Inter-Atrial Shunts for Pulmonary Hypertension: Group I and Group II

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Cardiovascular Research Foundation
Disclosure Statement of Financial Interest

I, Daniel Burkhoff have the following financial interest, arrangement or affiliation that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation:

Hemodynamic Core Lab/Consultant to Corvia Medical
# World Health Organization Classifications for Pulmonary Hypertension

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Abbreviations: COPD: chronic obstructive pulmonary disease
RV and LV Mechanics in WHO I PAH

Small LV, Large RV

↑↑ PAP, ↑↑PVR

↑↑CVP, ↓PCWP, ↓CO
RV and LV Mechanics in PAH vs PH HFpEF/HFrEF

WHO II PH-HFpEF (or HFrEF)

Normal LV, Normal RV
↑PAP; nl or mild ↑PVR
NI CVP, ↑↑PCWP, ↓CO at peak Ex
Interatrial Shunts in WHO I and II PH
Treatment Goals

WHO I

- Right→Left shunt to increase LV filling and CO
- Reduce CVP

WHO II

- Left→Right shunt to reduce PCWP, especially during exercise
# World Health Organization Classifications for Pulmonary Hypertension

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**Abbreviations:** COPD: chronic obstructive pulmonary disease
ACCF/AHA 2009 Expert Consensus Document on Pulmonary Hypertension

PAH Treatment Algorithm

Anticoagulation ± Diuretics ± Oxygen ± Digoxin

Acute Vasoreactivity Testing*

Positive

Lower Risk‡

ERAs or PDE-5 Is (oral) Epoprostenol or Treprostinil (IV) Iloprost (inhaled) Treprostinil (SC)

Higher Risk§

Epoprostenol or Treprostinil (IV) Iloprost (inhaled) ERAs or PDE-5 Is (oral) Treprostinil (SC)

No

Continue CCB

Reassess: consider combo-therapy

Investigational protocols

Atrial septostomy Lung transplant†

Negative

Oral CCB†

Sustained response

Yes

Continue CCB

Circulation 2009
# Treatment Algorithm for PAH: ESC/ERS (2016)

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class - Level</th>
</tr>
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<tbody>
<tr>
<td><strong>Measure/treatment</strong></td>
<td>WHO-FC II</td>
</tr>
<tr>
<td>Hospitalization in intensive care unit is recommended in PH patients with high heart rate (&gt;110 b/min), low blood pressure (Systolic blood pressure &lt;90 mmHg), low urine output and rising lactate levels due or not due to comorbidities.</td>
<td>-</td>
</tr>
<tr>
<td>Inotropic support is recommended in hypotensive patients.</td>
<td>-</td>
</tr>
<tr>
<td>Lung transplantation is recommended soon after inadequate clinical response on maximal medical therapy.</td>
<td>-</td>
</tr>
<tr>
<td><strong>Balloon</strong> atrial septostomy may be considered where available after failure of maximal medical therapy.</td>
<td>-</td>
</tr>
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</table>
# Acute Hemodynamic Effects After Septostomy

<table>
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<tr>
<th>Parameter</th>
<th>Before</th>
<th>After</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRAP, mmHg</td>
<td>14.6 ± 8.0</td>
<td>11.6 ± 6.3</td>
<td>0.001</td>
</tr>
<tr>
<td>mLAP, mmHg</td>
<td>5.7 ± 3.3</td>
<td>8.1 ± 4.0</td>
<td>0.001</td>
</tr>
<tr>
<td>CI, L/min/m²</td>
<td>2.04 ± 0.69</td>
<td>2.62 ± 0.84</td>
<td>0.001</td>
</tr>
<tr>
<td>SaO₂ %</td>
<td>93.3 ± 4.1</td>
<td>83.0 ± 8.5</td>
<td>0.001</td>
</tr>
<tr>
<td>mPAP, mmHg</td>
<td>64.3 ± 17.6</td>
<td>65.7 ± 18.3</td>
<td>0.169</td>
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*Rich and Lam, AJC1983; 51: 1550-51*
Graded balloon dilation atrial septostomy in severe primary pulmonary hypertension

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<th>1 year Survival</th>
<th>2 year survival</th>
<th>3 year survival</th>
</tr>
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<tr>
<td>Atrial septostomy</td>
<td>92%</td>
<td>92%</td>
<td>92%</td>
</tr>
<tr>
<td>Historical Controls</td>
<td>73%</td>
<td>59%</td>
<td>52%</td>
</tr>
<tr>
<td>NIH Registry</td>
<td>61%</td>
<td>49%</td>
<td>38%</td>
</tr>
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</table>
Comments (courtesy of Stuart Rich, Northwestern):

- Clinical response is unpredictable. Some patients have a dramatic improvement, others may not.
- Hypoxemia is generally well tolerated.
- Guidelines suggest do not do AS if RA pressure >20 mmHg or O2 sat on room air <90%.
- Staged procedures may be preferred: start with small hole and increase as tolerated if no clinical response.
- Currently underutilized as physicians think drugs work better which they usually do not.
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*Abbreviations: COPD: chronic obstructive pulmonary disease*
Interatrial Shunt for PAH-HFpEF?

REDUCE LAP-HF TRIAL II (Corvia)
- NYHA II/III/IVa
- LVEF ≥ 40%
- PCWP > CVP by ≥5 mmHg
- RAP < 14 mmHg
- PVR < 4 WU
- TAPSE > 14 mm

RELIEVE HF (V-Wave)
- NYHA III/IVa
- No EF restriction
- PAS <70 mmHg / PVR<4 WU
- TAPSE > 12 mm
AoP
PCWP
PAP
CVP
ASD Flow

Shunt

O$_2$ Sat

left $\rightarrow$ right
Continuous L $\rightarrow$ R Flow

45 Days after implant
REDUCE LAP-HF I RCT: Results

CONTROL

IASD

Feldman et al, Circulation 2018
ΔPCWP: Baseline vs 1 Month

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<tr>
<th>Outcome at 1 Mo</th>
<th>IASD Patients (N=22)</th>
<th>Control Patients (N=22)</th>
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<td>PCWP, peak, mmHg</td>
<td>-3.5±6.4 (n=17)</td>
<td>-0.5±5.0 (n=17)</td>
</tr>
<tr>
<td>PCWP, workload-corrected, mmHg/W/kg</td>
<td>-5.7±27.3 (n=16)</td>
<td>10.3±45.9 (n=17)</td>
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*P<0.05
**P<0.01

Feldman et al, Circulation 2018
Interatrial Shunts

WHO I
• R→L to increase LV filling and CO and decrease CVP
• Arterial desaturation limiting factor
• No randomized trials, but improved outcomes vs historical controls

WHO II
• Subgroup of WHO II patients included in trials
  • Upper limits to PVR, RVF and CVP for inclusion
• L→R to reduce PCWP
• Hemodynamic studies show ↓PCWP despite ↑Ex Tol
• Randomized studies underway
• Multiple device-based options under development and investigation