Continuous Inter-Atrial Shunting: Latest Clinical Insights

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Disclosures

Consulting fees from Corvia Medical for Hemodynamic Core Lab
IASD: Rationale

• HFpEF (LVEF > 50%) and HFmrEF (LVEF 40-50%):
  - Increasing in prevalence
  - High morbidity/mortality
  - No proven therapies
  - Heterogeneous syndromes
  - Common pathophysiologic thread: ↑LA pressure at rest or with exertion

Borlaug et al.  Circ. Journal 2013
Exercise hemodynamics in HFpEF

At REST

AFTER 1 MIN. OF EXERCISE
Importance of Exercise-Induced ↑LA pressure in HFpEF


![Graph showing survival rates with PCWP data]

Work corrected PCWP < 25.5 mmHg/W/kg

Work corrected PCWP > 25.5 mmHg/W/kg

p = 0.03
Both CVP and PCWP Increase with Exercise in HFpEF/HFmrEF

Wessler et al, Circ HF 2018
Exercise induced PCWP increase is greater than CVP increase

The LA-RA gradient is the driving pressure for atrial decompression

Wessler et al, Circ HF 2018
InterAtrial Shunt Device

Simulation using exercise hemodynamic data from HFpEF patients

Kaye…Burkhoff. J Card Fail 2014
Interatrial shunt for passive LA decompression

Corvia Medical IASD
Interatrial shunt for passive LA decompression

VWave

5mm central opening

Right Atrium

Interatrial septum

Self-expanding Nitinol frame

Exit hood may limit paradoxical emboli

Full ePTFE encapsulation
- Channels flow
- Prevents late lumen loss

Hourglass shape
- Secure and atraumatic septal retention
- Minimal ID 5.1 mm with venturi efficiency

Left Atrium
Interatrial shunt for passive LA decompression

Occlutech
Interatrial shunt for passive LA decompression
Corvia Implant
Continuous L → R Flow

45 Days after implant
Corvia Implant
Continuous L→ R Flow

Subcostal view

Subcostal view (zoomed)

12-month echo
Results of IASD Open-Label Study (n=64)

Inclusion criteria:
- Open label
- LVEF ≥ 40%
- NYHA class II-IV
- Elevated PCWP
  - ≥ 15 mmHg (rest) or
  - ≥ 25 mmHg (supine bicycle exercise)

Acceptable safety profile at 12, 24 months

*\( p < 0.05 \), **\( p < 0.01 \) vs. baseline

Hasenfuß G., Kaye D. Lancet 2016
Baseline PCWP-CVP Pressure Gradient Correlates with Decrease in PCWP at 6 Months

Peak Exercise
REDUCE LAP-HF I RCT: Results

CONTROL

IASD

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

**Outcome at 1 Mo**

<table>
<thead>
<tr>
<th></th>
<th>IASD Patients (N=22)</th>
<th>Control Patients (N=22)</th>
</tr>
</thead>
<tbody>
<tr>
<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>
</tr>
</tbody>
</table>

**Feldman et al, Circulation 2018**

*P<0.05 **P<0.01
IASD Treatment Reduced Incidence and Delayed Time to 1st IV Diuresis

108 More Days until 1st IV Diuresis Event

<table>
<thead>
<tr>
<th></th>
<th>IASD</th>
<th>Control</th>
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<tbody>
<tr>
<td>178</td>
<td>70</td>
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</table>

Cumulative Incidence of Heart Failure Event Requiring IV Treatment

<table>
<thead>
<tr>
<th>Time after Randomization (Days)</th>
<th>No. At Risk Treatment</th>
<th>No. At Risk Control</th>
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<tbody>
<tr>
<td>0</td>
<td>21.5 21.0</td>
<td>22.0 22.0</td>
</tr>
<tr>
<td>30</td>
<td>21.0</td>
<td>18.0</td>
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<td>90</td>
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<td>180</td>
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<tr>
<td>270</td>
<td>11.5</td>
<td>11.0</td>
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<tr>
<td>365</td>
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p=0.064
REDUCE LAP-HF II Pivotal RCT

PROSPECTIVE, MULTICENTER, 1:1 RANDOMIZED, SHAM-CONTROLLED, BLINDED TRIAL

- Rigorous non-invasive and invasive exercise hemodynamic screening
- Primary endpoint (12 mo.):
  - CV mortality
  - Non-fatal ischemic stroke
  - Rate of total HF hospitalizations
  - KCCQ
- Powered secondary endpoints:
  - Change in NYHA class
  - Change in KCCQ
REDUCE LAP-HF II

Key Inclusion Criteria and Execution

- Site reported EF ≥40%
- Invasive (exercise) HF diagnosis
  - Exercise PCWP >25 mm Hg
  - PCWP-RA gradient
- Sham control procedure
- Double blinding for 2 years
  - Patient
  - Managing HF MD
Summary

- Rapid and profound rise in PCWP with exertion in heart failure, particularly HFpEF and HFmrEF
- Persistent and significant Left-to-Right atrial pressure gradient on exertion
- Exercise hemodynamic are important for optimal patient selection
- IASD decreases PCWP while prolonging exercise time and peak Watts
- Preliminary results show symptomatic improvement and decrease in rate of HF decompensation