Surgical Management of Lymphatic Complications After Univentricular Heart Repair

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No disclosures
50 yrs of Evolution

- Optimized Fontan candidacy
  - Normal pulmonary anatomy and Low PVR.
  - No pulmonary venous obstruction
  - Preserved ventricular function.
  - Preserved AVV function
  - Staged palliation.

- Optimized Fontan surgical Technique: Extr. Conduit
  - Refinement of CPB management and End organ protection at Fontan
  - Technical perfection of Fontan Pathway pathway
  - Prevention of atrial arrhythmia (no-touch Atrium)
  - Preservation phrenic nerve
Fontan Kreutzer in 2018

• Extra cardiac conduit Fontan (ECC) 20 year follow up
• Survival of 92 %. (Aus NZ Fontan Registry)
• Not a “failed strategy”
• Excellent Survival (better than many Bivent Repairs)
• QOL is reasonable
• Dark clouds on the horizon
  • Fontan failure w preserved V. Fx.
  • Fontan failure w S Ventricle Failure
• What is a Fontan failure? Let’s be honest.

• A suboptimal management is *our* failure not Fontan’s
  • Most SV CHD have normal pulmonary arteries at birth.
  • Sub aortic stenosis can and should be avoided since birth.
  • Chronic volume overload (long standing loose bands, large BT shunts)
  • Phrenic nerve palsy is always iatrogenic.
  • Technical perfection of the Fontan Pathway can and should be always present.
  • Optimal CPB management. TCA, Organ protection @ Fontan Kreutzer
  • Lymphatic failure can be identified pre Fontan and may be prevented.
The lymphatic Circulation

- Perfect system favouring forward flow
- Contraction of Lymphatic Vessels.
  - Pacemaker cells.
  - Valves every 1/3 mm
  - Pulsatile flow.
  - “Twist” of lymphatic vessels
- A lymphatic “Heart”
  - Rate
  - Contractility.
  - Preload
  - Afterload

STS/EACTS Latin America Cardiovascular Surgery Conference 2018
the lymphatic circulation

- Thoracic duct carries 85% of the total lymph flow
- Right Lymphatic Duct.
- Dormant Lymphovenous Communications.
  - To systemic veins
  - To pulmonary veins on left lung (rare)
- Lymph = 1% of Venous Return.
  - 10/20 x increase in right heart Failure
  - Increased Preload.
- Cessation of Drainage at CVP of 22 mm Hg.
  - Increased Afterload
Fontan Kreutzer Lymphodynamics

• Normally lymphatic circulation drains to the lowest pressure site
  • To intrathoracic veins.
  • Drainage increases with inspiration
  • Drainage increases with diastole.
  • “Suction” of Lymph.

• Another True Fontan paradox
  • Lymph is required to drain at a similar or higher pressure than it is produced by hydrostatic pressure.
  • Increased “afterload” for the Lymphatic Circ.

• In Fontan physiology, lymphatic circulation drains to high pressure site
  • No diastole
  • Only Inspiration to increase thoracic duct flow
Lymphatics and Fontan circulation

Fontan circulation operates at or above the functional limits of the lymphatic circulation

• Lymph drainage compromised
  • High CVP (12-15 mm Hg) Increased Afterload. Cessation of TD flow at 20-25 mmHG
  • Mechanical obstruction (Innom Vein thrombosis)
  • Stasis in thoracic duct. Thoracic duct dilation and valve incompetence
  • No opening of dormant communications.

• Early Lymph Complications
  • Pleural effusions, Pulmonary lymphatic edema, Ascites.

• Late Complications
  • Effusions, Ascites, PLE, plastic bronchitis.
  • Chronic Lymphostasis. Liver fibrosis, Renal Failure, Lung Fibrosis, Myocardial Fibrosis?

