TECHNIQUES AND EVOLUTION OF THE FONTAN PROCEDURE

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The Cardiac Center at
The Children’s Hospital of Philadelphia
Surgery for Single Ventricle - History

1943:  *Starr* - Destroys 75% of RV Muscle with Cautery without Increased Systemic Venous Pressure

1945:  *Blalock and Taussig* - Systemic to Pulmonary Artery Shunt

1958:  *Glenn* - Superior Vena Cava to Right Pulmonary Artery Shunt “Classic Glenn Shunt”

1968:  *Fontan and Baudet* - First “Physiologic” Correction of Tricuspid Atresia (Reported in 1971)

1971:  *Kreutzer* - First Atrio-Pulmonary Fontan (Reported in 1973)

1972:  *Azzollina* - Bidirectional Glenn Shunt
Surgery for Single Ventricle - History

1978: Prostaglandin E\textsubscript{1} Introduced into Clinical Trials

1983: \textit{Norwood} - Stage I Palliation For Hypoplastic Left Heart Syndrome

1987: \textit{Puga} - Complete Exclusion of Right Side of Heart

1988: \textit{Laks} - Adjustable Atrial Communication

1988: \textit{de Leval} - “Total Cavopulmonary Connection”

1990: \textit{Bridges} - Routine Fixed Baffle Fenestration with Transcatheter Closure

1990: \textit{Marcelletti} - Extracardiac Fontan
Fontan Physiology

- All systemic venous return is routed so as to flow passively into the pulmonary arteries
  - Increased PVR or EDP results in low cardiac output
  - Maneuvers which increase heart rate or contractility may not improve cardiac output in this setting
- Allowing a R-L shunt at the atrial level ("fenestrated Fontan") has proven valuable in this palliation
“The Ten Commandments”

1) Minimum Age 4 Years
2) Sinus Rhythm
3) Normal Caval Drainage
4) Right Atrium of Normal Volume
5) Mean PA Pressure < 15 mmHg
6) Pulmonary Vascular resistance < 4 U/m²
7) PA to Aorta Diameter Ratio > 0.75
8) Normal Ventricular Function (EF > 0.60)
9) Competent Left Atrioventricular Valve
10) No PA Distortion from Previous Shunts
Current Exclusion Criteria

1) Severe Ventricular Dysfunction
2) Pulmonary Vascular Resistance
   > 4 U/m²
Procedural Modifications

**Valveless Atriopulmonary Connection**
- Exclusion of Rudimentary Right Ventricle

**Total Cavopulmonary Connection**
- Right Atrium Does Not Function as a Pump
- Minimize Flow Disturbances and Energy Losses
- Decrease Portion of RA Exposed to Elevated Pressures

**Extracardiac Fontan**
- No Exposure of RA to Elevated Pressures
- No Atrial Suture Lines
Procedural Modifications

**Interim Superior Cavopulmonary Connection**
- Volume Unloading of Ventricle
- Regression of Ventricular Hypertrophy Prior to Fontan Completion
- Correction of PA Distortion or Valvular Regurgitation

**Baffle Fenestration**
- Allows Right-to-Left Shunting to Maintain Ventricular Filling and Cardiac Output
- Decrease Systemic Venous Pressures
- Decreased Incidence of Prolonged Effusions
Fontan Technical Approaches

- Intracardiac Lateral Tunnel
- Extracardiac Lateral Tunnel
- Extracardiac Conduit
- Intra/Extracardiac Conduit
- With or Without Fenestration
- With or Without CPB
- With or Without Aortic Crossclamping
- With or Without DHCA
- Catheter-Based Completion (Internal Conduit)

Given Current Excellent Results With Fontan, Not Yet Apparent That There Is Clear Superiority Of Any Approach
Lateral Tunnel Fenestrated Fontan

LATERAL TUNNEL
CAVOPULMONARY FONTAN - 1

ADVANTAGES:

• Simple to construct (especially after hemi Fontan)
• More efficient hydrodynamics, less energy loss
• Growth of native atrial component of conduit may prevent obstruction - can complete Fontan at younger age
• Easy to fenestrate
DISADVANTAGES:

- SVC-PA connection may need to be enlarged
- Intraatrial suture lines may predispose to arrhythmias
- Intraatrial thrombotic surface
- Difficult if anomalous PV return
ADVANTAGES:

