Hypoplastic Left Heart Syndrome

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Hypoplastic Left Heart Syndrome

• Introduction
• Clinical presentations
• Diagnostic tests
• Treatment options
• Outcomes
Hypoplastic Left Heart Syndrome

• First defined by Drs. Jacqueline Noonan and Alexander Nadas in 1968

• Two conditions required for diagnosis
  – Left heart hypoplasia (underdevelopment), involving
    • mitral valve atresia or severe stenosis
    • left ventricular hypoplasia
    • aortic valve atresia or severe stenosis
    • ascending aortic hypoplasia
  – The left heart’s inability to perfuse the entire aorta adequately
    • Making aortic perfusion dependent upon the patent ductus arteriosus (PDA) and pulmonary artery
Hypoplastic Left Heart Syndrome (HLHS)
Hypoplastic Left Heart Syndrome

• 2-3% of all congenital heart disease
• 2/10,000 births (about 4/year in our region)
• Anomalies may coexist
  – Turner syndrome XO, Trisomy 13, 18
  – CNS anomalies
  – GI anomalies
• Family History may be positive for left heart lesions
  – Bicuspid aortic valve
  – Coarctation of the aorta
  – Subaortic stenosis
Hypoplastic Left Heart Syndrome

- Arguably the most serious heart defect
- The most difficult defect to treat surgically
- Uniformly fatal until the early-mid 1980’s
- With development of three staged operations the survival has increased significantly
- Oldest survivors are reaching 30 years of age
- Long term outcome studies are limited
Hypoplastic Left Heart Syndrome
Pathophysiology

- Minimal/no flow across aortic valve
- RV/PA perfuse aorta via PDA
- Pulmonary venous return must cross PFO/ASD
Hypoplastic Left Heart Syndrome

• Optimum circulation requires
  – Unrestrictive PDA (patent ductus arteriosus)
    • Can be opened/maintained open with Prostaglandin E IV after diagnosis is made
  – Unrestrictive PFO (patent foramen ovale)
    • When too small, may be enlarged with catheter-directed balloon septostomy
    • No PFO a bad prognostic sign
  – Good right ventricular systolic function
  – Competent tricuspid and pulmonic valves
  – Absence of complicating factors
    • ? Mitral stenosis-aortic atresia
    • Coronary sinusoids
Hypoplastic Left Heart Syndrome with Intact Atrial Septum (No PFO)

- Mortality very high with no/tiny atrial defect
  - Untreated, leads to death within first day

- Intervention in most hands carries very high risk
  - In utero atrial septostomy
  - Immediate postnatal catheter-directed septostomy
  - Immediate postnatal institution of CP bypass (ECMO)
    - Surgical atrial septostomy
    - Hybrid procedure
HLHL Intact Atrial Septum
Possible Fetal Intervention
Hypoplastic Left Heart Syndrome
Clinical Presentations—Prenatally

• Abnormal fetal sonogram (4 chamber view) leads to prenatal diagnosis

• Advantages of prenatal diagnosis
  – Preparing the family for the diagnosis and its possible treatments
  – Planning prenatal care and delivery at a tertiary center
  – Post operative survival is not significantly better, but
    • Prenatally diagnosed cases can be treated before the circulation destabilizes and leads to end organ damage
      – Less preop acidosis and renal dysfunction, fewer postop seizures
  – Prenatally diagnosed cases tend to be lower weight and delivered earlier (risk factor)
Hypoplastic Left Heart Syndrome
Clinical Presentation—Postnatally
PDA large

- All systemic and pulmonary venous return mixes at right atrial level
- Cyanosis usually not visible
- Screening pulse oximetry *usually* abnormal
- Possible murmur, increased precordial activity to palpation
Hypoplastic Left Heart Syndrome
Presentation Postnatally—Symptomatic
PDA restrictive

- As PDA closes, suddenly
  - Aortic perfusion decreases
  - Pulmonary blood flow increases

- Symptoms/signs
  - Tachypnea, dyspnea
  - Lethargy or irritability
  - Pallor
  - Tachycardia
  - Mild cyanosis
  - Single S2
  - Usually no murmur
  - Hepatomegaly
  - Diminished pulses