Lymphostasis

Paralysis

Ectasia

Muscular dysfunction

Valve incompetence

Lymphatic dysplasia

Lymphedema

Lymphangiogenesis

Hyperplasia

Regeneration
Wound-healing
Angiofollicular hyperplasia

Benign
Lymphangioma
• Angiomyoma
• Angiolipoma
• Angiofibroma

Malignant
Kaposi's sarcoma
Lymphangiosarcoma

Fibrosis

Inflammation infection

Injury

Lipogenesis

Immunosuppression

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PLE is the tip of the iceberg

- Fontan Kreutzer: a vicious cycle for GI tract
  - Elevated CVP and mild Portal Hypertension
  - Decreased mesenteric perfusion
    - Elevated Mesenteric Vascular Resistance.
  - Lymphostasis & Chronic splachnic inflammation
    - Increased Lymph production.
    - Impaired lymphatic drainage
    - Lymphostasis, Inflammation & Fibrosis
  - PLE.
    - Lymphatic decompression into low pressured gut lumen.
Lung “lymphodynamics”

• “you can’t have pulmonary edema in a Glenn or Fontan”
  - You can’t have Hydrostatic pulmonary edema.
  - Constant tendency to fluid accumulation in the lung in the Glenn and Fontan

<table>
<thead>
<tr>
<th>Typical values of pulmonary pressures (mmHg)</th>
</tr>
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<tbody>
<tr>
<td>PAP (mean)</td>
</tr>
<tr>
<td>Normal Circulation</td>
</tr>
<tr>
<td>Fontan Kreutzer or Glenn</td>
</tr>
</tbody>
</table>

• Early: Pulmonary congestion /Effusions.
• Late: Lung fibrosis & Plastic Bronchitis.
Plastic bronchitis airway casts from children with Fontan physiology are composed of fibrin and are **cellular** and **inflammatory** in nature, providing evidence that their formation cannot be explained simply by lymph leak into the airways. A derangement in **inflammation resolution** likely contributes to cast formation.

Heart lymphatics

- Extensive Lymphatic network. Drains into Thoracic Ducts
- FX
  - Fluid Balance
  - Removal of Inflammatory mediators
  - Healing.
- Disruption of the lymphatic circulation results in the development of Myocardial fibrosis in dogs
- Fontan circulation
  - Coronary venous drainage @ normal pressure.
- 30 % of adult Fontans show Myocardial Fibrosis by MRI.
- Stiff hearts w diastolic dysfunction.
- A longlife process of Lymphostasis, and chronic inflammation resulting in fibrosis?

KLINE IK, MILLER AJ, KATZ LN.
Fontan Lymphatic complications Diagnosis & intervention

M Itkin & Y Dori U. Penn

• Non contrast MRI (T2 weighted)
  • Classification of Abnormalities.
  • Identification of TD and abn.

• CDMRL
  Aug;98(2):634-4
  Circulation. 2016 Mar 22;133(12):1160-70
  Itkin et al. JACC 2017

• Transabdominal Catheterization of TD.

• Lymphangiography and Lymphodynamics

• Intervention on PLE and PB

Maximal Intensity Projections (MIP) of MRI Lymphangiograms in 4 patients. Diagnosis listed in top left corner. (List of abbreviations: PLE-protein losing enteropathy, PB-plastic bronchitis, LE-lymphangiectasia, LC-lymphatic collaterals, TD-thoracic duct, Edema)
Late Fontan end Organ Fibrosis

• Mandatory liver/renal/lung surveillance.
• Shall we wait for the inevitable? Organ Fibrosis
• Therapeutic options are limited and primarily used for failing pts.
• An elevated CVP is inherent to the Fontan circulation
• Increased lymph production is inherent to the Fontan circulation
• Impaired lymphatic drainage may NOT be inherent to Fontan circulation
LYMPHATIC DECOMPRESSION IN FONTAN
The holy grail?


- 40 dogs with TR and PS “Fontan” reproduction. (High CVP, low LAP)
- 20 x Increased production of Lymph (ascites, heart failure)
- Increased CVP w Cessation of TD flow.
- @ Day 3 Thoracic Duct to Pulmonary Vein shunt
  - Increased lymph drainage
  - Complete Resolution of ascites
  - Increased Na and Water Excretion.
  - Reduction of CVP from 15 to 10 mmHg
    - Increased Cardiac Index?
  - “Experimental evidence that the manifestations of circulatory congestion can be relieved in dogs with isolated right-heart failure when the TD is anastomosed to a normotensive pulmonary vein”
Hraska procedure

- TD decompression via Innominate vein-left atrium anastomosis for PLE.
  - Inn vein take down.
  - Fenestration
  - Decompression of the Fontan through the brain veins/transverse sinus

TD decompression: How and when?