- Simple to construct - may be done without CPB or cross-clamp
- Suitable for most anatomy - especially if anomalous PV return
- Very suitable after bidirectional Glenn shunt
- Few atrial sutures lines - may have fewer arrhythmias
- No exposure of foreign surface in systemic atrium
- No exposure of atrium to elevated venous pressures
- Can offset anastomosis to PA to balance PBF
EXTRACARDIAC FONTAN - 2

DISADVANTAGES:

- Size must be adequate - limits use in small children
- Longitudinal growth may cause stenosis
- ? Thrombosis
- Hard to effectively fenestrate
- Optimal conduit material/size not known
FENESTRATED FONTAN

ADVANTAGES:

• Maintains ventricular preload during stress (maintains cardiac output)
• Decreases risk of effusions
• $O_2$ saturation may **increase** during exercise

DISADVANTAGES:

• Improved C.O. at expense of desaturation ($O_2$ delivery maintained)
• Risk of thromboembolism
FENESTRATED FONTAN

- Hepatic vein exclusion
- Adjustable fenestration
- “Fixed” fenestration
  - Single hole
  - Multiple small holes
- Shunts
18 Years of the Fontan Operation at a Single Institution

Results from 771 consecutive patients

Lindsay S. Rogers MD, Andrew C. Glatz MD, Chitra Ravishankar MD
Thomas L. Spray MD, Susan C. Nicolson MD, Jack Rychik MD
Christina Hayden Rush BSN, J. William Gaynor MD, David J. Goldberg MD
Previously Reported Risk Factors

• **Mortality**
  – Elevated PA pressure, CAVV, poor function
  – Longer operative time

• **Prolonged Effusion**
  – Elevated PA pressures & lower baseline saturation
  – Absence of a fenestration & extracardiac conduit

• **Prolonged Hospital Stay**
  – Extracardiac conduit & longer operative times

Methods

• Retrospective chart review (2005-2009)
  – Added to previously compiled data

• Inclusion criteria
  – Fontan operation at The Children’s Hospital of Philadelphia

• Exclusion criteria
  – Previous Fontan operation

• 771 consecutive patients (1/1/92 - 12/31/2009)

• Primary Endpoints
  1. Death or Fontan take-down within 30 days
  2. Duration of pleural effusion (surgery – last chest tube pulled)
  3. Length of hospital stay
Center Fontan Volume

(Average/year = 43)
Demographic Variables Across Eras

Median Age at Stage Two (mos)

- ERA 1
- ERA 2
- ERA 3

*p < 0.001*

Median Age at Fontan (years)

- ERA 1
- ERA 2
- ERA 3

*p < 0.001*
Systemic Ventricular Morphology

<table>
<thead>
<tr>
<th>Era</th>
<th>RV (non-HLHS)</th>
<th>LV</th>
<th>HLHS</th>
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<tbody>
<tr>
<td>ERA 1</td>
<td></td>
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<tr>
<td>ERA 2</td>
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<tr>
<td>ERA 3</td>
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</table>

\[ p = 0.012 \]
Preoperative AVVR > Mild

p < 0.001
Pre-Fontan Cardiac Catheterization (n=668)

Mean PA Pressure $p = 0.1$

Ventricular EDP $p < 0.001$

n=219 (96%)

n=185 (95%)

n=264 (76%)
Support Times Across Eras

<table>
<thead>
<tr>
<th>Era</th>
<th>TST</th>
<th>CPB</th>
<th>ACC</th>
<th>DHCA</th>
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<tbody>
<tr>
<td>Era 1</td>
<td>58</td>
<td>30</td>
<td>15</td>
<td>10</td>
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<tr>
<td>Era 2</td>
<td>60</td>
<td>35</td>
<td>12</td>
<td>8</td>
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<tr>
<td>Era 3</td>
<td>65</td>
<td>30</td>
<td>10</td>
<td>5</td>
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*p < 0.001*
Mortality

Early Death: 9%
Takedown: 1%

ERA 1: p<=0.001
ERA 2
ERA 3
Effusion Across Era

Duration of effusion (days)

Era 1

Era 2

Era 3

p < 0.001

p < 0.001
Hospitalization Across Era

\[ p < 0.001 \]

