Disclosure

- I have no relevant financial relationships with any companies related to the content of this course.

Objectives

- To provide an overview of pediatric cardiac transplantation
  - What is the pediatric population that requires a OHT?
  - How do they do?
- Describe the changing face of congenital transplantation
  - Shifting single ventricle population
- Discuss challenges of transplantation for failing Fontans
  - Plastic bronchitis/Protein losing enteropathy
  - Early phase graft loss
A nod to history

- First cardiac transplant:
  - 12/3/1967: Christiaan Barnard - Cape Town
- First infant cardiac transplant
  - 12/6/1967: Adriano Kantrowitz – Brooklyn
    - No immunosuppression
- 1984 Loma Linda – Baby Fae
  - Managed with CSA – died POD #20
- First successful Neonatal Transplant: November 15, 1985
  - Leonard L. Bailey – Loma Linda, California
  - Still alive as of 11/17

So where have we come to?

United States

Who gets a transplant?

- < 1 year old
- 1 – 5 years old
- 6 – 10 years old
- 11 – 18 years old
Patients Bridged with Mechanical Circulatory Support

Ventricular Assist Devices - Berlin Heart
- Para-corporeal VAD
- Pulsatile flow
  - Adults think we’re nuts!
  - Complication profile is not great
    - Neurologic concerns/strokes
  - But it’s what we got!

Pulsatile outcome (Berlin)

Ventricular Assist Devices - Heartware
- Intra-corporeal VAD
- Continuous flow
  - Standard of care for adults
    - Big two are Heartware (HVAD) and Heartmate II
  - Complication profile is dramatically better
  - But it’s gotta fit!
  - Almost for sure >40kg
  - Probably 20-40kg (been done down to ~15 kgs)
  - Discharge possible!
Continuous flow outcomes


Outcomes– ERA effect

Outcomes–2004-2015 conditional
Outcomes quality of life

- No Activity Limitations
- Performs with Some Assistance
- Requires Total Assistance

1 Year (N = 2,134) 5 Year (N = 1,415) 10 Year (N = 554)

- 0%
- 20%
- 40%
- 60%
- 80%
- 100%

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Congenital Heart Disease

- This population is changing
- Shift from early mortality

Congenital Heart Patients

Trends in the Indications and Survival in Pediatric Heart Transplant: A 24-year Single-Center Experience in 367 Patients

References:

Heart transplantation is the only viable treatment option for end-stage heart failure caused by congenital heart disease (CHD). A multifaceted approach to the management of patients with CHD is well documented. This study describes the outcomes of patients with CHD who underwent heart transplantation at a single institution over a 24-year period. The results showed that heart transplantation in CHD patients is an effective treatment option with excellent outcomes.
### Congenital Heart Patients

1986-1993

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<tr>
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<td>11/50 (22%)</td>
<td>40/116 (34%)</td>
<td>70/141 (49%)</td>
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<tr>
<td>CHD</td>
<td>37/50 (74%)</td>
<td>69/116 (60%)</td>
<td>67/141 (48%)</td>
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<td>Single V (% of CHD)</td>
<td></td>
<td></td>
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<tr>
<td>Without palliation</td>
<td>30/37 (81%)</td>
<td>33/70 (47%)</td>
<td>12/67 (18%)</td>
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<tr>
<td>After palliation</td>
<td>3/37 (8%)</td>
<td>9/70 (13%)</td>
<td>16/67 (24%)</td>
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<tr>
<td>After failed Fontan</td>
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<td>Biventricular CHD</td>
<td>3/37 (8%)</td>
<td>17/70 (24%)</td>
<td>15/67 (22%)</td>
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<td>Redo transplant</td>
<td>2/50 (4%)</td>
<td>7/116 (6%)</td>
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1994-2001

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2002-2009

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### Shift away from primary transplant for HLHS/single ventricle

- “Transplantation for heart failure related to failed SV palliation has become the most common indication for patients with CHD”

### Future of OHT???

- If we add most of the neonatal palliations back later

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### Increasing incidence of cardiomyopathy??

- Shifting Single Ventricles
  - 1986-93: 30/37 without palliation
  - 81% of CHD and 60% of TOTAL transplant volume!