- Modified Hraska Procedure.
  - PTFE graft
  - Vein homograft
  - Subclavian vein flow to “flush” the system
- Failing Fontan with PLE/PB +/- Organ Failure
- W
- Early failure, Ascites and Hidrothorax
- Concomitant to Fontan procedure for high risk patients?
  - Thoracic Lymphangiectasia by MRI.
  - Elevated PVR
  - Systolic/diastolic dysfunction
# Clinical experience in Failing Fontans

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>Weight (kg)</th>
<th>Diagnosis</th>
<th>Time since Fontan</th>
<th>PLE</th>
<th>Ascites</th>
<th>Effusions</th>
<th>Plastic Bronc.</th>
<th>Procedure</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>15</td>
<td>Heterotaxy syndrome, asplenia, common AVVR,</td>
<td>2y</td>
<td>yes</td>
<td>Yes, massive</td>
<td>Yes, Bilat</td>
<td>No</td>
<td>R Glenn take down, AVVR.</td>
<td>Late death, Pulm Hemorrhage 3m.</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>HLHS</td>
<td>4m</td>
<td>yes</td>
<td>Yes, massive</td>
<td>Yes, Bilat</td>
<td>Nio</td>
<td>Hraska</td>
<td>Alive, 8m, Class II</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
<td>Heterotaxy syndrome, asplenia, depressed RV function.</td>
<td>1m</td>
<td>no</td>
<td>Yes</td>
<td>Yes, Bilat</td>
<td>No</td>
<td>Hraska</td>
<td>Early death, Vent Dysfx</td>
</tr>
<tr>
<td>6</td>
<td>21</td>
<td>PA IVS Stenotic BDG</td>
<td>2y</td>
<td>No</td>
<td>no</td>
<td>Yes, right</td>
<td>yes</td>
<td>Hraska</td>
<td>Alive recurrent PB</td>
</tr>
</tbody>
</table>
Case IV

- 6 y/old. 2 yrs post Fontan
- Plastic Bonchitis. 2 episodes per month
- Hraska procedure with LIJ ligation.
- Recurrent PB.
- Embolization and complete cessation.
- First case of combined Lymphatic decompression and intervention for Lymphatic complications
Case II

- 3 y/old. 4 m post Fontan
- Unbalanced AV Canal status post Norwood and Glenn
- Cachectic patient, 8 kg, ventilated 45 d.
- Fontan Failure with chronic ascites and Hydrothorax (600/800 ml/d)
- TD decompression
  - “Classic Hraska”
- Complete cessation of Effusions and Ascites in 6 days.
- Nutritional support, discharged home on Oxygen.
- Fup 8m, 10.5 Kg, Right effusions.
chest x-ray
Pre/Post Hraska 4th PO day
Fontan Outcome of 83 Glenn Patients With Pre Fontan T2 MRI Imaging (mandatory!!)