Duration of hospitalization (days)

Era 1: 12
Era 2: 6
Era 3: 8
## Death or Fontan Take-Down

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate</th>
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<th>Multivariate ($R^2 = 0.29$)</th>
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<tr>
<td></td>
<td>OR</td>
<td>p</td>
<td>OR</td>
<td>p</td>
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<tr>
<td>Weight at Fontan (kg)</td>
<td>1.03</td>
<td>0.03</td>
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<td>Time from stage II (mos)</td>
<td>0.93</td>
<td>0.003</td>
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<tr>
<td>Common AV valve</td>
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<tr>
<td>Mean PA pressure (mmHg)</td>
<td>1.25</td>
<td>&lt;0.001</td>
<td>1.27</td>
<td>&lt;0.001</td>
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<tr>
<td>Ventricular EDP (mmHg)</td>
<td>1.29</td>
<td>&lt;0.001</td>
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<tr>
<td>Fontan type--extracardiac</td>
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<td>0.031</td>
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<tr>
<td>Creation of fenestration</td>
<td>0.38</td>
<td>0.028</td>
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<tr>
<td><strong>Fenestration type</strong></td>
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<tr>
<td>Single punch or side-side</td>
<td>0.16</td>
<td>0.001</td>
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<td>Use of MUF</td>
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<td>Total support time (15 min)</td>
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<td>ACC (15 min)</td>
<td>1.75</td>
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<td>DHCA (15 min)</td>
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<td>&lt;0.001</td>
<td>1.65</td>
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# Prolonged Effusion

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<th>Univariate</th>
<th>Multivariate ($R^2 = 0.083$)</th>
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<td>OR</td>
<td>p</td>
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<td>HLHS</td>
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<tr>
<td>Dominant RV</td>
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<tr>
<td>Mean PA Pressure (mmHg)</td>
<td>1.08</td>
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<tr>
<td>Ventricular EDP (mmHg)</td>
<td>1.08</td>
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<tr>
<td>Use of MUF</td>
<td>0.32</td>
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<td>Creation of Fenestration</td>
<td>0.49</td>
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<tr>
<td><em>Fenestration Type</em></td>
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<tr>
<td>Single punch or side-side</td>
<td>0.35</td>
<td>&lt;0.001</td>
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<tr>
<td>Total support time (15 min)</td>
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<td>CPB (15 min)</td>
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<tr>
<td>ACC (15 min)</td>
<td>1.27</td>
<td>0.013</td>
</tr>
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</table>
Summary

• Important changes in patient and operative characteristics, and operative techniques over time

• Death and Fontan take-down are now rare outcomes

• Morbidity increased slightly in most recent era
  – Increased support time for extra cardiac conduit
  – Increasing need for additional procedures
  – More marginal candidates with suboptimal hemodynamics
  – Consistent with other recent reports

• Many unmeasured variables exist that may have significant impact on outcomes

• Early outcomes now excellent; impact of changes on late outcomes still not clear
COMPLICATIONS OF FONTAN

EARLY:

- Low cardiac output
- Fluid retention/effusions
- High venous pressures

LATE:

- Protein-losing enteropathy
- Atrial arrhythmias
- Ventricular dysfunction
- AV valve regurgitation
- Pulmonary AV malformations
- Thromboembolism
TREATMENT OF EARLY COMPLICATIONS OF FONTAN

- Low cardiac output
- Fluid retention/effusions
- High venous pressures

1. Fenestration
2. Takedown to BDG
Results

- 592 patients
- Pre-Op Cath data available in 83.4%
- Prior SCPC 96.8%, Fenestration 91%, MUF 95.9%, DHCA 97.5%
- ECC 60% vs LT 40%
- EFF 11 patients (1.9%)
Results

Overall mortality for entire cohort of 0.8%
Incidence of Early Fontan Failure of 1.9% with an early survival of 54.5%
Early and mid-term survival after Early Fontan Failure treated with takedown of 80%
LATE COMPLICATIONS – PREVENTION

Protein-losing enteropathy:
- Decrease effusions early postop
- Fenestration

Atrial arrhythmias:
- Avoid interference with SA node blood supply (bidirectional Glenn vs. Hemi)
- Avoid atrial suture lines (lateral tunnel)
- Early staged repair
- Ablation of reentrant circuits