- So what happens if we take OUT most of those early HLHS?
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**The “Failed Fontan”**

- Uni-ventricular heart with “heart failure”
  - Different from “typical” adult heart failure
    - Ventricular dysfunction (or NOT)
    - AV valve regurg
    - Arrhythmia
    - Hepatic insufficiency
    - Protein losing enteropathy (PLE)
    - Plastic Bronchitis (PB)
  - They just DON’T fit a box in UNet!
Survival after OHT for Failed Fontan

- What do they look like?
  - Multiple prior operations
  - Elevated Panel Reactive Antibody (PRA)
  - Poor nutritional status
  - Multi-organ system dysfunction typical

OHT for Failed Fontan: Lurie Children’s

- 224 Transplants: 1988 – 2013
- 23 failed Fontan
  - Mean age: 14.9 years (4.4 – 47 years)
  - Mean interval since Fontan 8.3 years
- Mean # Prior operations = 3.7
- PLE (n = 15)
- Plastic Bronchitis (n = 2)
- s/p Fontan Conversion (n = 8)
- Ventilator (n = 8)

Results

- 5 early deaths (23%)
  - No clear risk factors (likely due to n)
  - Renal failure a concern
- PLE resolved in all survivors
- Plastic Bronchitis resolved in all survivors
- Pulmonary AVMs resolved as well
Protein Losing Enteropathy

- Protein loss through the GI tract
  - In CHD dominantly reported in single ventricle pts after Fontan
- Etiology unclear
  - Increased hydrostatic pressure
  - Non-pulsatile flow
  - Altered cardiac output
- Seen despite "optimal" Fontan hemodynamics
  - With preserved and decreased function
- Many potential treatments described
  - Historically significant mortality/morbidity

PHTS PLE Project

- Compared transplantation after Fontan with vs without PLE
  - 96 patients with PLE vs 260 without
  - Patients with PLE were:
    - Older (12.2 vs 8.7yrs)
    - Larger (BSA 1.1 vs 0.9m²)
    - Lower serum Bil (0.5 vs 0.9mg/dl)
    - Lower BNP (59 vs 227pg/ml)
    - Lower Albumin (2.7 vs 3.8 gm/dl)
    - Lower PCW (10.5 vs 14mmHg)
    - Less PB (9.1 vs 26.1%)
    - Less intubation (3.1 vs 13.1%)

Plastic Bronchitis

- Formation of occlusive airway casts
  - In CHD dominantly reported in single ventricle pts after Fontan
- Etiology/treatment unclear
PHTS Plastic Bronchitis project

- Multicenter prospective database in pediatric OHT
- Captures ~85% of peds OHT
- 10/35 centers had patients with PB
- 14 TOTAL patients
- 10 patients underwent OHT
- Early mortality was higher
- Conditional (after 30 d) and late (to 5 year) survival was equivalent
- Plastic Bronchitis resolved in ALL survivors
- Same shown repeatedly for PLE

Gossett et al. JACC 2013;61:985-986

Survival after OHT for Failed Fontan

Bernstein et al. Circ 2006; 114:273-80

Current Era

Simpson et al. ATS 2017; 103:1315-21
ACHD vs non-CHD

Supporting the SV to OHT

- All of our outcomes are hurt by early phase mortality
  - Earlier referral
    - Better listing concepts/criteria
  - Better prediction and prevention of comorbidities
  - Better options for reversing end organ injury through support?

Supporting the SV to OHT

- VAD support for the SV
  - Very limited numbers
    - ~15-20% of Pedimacs implants for SV overall *
    - ~5% for Fontan *
  - Devices applied:
    - Heartware (systemic); TAH; Jarvik VAD (FTN); Berlin (FTN, systemic); Heartmate; Tandem (systemic)
    - Certainly others!
  - Mortality and morbidity too high-- We MUST do better!

Conclusions

- World wide OHT numbers are relatively static
- Organ availability must increase
- Longer waiting times mitigated by improved medical therapies
- VAD therapies in pediatrics lag far behind adult counterparts
- More congenital patients will be coming!
  - Higher up front mortality, but better long term!
  - Single ventricle patients are challenging, but will be the future
  - We must find better support options to maximize outcomes

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* Pedimacs unpublished communications
Remind me why we do this???

Tony Hines, Transplant Patient, Elves at 53

Thank you!

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