May masquerade as “sepsis”
Hypoplastic Left Heart Syndrome

Diagnosis

- Echocardiography is crucial to assess
  - LV size and function
  - Mitral and aortic valve size and function
  - Ascending aortic size
  - Patent ductus arteriosus
  - Patent foramen ovale
  - Associated cardiac anomalies
    - Pulmonary venous return anomalies
    - Tricuspid incompetence
    - RV dysfunction
Hypoplastic Left Heart Syndrome
Hypoplastic Left Heart Syndrome Diagnosis

• ECG
  – To rule out arrhythmias

• Chest X ray
  – Mainly to exclude pulmonary disease

• Arterial/venous blood gas
  – Mainly to exclude acidosis (from poor aortic perfusion)

• Cardiac catheterization
  – In case of HLHS with mitral stenosis/aortic atresia
    • Assess coronary sinusoids
      – Which may complicate intraoperative and postoperative coronary perfusion
Hypoplastic Left Heart Syndrome
Treatment Options

• Surgical
  – Norwood palliation
    • 1. Norwood procedure (within first week)
    • 2. Bidirectional Glenn operation (3-15 months)
    • 3. Total caval pulmonary connection (2-5 years)
  – Hybrid palliation
    • 1. Hybrid procedure (within first week)
    • 2. Combination Norwood and bidirectional Glenn procedure (>3 months)
    • 3. Total caval pulmonary connection (2-5 years)
  – Cardiac transplantation
    • Rarely considered since risk of awaiting a donor heart is greater than the risk of the Norwood procedure

• Palliative care
• Open heart operation
• Main pulmonary artery anastomosed to ascending aorta and arch
• Pulmonary artery bifurcation connected to
  – Aortic arch (BT shunt)
  – Right ventricle (Sano)
• Foramen ovale enlarged
Transplantation-Free Survival and Interventions at 3 Years in the Single Ventricle Reconstruction Trial
Jane W. Newburger, MD, MPH; Lynn A. Sleeper, ScD; Peter C. Frommelt, MD; Gail D. Pearson, MD, ScD; et. Al. for the Pediatric Heart Network Investigators

- Multicenter study of babies with HLHS born since 2005 who had the Norwood procedure
- Assessed transplant-free survival at 1 year of age, then after 3 years and 5 years of age
- Compared survival between Norwood BT shunt and Norwood Sano patients

<table>
<thead>
<tr>
<th>Survival</th>
<th>Norwood BT Shunt</th>
<th>Norwood Sano</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>64%</td>
<td>74%</td>
</tr>
<tr>
<td>3 years</td>
<td>61%</td>
<td>67%</td>
</tr>
<tr>
<td>5 years</td>
<td>60%</td>
<td>64%</td>
</tr>
</tbody>
</table>
Norwood Procedure Outcomes


![Graph showing outcomes for Norwood Procedure](image)

- **Explained:**
  - Proportion Free of Death and Transplant
  - Years since Randomization
  - Logrank P-Value = 0.14
  - Wilcoxon-Gehan P-Value = 0.07

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>MBTS</th>
<th>RVPAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>275</td>
<td>175</td>
<td>202</td>
</tr>
<tr>
<td>168</td>
<td>159</td>
<td>183</td>
</tr>
<tr>
<td>127</td>
<td>77</td>
<td>85</td>
</tr>
<tr>
<td>30</td>
<td></td>
<td>43</td>
</tr>
</tbody>
</table>
Norwood Procedure—Complications