Ventricular dysfunction:
- Staged reconstruction
- Avoid ischemia if possible
SUBSTRATE FOR ARRHYTHMIAS AFTER FONTAN

- Atrial suture lines
- Isthmus between IVC and TV annulus
- Elevated RA pressure
- Dilated right or left atrium
- AV valve regurgitation
- Sinus node dysfunction
- Chronotropic impairment
TACHYARYRHYTHMIAS AFTER FONTAN

- Incidence 4-24%, increases with increasing followup interval
- Atrial flutter most common, but also JET, EAT, atrioventricular reciprocating tachycardia
- Poorly tolerated in Fontan circulation
- Not clearly related to hemodynamics or to type of atriopulmonary connection (except maybe extracardiac ... followup too short)
- Difficult to control medically
BRADYARYRHYTHMIAS AFTER FONTAN

- Sinus node dysfunction most common cause
- May be more frequent when Fontan “staged” with BDG or Hemifontan
- More frequent with TCPC than Atriopulmonary Fontan
- Incidence with Extracardiac Fontan unknown, but appears to be similar to TCPC
SINUS NODE DYSFUNCTION

- Bidirectional Glenn vs HemiFontan
- Early pacer insertion if resting bradycardia
- Atrial flutter more common early after extracardiac Fontan
Early mortality may be slightly higher, occasionally complex reconstruction necessary

Most commonly needed for ventricular dysfunction or PLE (often with systemic AV valve regurgitation)

PLE usually, but not always, resolves ...may be related to ventricular compliance

Heart transplant alone or heart/single lung if PAVM’s

Limited experience with VAD as bridge to transplant
THROMBOEMBOLISM

• May be a major long-term problem

• Incidence of clinically recognized thromboemboli 3-20%

• Higher incidence (up to 33%) of “silent” thrombi noted by TEE

• CHOP: Freedom from echo thrombus 92%, 90%, and 84% at 1,3,&8 years post Fontan

• Multiple causes: Venous stasis, low cardiac output, enteric protein loss, coagulation abnormalities, arrhythmias
FONTAN TYPE: Survival

From: Khairy, P and Poirier, N Circulation 2012;126:2516-25
LT VS EC FONTAN

From: Khairy, P and Poirier, N Circulation 2012;126:2516-25
LT VS EC FONTAN: Arrhythmias

Figure 3. Freedom from intraatrial reentrant tachycardia following the intracardiac lateral tunnel versus extracardiac conduit Fontan. Values are adjusted for predominant rhythm and child health questionnaire physical summary score. Number of patients at risk in each surgical group is shown in the adjoining panel. Adapted from Stephenson et al²⁴ with permission from the publisher. Copyright © 2010, Elsevier.

From: Khairiy, P and Poirier, N Circulation 2012;126:2516-25
LT VS EC FONTAN: Arrhythmias

<table>
<thead>
<tr>
<th>Year</th>
<th>First Author</th>
<th>n</th>
<th>Follow-Up, y</th>
<th>Arrhythmia Prevalence, %</th>
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<td>2000</td>
<td>Cohen MI</td>
<td>30</td>
<td>N/A</td>
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<tr>
<td>2001</td>
<td>Azakie A</td>
<td>60</td>
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<td>7</td>
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<td>2003</td>
<td>Kumar SP</td>
<td>33</td>
<td>3.0±2.2</td>
<td>28</td>
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<tr>
<td>2004</td>
<td>Nürnberg JH</td>
<td>45</td>
<td>4.4 (1.6–7.2)</td>
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<tr>
<td>2007</td>
<td>Fiore AC</td>
<td>49</td>
<td>3.0±2.3</td>
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<td>41</td>
<td>1.0</td>
<td>52</td>
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<td>63</td>
<td>Up to 8 y</td>
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<td>Sarkis V</td>
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<td>20</td>
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<tr>
<td>2011</td>
<td>Chungsomprasong</td>
<td>64</td>
<td>Actuarial 5-y</td>
<td>12</td>
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</table>

ECC indicates extracardiac conduit; LT, lateral tunnel; N/A, not available; NS, not significant; SND, sinus node dysfunction; and SVT, supraventricular tachycardia.

