascular Resistance (mmHg)

**Experimental Group Hematocrit**

- Hematocrit (%)

Time (hours) vs Cardiac Index

Time (hours) vs Pulmonary Vascular Resistance

Time (hours) vs Hematocrit
Conclusions

- Total cavopulmonary diversion using a magnetically levitated ventricular assist device is feasible in an acute newborn lamb model
- Yields stable hemodynamics and adequate pulmonary gas exchange throughout the entire study
- PVR remained stable without evidence of elevation throughout the entire study
- Maintains a stable hematocrit with no evidence of excessive bleeding or thrombosis
- Data supports the indication for longer-term, survival studies

Future Considerations Using a Long-Term Device

- If the PVR continues to drop and reaches normal levels, can the animal be converted to an unassisted univentricular Fontan circulation after device weaning?
- What will be the effect of longer-term cavopulmonary assist on chronic maturation of the newborn transitional pulmonary vasculature?
- Can this serve as a bridge to neonatal Fontan repair of single ventricles?