in addition to shock, CHF, need for ECMO

Approximately 50% have major morbidities

Table 1. Clinical Events From Norwood to 3 Years of Age by Shunt Type

<table>
<thead>
<tr>
<th>Outcome</th>
<th>All (n=549)</th>
<th>MBTS (n=275)</th>
<th>RVPAS (n=274)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death or cardiac transplantation</td>
<td>197</td>
<td>107</td>
<td>90</td>
<td>0.15</td>
</tr>
<tr>
<td>Death (before transplantation)</td>
<td>177</td>
<td>97</td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>Cardiac transplantation</td>
<td>20</td>
<td>10</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Death/transplantation ≤ 1 y</td>
<td>172</td>
<td>100</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>Death/transplantation &gt; 1 y—≤ 3 y</td>
<td>25</td>
<td>7</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Incidence per 100 patient- y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac surgeryies</td>
<td>164.3</td>
<td>167.9</td>
<td>161.0</td>
<td>0.37</td>
</tr>
<tr>
<td>Catheter intervention</td>
<td>43.1</td>
<td>30.2</td>
<td>54.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Interventional catheterizations</td>
<td>31.2</td>
<td>23.9</td>
<td>37.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Complications</td>
<td>289.7</td>
<td>296.1</td>
<td>284.0</td>
<td>0.23</td>
</tr>
<tr>
<td>Patients, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pacemaker placed</td>
<td>12/549 (2.2)</td>
<td>5/275 (1.8)</td>
<td>7/274 (2.6)</td>
<td>0.58</td>
</tr>
<tr>
<td>Thrombotic event</td>
<td>77/549 (14.0)</td>
<td>38/275 (14.2)</td>
<td>38/274 (13.9)</td>
<td>1.000</td>
</tr>
<tr>
<td>Stroke</td>
<td>34/549 (6.2)</td>
<td>12/275 (4.4)</td>
<td>22/274 (8.0)</td>
<td>0.08</td>
</tr>
<tr>
<td>Seizure</td>
<td>64/549 (11.7)</td>
<td>29/275 (10.5)</td>
<td>35/274 (12.8)</td>
<td>0.43</td>
</tr>
<tr>
<td>PLE</td>
<td>7/549 (1.3)</td>
<td>2/275 (0.7)</td>
<td>5/274 (1.8)</td>
<td>0.29</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>0/549 (0.0)</td>
<td>0/275 (0.0)</td>
<td>0/274 (0.0)</td>
<td>...</td>
</tr>
<tr>
<td>Plastic bronchitis</td>
<td>1/549 (0.2)</td>
<td>0/275 (0.0)</td>
<td>1/274 (0.4)</td>
<td>0.499</td>
</tr>
</tbody>
</table>

MBTS indicates modified Blalock-Taussig shunt; PLE, protein-losing enteropathy; and RVPAS, right ventricle-to-pulmonary artery shunt.

*P values for incidence rate and proportion comparisons are based on Poisson regression and Fisher exact test, respectively. P value for comparison of 3-year death/transplantation is based on Wald test of the point-wise Kaplan-Meier event rate estimates at 3 years.
Norwood Procedure—Outcomes
Mitral Stenosis and Aortic Atresia—A Risk Factor for Mortality After the Modified Norwood Operation in Hypoplastic Left Heart Syndrome
Stephanie L. Siehr, MD, Katsuhide Maeda, MD, Andrew A. Connolly, MD, Theresa A. Tacy, MD, et. al. (Ann Thorac Surg 2016;101:162–8)

- 74 patients with HLHS from 2005-2013 underwent Norwood procedure
- 14 with Mitral stenosis-aortic atresia (MS-AA)
- 60 other usual variants
- Mortality < 30 days post op
  - 4/14 MS-AA (29%)
  - 4/14 other (7%)
- But, there were interstage and later deaths
- Survival by 6-8 years: 60-70%
Norwood Procedure—Outcomes
Preoperative Trophic Feeds in Neonates with Hypoplastic Left Heart Syndrome  
Rune Toms, MD,† Kimberly W. Jackson, MD,* Robert J. Dabal, MD,‡ Cristina H. Reebals, NNP,† and Jeffrey A. Alten MD*  
*Congenit Heart Dis. 2015;10:36–42