From: Khairy, P and Poirier, N Circulation 2012;126:2516-25
CONCLUSIONS

• Recent modifications of Fontan procedure have had profound impact on early mortality and morbidity - impact on late morbidity remains unknown
• Further modification (extracardiac Fontan, etc) may have significant effect on late morbidity, but data not yet available
• Durability of Fontan better than expected - proportion of patients who will come to transplant remains unclear
• Technical modifications may be less important than preservation of ventricular function
• Benefits of fenestration in “high risk” patients demonstrated - benefits in low risk not clear but effusions less, may have effect on late PLE
• While age no longer a risk factor for Fontan, optimal timing of completion Fontan remains controversial
• Late morbidity and benefits of newer surgical modifications await careful followup studies
• Revision of Fontan -(Conversion to extracardiac, fenestration, Maze, pacing) may offer significant improvement in functional status if performed before ventricular function deteriorates
MECHANISMS OF FONTAN FAILURE

PREVENTABLE:
- Early protection of pulmonary vascular bed
- Early reduction of volume load on single ventricle

TREATABLE:
- Loss of sinus rhythm
- Atrial arrhythmias
- PA distortion/stenosis
- RA enlargement
- PV compression
- AVV regurgitation
- Subaortic obstruction

Fontan Conversion
With or Without Maze
MECHANISMS OF FONTAN FAILURE

IMMUTABLE VENTRICULAR DYSFUNCTION:
Ventricular morphology
Heterotaxy syndromes
Abnormal myocardial substrate
Diastolic dysfunction from chronic volume underload/overload

SYSTEMIC EFFECTS:
PLE
Plastic bronchitis
Pulmonary AV malformations
Systemic arterial or venous collaterals

Transplant
Conversion or Transplant
FONTAN “FAILURE”

- Goal of Fontan modifications and staging is to preserve ventricular function
- Conversion/arrhythmia control effective if ventricular function preserved
- Occasionally conversion can improve ventricular function (loading conditions)
- “Failed” Fontan when ventricular function significantly depressed
PULMONARY VASCULAR BED

• PVR clearly important in early Fontan failure but also may be important in late failure
• Fontan physiology promotes increase in PVR (de Leval)
• Lack of pulsatility/energy to keep vascular bed open, increasing impedance
• Middle Zone (Zone 2) smaller in Fontan circulation (decreased capacitance)
• Increased lymphatic pressure may increase resistance

Chronic thromboembolism

Difficult to measure PVR in Fontan circulation
TRANSPPLANT AND PVR

- Transplant may improve PVR by ventricular/pulmonary coupling and good LV function
- Old adage “PVR low enough for transplant if alive with Fontan circulation” not absolute
- Denver group reported elevated PVR post-transplant for late-failing Fontan
- Reports of transplant for Fontan suggest high incidence of graft failure (??? Related to PVR)
- Unclear whether vascular remodeling occurs after transplant with pulsatile PBF
VENTRICULAR DYSFUNCTION
Difficult to quantify ventricular dysfunction that precludes revision:

• No significant experience has been reported
• Ventricular function can improve after revision (loading)
• Function (ejection fraction) hard to quantitate, especially with RV
• VEDP > 12 suggests severe dysfunction, but may not be accurate due to chronic volume underload
• Exclude anatomic causes (subaortic stenosis)
Function may deteriorate after AVVR repair
RELATIVE INDICATIONS FOR TRANSPLANT

- Severe systolic ventricular dysfunction
- VEDP > 12 after volume load in absence of arrhythmias or other cause
- PLE in absence of treatable hemodynamic/anatomic lesions
- Pulmonary AVM’s with cyanosis
- Early hepatic dysfunction
- Ventricular dysfunction with severe AVVR
- Non-revisable Fontan
- Failed Fontan revision
## SURGICAL RESULTS OF TRANSPLANT FOR FAILING FONTAN

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Hospital Mortality</th>
<th>Follow-Up (mos)</th>
<th>Survival Estimate</th>
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<td>Hsu et al\textsuperscript{1}</td>
<td>9</td>
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<td>23</td>
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<td>Carey et al\textsuperscript{8}</td>
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<td>Michielon et al\textsuperscript{10}</td>
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<td>Mitchell et al\textsuperscript{17}</td>
<td>15</td>
<td>7%</td>
<td>60</td>
<td>82%</td>
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SUMMARY