<table>
<thead>
<tr>
<th>Classification of T2 Lymphatic Abnormalities</th>
<th>Type 1/2</th>
<th>Type 3</th>
<th>Type 4</th>
<th>p</th>
<th>Type 1/2 vs Type 3</th>
<th>Type 1/2 vs Type 4</th>
<th>Type 3 vs Type 4</th>
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<tr>
<td>TCPC Completion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>52 (98.1%)</td>
<td>16 (94.1%)</td>
<td>6 (46.2%)</td>
<td>&lt;0.001</td>
<td>0.429</td>
<td>&lt;0.001</td>
<td>0.009</td>
</tr>
<tr>
<td>No</td>
<td>1 (1.9%)</td>
<td>1 (5.9%)</td>
<td>7 (53.8%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCPC Takedown</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Yes</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>1 (7.7%)</td>
<td>0.066</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
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<tr>
<td>No</td>
<td>53 (100%)</td>
<td>17 (100%)</td>
<td>12 (92.3%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transplant</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>3 (23.1%)</td>
<td>0.023</td>
<td>n/a</td>
<td>0.036</td>
<td>0.179</td>
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<tr>
<td>No</td>
<td>53 (100%)</td>
<td>17 (100%)</td>
<td>10 (76.9%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alive</td>
<td>53 (100%)</td>
<td>17 (100%)</td>
<td>8 (51.5%)</td>
<td>&lt;0.001</td>
<td>n/a</td>
<td>&lt;0.001</td>
<td>0.009</td>
</tr>
<tr>
<td>Deceased</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>5 (38.5%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Duration of Effusions (d)</td>
<td>6.88 (3.45)</td>
<td>12.13 (9.99)</td>
<td>14.75 (6.85)</td>
<td>&lt;0.001</td>
<td>0.006</td>
<td>0.029</td>
<td>1</td>
</tr>
<tr>
<td>Mean Duration of Hospital Stay (d)</td>
<td>9.31 (3.23)</td>
<td>24.44 (29.12)</td>
<td>25.5 (7.05)</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>0.085</td>
<td>1</td>
</tr>
<tr>
<td>Age (y)</td>
<td>Weight (kg)</td>
<td>Diagnosis</td>
<td>Pre Fontan MRI classification type</td>
<td>Chest tube duration (days)</td>
<td>Procedure</td>
<td>outcome</td>
<td>Follow UP</td>
</tr>
<tr>
<td>--------</td>
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<td>----------------------------</td>
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<td>-----------</td>
</tr>
<tr>
<td>22</td>
<td>55</td>
<td>DILV, SLL, Rest BVF, S/P Banding and Glenn</td>
<td>4</td>
<td>2</td>
<td>Modified Hraska. LIJV to RSVC graft</td>
<td>Alive</td>
<td>20 m, Class I</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>HLHS S/P Norwood and Glenn</td>
<td>4</td>
<td>5</td>
<td>Hraska</td>
<td>Alive</td>
<td>6 m. Class I</td>
</tr>
<tr>
<td>3</td>
<td>11</td>
<td>DORV MA, S/P banding atrial septectomy and Glenn</td>
<td>3</td>
<td>7, Right Hidrothorax.</td>
<td>Hraska</td>
<td>Alive</td>
<td>2m Class 1.</td>
</tr>
<tr>
<td>2</td>
<td>13</td>
<td>HLHS</td>
<td>4</td>
<td>3</td>
<td>Hraska</td>
<td>Alive</td>
<td>2 m Class I</td>
</tr>
</tbody>
</table>
Case I

- 22 y/o criss cross heart, S/P Glenn and PA banding @ 4 yrs.
- Severe cyanosis
  - Sat 70/75 %
  - PA pressure 15 mm Hg.
  - Massive Lymphangiectasia by MRI
- MRI CHOP class:
  - Type 4 Abnormalities
  - TD dilatation and Tortuosity
  - Pulmonary Lymphangiectasia

TD aneurism 6,4 mm Diameter
Case I

- TD decompression
  - Extracardiac conduit Fontan
  - Fenestration via subclavian vein
  - PTFE graft LIJ-SVC
- Extubated POD #1, No effusions
- Alive 20 m after FK
- Class I
Lymphatic decompression in Fontan Kreutzer

• Potential benefit
  • Improved lymphatic drainage (decreased Afterload)
  • Lower CVP: Lymph flow outside Fontan flow. (Decreased Preload)
  • Ideal Fenestration: no systemic desaturation
  • Decreased hepatic congestion. Fibrosis and cirrhosis?
  • Prevention of PB and PLE
  • Resolution of PB and PLE post Fontan?
    • Word of Caution. Concomitant intervention.
  • Resolution of ascites, pleural effusions.
  • Increased cardiac index.

• Potential detriment
  • Unknown effects of lymphatic flow (Inflammatory mediators, Bacteria, etc) to the left sided circulation without pulmonary first pass.
  • Technical difficulties, leaks and blockade of lymphatic drainage.
Summary

• Lymphatic Intervention is here and it may benefit outcome
  • Interventional Cath for PLE and PB.
  • Surgical Lymphatic decompression may
    • Ameliorate fibrosis and End Organ Failure
    • Improve cardiac output.
    • Prevent or treat Fontan Lymphatic Failure.
      • Early
      • Late