Table 2. Preoperative, Intraoperative, and Postoperative Outcomes

<table>
<thead>
<tr>
<th>Variable</th>
<th>No Pre-Op Trophic Feeds (n = 14)</th>
<th>Yes Pre-Op Trophic Feeds (n = 31)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPB time, minutes</td>
<td>171 (153.5, 262.5)</td>
<td>189 (162, 214)</td>
<td>.91</td>
</tr>
<tr>
<td>ACC time, minutes</td>
<td>77 (65.5, 94.5)</td>
<td>80 (67, 100)</td>
<td>.73</td>
</tr>
<tr>
<td>OR fluid balance, mL/kg</td>
<td>296 (165, 477)</td>
<td>159 (112, 271)</td>
<td>.02</td>
</tr>
<tr>
<td>Peak inotrope score</td>
<td>15.4 (6.3, 16.5)</td>
<td>11.7 (10.9, 18.2)</td>
<td>.15</td>
</tr>
<tr>
<td>Peak lactate, mmol/L</td>
<td>15 ± 6.5</td>
<td>11.4 ± 5.3</td>
<td>.06</td>
</tr>
<tr>
<td>Fluid balance at 48 h, mL/kg</td>
<td>92 (2, 171)</td>
<td>-30 (-155, 89)</td>
<td>.03</td>
</tr>
<tr>
<td>Postoperative infection, n (%)</td>
<td>3 (21)</td>
<td>7 (23)</td>
<td>1</td>
</tr>
<tr>
<td>Low ALC first 72 h</td>
<td>1190 (972, 1906)</td>
<td>1195 (868, 1748)</td>
<td>.79</td>
</tr>
<tr>
<td>Lowest albumin in first 72 h</td>
<td>2.7 (2.5, 2.8)</td>
<td>2.9 (2.6, 3.1)</td>
<td>.11</td>
</tr>
<tr>
<td>Duration mechanical ventilation, days</td>
<td>8.3 (5, 11.5)</td>
<td>5.5 (4, 8.8)</td>
<td>.006</td>
</tr>
<tr>
<td>Day of first postoperative feed</td>
<td>5 (3, 6)</td>
<td>4 (2, 5)</td>
<td>.51</td>
</tr>
<tr>
<td>Days to full feeds</td>
<td>10.5 (7.1, 14.3)</td>
<td>7 (5.1, 10.8)</td>
<td>.059</td>
</tr>
<tr>
<td>ICU LOS, days</td>
<td>14 (8.5, 18.8)</td>
<td>9.5 (7.8, 16.3)</td>
<td>.252</td>
</tr>
<tr>
<td>Hospital LOS, days</td>
<td>29 (12.5, 54.5)</td>
<td>18.5 (13, 27)</td>
<td>.198</td>
</tr>
</tbody>
</table>

ACC, aortic cross clamp; ALC, absolute lymphocyte count; CPB, cardiopulmonary bypass; ICU, intensive care unit; LOS, length of stay; OR, operating room.

significant pre- or postoperative feeding intolerance or NEC. There were no differences between groups in hospital course or outcome.

Discussion  
In this retrospective study, we add to the growing evidence suggesting that routine preoperative trophic feeds may mitigate the negative impact of hypoperfusion on gut function in neonates with HLHS.
Norwood Procedure
Does Timing Make a Difference?

• Earlier stage 1 palliation is associated with better clinical outcomes and lower costs for neonates with hypoplastic left heart syndrome.


• Excellent survival statistics, but mortality increased daily from day 4 on
2nd Operation: Bidirectional Glenn Anastomosis or…
Bidirectional Glenn Anastomosis Outcomes

- Lowest Mortality of the three operations
- < 5% in most institutions
- Interstage mortality (deaths after discharge from Norwood procedure and before Glenn) reduce numbers of high risk patients for Glenn
- Performed 3 months-15 months
Hybrid Operation

- Stent placed in PDA
- Pulmonary artery branches banded to reduce flow/pressure
3rd Operation: Total Caval Pulmonary Connection

Fontan operation

Superior vena cava and Gore-tex® conduit attached to pulmonary artery

Inferior vena cava attached to Gore-tex® conduit

A fenestration (small hole) allows blood flow between right atrium and conduit

Fontan operation with extracardiac conduit
Total Caval Pulmonary Connection
“Fontan Operation”