• Increasing numbers of Fontan patients are reaching adulthood, suggesting increasing number eventually needing transplant
• Despite design modifications, continued late attrition will likely occur
• Fontan revision advised for patients with preserved ventricular function or arrhythmias, but longterm followup lacking
• Transplant only option when revision not possible or failed
• Transplant for failed Fontan higher risk, but reasonable results with careful selection (donor & recipient)
SUMMARY

• Long-term followup not available for either transplantation or revision
• Revision results may be less favorable in absence of atriopulmonary Fontan or arrhythmias
• Late outcomes may be better for newer Fontan techniques, but data not available and rhythm issues still likely
• Ultimately, revision may just delay onset of irreversible ventricular dysfunction
The Continuing Evolution of the Fontan Procedure

<table>
<thead>
<tr>
<th>Year</th>
<th>RA-RV/PA Conduit</th>
<th>RA-PA Connection</th>
<th>Lateral Tunnel</th>
<th>Intermediate BDG/HemiFontan</th>
<th>Fenestration</th>
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<td>2000</td>
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<td>2005</td>
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</table>

20-30 Year Outcome Following the Fontan Operation

Mortality: 25% 15% 10% <5%

Age at Surgery: 8 6 4 2

Problematic Effusions

~2 ~2

Less Problematic

3 4+

~2 ~2
The Continuing Evolution of the Fontan Procedure


RA-RV/PA Conduit
RA-PA Connection
Lateral Tunnel
Intermediate BDG/HemiFontan
Fenestration
Extracardiac Conduit
Off Pump Fontan

Limited Mid-term Follow-Up Data

Mortality 25% 15% 10% <5%
Age at Surgery 8 6 4 2

~2 ~2 3 4+
FUNCTIONAL STATUS

Long term survivors of the Fontan Procedure
Gentles TL et al. JTCVS 1997

• 91% of survivors NYHA Class I or II

• Factors related to poor outcome (9%)
  – Older age at Fontan
  – Arrhythmia
  – PLE
  – Longer Duration of Follow-Up
    • ? inherent to Fontan circulation, or reflection of management strategies 15-25 years ago???
Results: WEIGHT

Cohen MI et al, Ped Cardiol 1999
Results: HEIGHT

<table>
<thead>
<tr>
<th>Birth</th>
<th>Hemi</th>
<th>Fontan</th>
<th>Years Post Fontan</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>65</td>
</tr>
</tbody>
</table>

Cohen MI et al, Ped Cardiol 1999
Medication Burden

Questionnaire Responses (n=363) in Fontan Patients
Median age at Fontan = 7 years
Age at response = 14 years

Gentles T et al, JTCVS 1997
Growing-Up with a Fontan:
Set Reasonable Expectations From the Beginning

• The Fontan Operation is not the “Last” Operation
  – It’s the last PLANNED operation
• The circulation will NEVER be a “normal” circulation
  – Life-long follow-up will necessary
  – Most children are similar to their peers in day-to-day activities
• Truly LONG-TERM outcomes are unknown
Summary and Recommendations

• Most “long-term” outcome studies represent truly early results of the (un)natural history following surgery for CHD
  – Most adverse outcomes are “time-dependant”
  – Have we ‘pushed back’ the mortality and morbidity; to be cared for by the next generation of physicians?
• Current 15-25 year follow-up studies are rare, and may no longer be relevant to our current practice
WHAT’S NEW?
FONTAN ASSIST

FIGURE 4. Comparison of pre- and post-operative connections under steady, pre-operative flow conditions. Streamlines are color-coded by vessel of origin (red—RSVC; blue—HepV/IVC; green—AZ; yellow—LSVC).

TABLE 8. Predictive accuracy.

<table>
<thead>
<tr>
<th>Pt</th>
<th>HFD (% LPA)</th>
<th>Connection resistance (mmHg * min/L)(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Surgical planning model</td>
<td>Post-op anatomy</td>
</tr>
<tr>
<td>1</td>
<td>23</td>
<td>35</td>
</tr>
<tr>
<td>2</td>
<td>25</td>
<td>35</td>
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<tr>
<td>3</td>
<td>58</td>
<td>91</td>
</tr>
<tr>
<td>4</td>
<td>52</td>
<td>54</td>
</tr>
<tr>
<td>90% #CInt.</td>
<td></td>
<td>14.3 ± 4.3</td>
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</tbody>
</table>

\(^a\)Pre-operative values using post-operative outflow splits; #CInt. = Confidence Interval.
PLE after Fontan: Frequency?