• Ultimate palliation for HLHS
  – Right ventricle functions as the left ventricle
  – Nearly all systemic venous return reaches the pulmonary artery directly
  – Long term issues
Redefining Expectations of Long-Term Survival After the Fontan Procedure
Twenty-Five Years of Follow-Up From the Entire Population of Australia and New Zealand
Yves d’Udekem, MD, PhD*; Ajay J. Iyengar, MBBS(Hons), BMedSci, GCALL*; John C. Galati, BSc, PhD; Victoria Forsdick, MBBS; Robert G. Weintraub, MBBS, FRACP; Gavin R. Wheaton, MBBS, FRACP, et. al. *Circulation. 2014;130:[suppl 1]S32-S38

• Freedom from Fontan Failure 10 years after the operation
  – HLHS group 79%
  – Other single ventricle group 92%
HLHS Long Term Follow up—Survival and Morbidity

• Long term survival
  – Equals the product of survivals of three operations
    • 80% x 95% x 79% = 60%
    • 60% is current survival to early school age

• Morbidity
  – Congestive heart failure, possible need for transplantation
  – Multi-system disease and complications
Late Consequences of the Fontan Operation
Jack Rychik, MD; David J. Goldberg, MD

Known Clinical Complications Seen in Survivors Late After Fontan Operation  *Circulation*. 2014;130:1525-1528.)

The Fontan operation is the third operation for HLHS

- Exercise intolerance
- Arrhythmia
- Thromboembolism
- Delayed somatic growth and development
- Delayed pubertal development
- Protein-losing enteropathy
- Plastic bronchitis
- Liver fibrosis
- Renal dysfunction
- Venous insufficiency, varicose veins
- Neurocognitive deficits
Early Developmental Outcome in Children With Hypoplastic Left Heart Syndrome and Related Anomalies
The Single Ventricle Reconstruction Trial
Jane W. Newburger, MD, MPH; Lynn A. Sleeper, ScD; David C. Bellinger, PhD, MSc; Caren S. Goldberg, MD, MS; et. al. for the Pediatric Heart Network Investigators

- 321/373 post Norwood patients had Psychomotor Development Index PDI and Mental Development Index MDI (normal score = 100 for each)
- Study group results
  - **PDI 74**
    - Risk factors for lower score
      - Clinical center
      - Birth weight < 2.5 kg
      - Prolonged hospitalization post Norwood
      - Interstage complications
  - **MDI 89**
    - Risk factors for lower score
      - Clinical center
      - Birth weight < 2.5 kg
      - Genetic syndromes/anomalies
      - Lower maternal education level
      - Longer mechanical ventilation post Norwood
      - Interstage complications
Hypoplastic Left Heart Syndrome

Summary

- Relatively rare, very serious diagnosis
- Over 50% diagnosed prenatally
- No longer fatal, but treatment carries morbidity as well as mortality
- Pre-, peri-, and postoperative management is receiving increased focus in many centers
- Low birth weight and associated anomalies increase operative mortality and morbidity
- Intact atrial septum remains a poor prognostic sign
Hypoplastic Left Heart Syndrome

Summary

• Truly long term outcome is not yet definable
  – Outcomes reported on websites or parents’ testimonials may be misleading or false
  – Current studies indicate 60% survival to 6-8 years of age
  – With improved management survival is hoped to reach 70% at 21 years of age

• Additional risk factors raise risk and must be regarded in decision making
  – Mitral stenosis/aortic atresia variant
  – Operation > 7 days
  – Smaller weight/earlier gestation
  – Associated anomalies/syndromes
Hypoplastic Left Heart Syndrome
Future Goals for Our Region and Others

• Further refinement of prenatal and postnatal diagnosis of HLHS and its anatomic variants
• Strive for delivery near term (only in Rochester?)
• Identify infants who will benefit from the hybrid procedure, rather than the Norwood procedure
• Devise new methods for cardiopulmonary bypass and myocardial perfusion during open heart surgery (particularly with HLHS and mitral stenosis/aortic atresia)