- **Mayo Clinic**: 427 pts, 47 developed PLE over 10 year period, cumulative risk of 13.4% (Feldt RH, *JTCVS* 1996;112:672)

- **International Multicenter Study**: 3,029 pts, 114 developed PLE, prevalence of 3.7% (Mertens & Gewillig, *JTCVS* 1998;115:1063)

- *time of onset of disease is variable*

- *wide spectrum of symptoms*
Outcome: Survival after Fontan Operation

Fig. 1. Survival curve for 427 30-day survivors of the Fontan operation. Time zero is 30 days after the operation.

(Mayo Clinic. Feldt RH, JTCVS 1996;112:672-680)
Survival after Diagnosis of PLE

Fig. 2. Survival curve after diagnosis of PLE in patients who have had the Fontan operation.

(Mayo Clinic. Feldt RH, JTCVS 1996;112:672-680)
Fig. 1. Survival analysis (Kaplan-Meier) of patients with PLL. The graph represents a Kaplan-Meier survival analysis. *Time zero* represents the date of diagnosis of PLL. The *vertical bars* represent the 95% confidence interval.

(Mertens L, *JTCVS* 1998;115:1063-73)
PLE After Fontan

• What is the pathophysiological mechanism?
  – Why after the Fontan operation?
  – Why in some patients and not others?
  – What is the link between post Fontan physiology and the development of enteric protein loss?
Cardiac Disorders and PLE

• **Heart Failure** (Davidson JD, *Lancet* 1961;1:899)


• **Inferior Vena Caval Obstruction after Mustard Operation** (Moodie DS, *JTCVS* 1976;72:379)

• **Glenn Shunt** (Gleason WA, *JTCVS* 1979;77:843)

• **Fontan Operation** (Crupi G, *Thorac Cardiovasc Surg* 1980;28:359)
What Is The Mechanism of PLE In Heart Disease?

• **Plausible Hypothesis (?):** Increased systemic venous pressure leads to dilated lymphatics (lymphangiectasis) with loss of protein into the gut lumen

• **However, in PLE after Fontan:**
  – lymphangiectasis not always seen!
  – histology commonly unrevealing!
  – PLE not commonly seen after bidirectional Glenn (increased pressure in thoracic duct)!
  – systemic venous pressures do not directly correlate with presence, or severity, of disease!
Hemodynamics in PLE After Fontan Operation

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ao Sat %</td>
<td>90</td>
<td>6.7</td>
<td>63-99</td>
</tr>
<tr>
<td>MV Sat %</td>
<td>64</td>
<td>8.8</td>
<td>41-71</td>
</tr>
<tr>
<td>PAP (mm Hg)</td>
<td>16</td>
<td>6</td>
<td>6-40</td>
</tr>
<tr>
<td>EDP (mm Hg)</td>
<td>10</td>
<td>6</td>
<td>0-37</td>
</tr>
<tr>
<td>PVR</td>
<td>2.9</td>
<td>1.6</td>
<td>0.3-7.7</td>
</tr>
<tr>
<td>CI (l/min/m²)</td>
<td>2.4</td>
<td>0.8</td>
<td>0.6-5.9</td>
</tr>
</tbody>
</table>

(Mertens L, *JTCVS* 1998;115:1063-73)
Can Success With Treatment Initiatives Help Explain The Pathophysiology of PLE After Fontan?

- Treat Hypoproteinemia
- Treat the Intestinal Mucosa
- Alter Cardiac Hemodynamics
Summary: Proposed Mechanism

1. **Chronic Low Cardiac Output State**
   - **Increased Mesenteric Vascular Resistance**
   - **Low Flow**
   - **Break in Intestinal Mucosal Integrity/PLE**

2. **Fontan**
   - **Angiotensin II mediated (?) (genetic component?)**
   - **Release of inflammatory mediators (?)**
   - **Stasis related alteration of charge (?)**

3. **Fenestration**
4. **Pacing**
5. **ACEI (?)**
6. **Nitric Oxide (?)**
7. **Steroids/Heparin**