Interatrial Shunts for Heart Failure

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Disclosures

Consulting: Abbott, AstraZeneca, Boehringer Ingelheim, Boston Scientific, CVRx, Edwards Lifesciences, Impulse Dynamics, VWave

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Elevated Left Atrial Pressure Causes Lung Congestion, Worsening Symptoms, and Hospitalizations

**Fast**
- Vascular
- Acute, Dynamic
- Impossible to treat with diuretics

**Slow**
- Volume
- Progressive, Dynamic
- Often difficult to treat with diuretics alone

<table>
<thead>
<tr>
<th>Precipitant</th>
<th>Sympathetic activation</th>
<th>Venous redistribution (fast)</th>
<th>Renal and dietary</th>
<th>Fluid retention (slow)</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑LAP</td>
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Lung Congestion

ADHF / hospitalization

Adapted from Fallick C, et al. Circ Heart Fail 2011
Lowering Left Atrial Pressure
Interatrial Shunting in Heart Failure

Mechanism of Action

- Excess LA volume shunted to RA
- ↓ Left atrial pressure (LAP)
- ↓ Pulmonary artery pressure
- Reduced pulmonary congestion and HF events
- Improved functional status and symptom relief
- Signs of reverse LV remodeling
- Maintenance of RV function
How a Small Interatrial Shunt Reduces LAP in Both HFrEF and HFpEF

Ventricular Pressure vs Volume

<table>
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<tr>
<th></th>
<th>HFpEF</th>
<th>HFrEF</th>
</tr>
</thead>
<tbody>
<tr>
<td>V_{30}</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Pressure (mmHg)</td>
<td>40</td>
<td>30</td>
</tr>
<tr>
<td>LV Volume (ml)</td>
<td>0</td>
<td>100</td>
</tr>
</tbody>
</table>

Pressure – Volume Curves of LV

- Shows small volume of blood flow across an interatrial shunt can lead to large pressure decreases in both HFrEF and HFpEF
- Reduction in Left Ventricular and Left Atrial Pressures should reduce acute HF episodes and improve symptoms

Evidence Supporting Interatrial Shunt Therapy in Chronic Heart Failure

- Patients with mitral valve stenosis and an atrial septal defect (ASD) have fewer symptoms than patients with an intact septum.
- Closure of ASDs in patients with unrecognized left ventricular dysfunction results in elevated LAP and pulmonary edema.
- Pre-clinical animal studies demonstrate hemodynamic, echocardiographic, and survival benefits with interatrial shunting.
- First-in-human and clinical pilot studies support the safety, feasibility, and potential effectiveness of interatrial shunting in heart failure.

References:
1. Lutembacher R. Arch Mal Coeur 1916
8. Rodés-Cabau J, et al. JACC Intv 2018
Favorable Effects of an Interatrial Shunt Device in Microembolization Model of Ischemic Heart Failure

N=21 sheep
14 V-Wave 5 mm Shunts
7 Controls

Shunting significantly improved:
LA, LV, RA, PA pressures LV systolic & diastolic function, and survival

A “Device Effect” is the likely cause of observations

*  p<0.05 vs. Control
** p<0.01 vs. Control
†  p<0.05 vs. Baseline

Eigler, et al. Cardiac Unloading with an Implantable Shunt in Heart Failure. Structural Heart 2017
Interatrial Shunt Devices* with Completed Pilot Studies

V-Wave Ventura Interatrial Shunt Device

Corvia Interatrial Shunt Device (IASD)

Occlutech Atrial Flow Regulator (AFR)

5 mm venturi orifice and septal footprint diameters

8 mm orifice plate, 19 mm diameter septal footprint

6-10 mm orifice plate, 22-26 mm diameter septal footprint

*Not sized to scale
Corvia First REDUCE LAP-HF Trial

• Prospective, non-randomized study
• Symptomatic HF (N=64)
• Preserved EF (>40%)
• Elevated PCWP at rest (>15 mmHg) or during exercise (>25 mmHg)
• Monitored by independent DSMB and CEC
• Assessed by independent Core-Laboratories
  • Echo
  • Hemodynamic
• Three year clinical follow-up
  • One year complete

First REDUCE-LAP Trial Results

V-Wave First-in-Human (FIH) Studies

Eligibility Criteria

Major Inclusion Criteria

- Chronic HF, ischemic or non-ischemic etiology
- HFrEF and HFpEF
- NYHA class III or ambulatory class IV
- On GDMT and device therapies
- HF-hospitalization or elevated BNP/NT-proBNP

Total 38 pts (30 HFrEF, 8 HFpEF)
  6 sites (Canada, EU, Israel)
  Median FU 28 months (18-48 months)

Shunting Improves Functional Outcomes

NYHA Class*

QoL Change*

6MWT Change (m)*

*p<0.04 (baseline vs. follow-up)

Rodes-Cabau J, et al. JACC Intv 2018;11:2300–2310
Occlutech Pilot Study

- Prospective, non-randomized, open-label, multi-center study
- Symptomatic NYHA class III or IV HF and pulmonary capillary wedge pressure (PCWP) ≥ 15mmHg at rest or ≥ 25mmHg at exercise, irrespective of left ventricular ejection fraction (EF ≥15%)
- Thirty-six patients enrolled
  - 16 HFrEF (LVEF 15%-39%)
  - 20HFpEF (LVEF ≥ 40%)
- Three-month follow-up reported
- 100% implant success and patency rate
Occlutech Trial Study Results

B. Individual patient level Δ6MWD FU vs. baseline
HFpEF

C. Individual patient level ΔKCCQ score FU vs. baseline
HFpEF

Paitazoglou C, wt al. EuroInterv 2019
Interatrial Shunting: Current Status

• Corvia, V-Wave, and Occlutech shunts have CE Mark

• No interatrial shunts are approved in the U.S.

• Pivotal trials of Corvia and V-Wave shunts are ongoing
  • REDUCE LAP HF II completed enrollment last summer (HFpEF only)
  • RELIEVE-HF enrolling (No LVEF restriction; HFrEF and HFpEF)
RELIEVE-HF Study Flow
Roll-in arm provides early look at results

* Up to 600 pts per Interim Analysis
High Procedure Success and Excellent Safety
RELIEVE-HF Roll-In Cohort Data (N=60)

Median Follow-up, months 7.2
Successful device implantation 100%
Shunt Patency on procedural TEE 100%
Shunt Patency at 6 and 12 months 100%
Device embolization/dislocation 0
Need for a second device 0
Procedure time, min 71 (IQR 56-88)
Length of Stay, days 1 (IQR 1-1.3)
MACNE at 30-Days 0
Device- or Procedure-related MACNE 0

MACNE (Major Adverse Cardiovascular and Neurological Events) includes: Deaths, Stroke and Thromboembolism, Tamponade, Shunt embolization requiring surgery, Need to remove or close shunt, Vascular complication requiring surgical repair.
Preliminary Data: Quality of Life in RELIEVE-HF Roll-In Cohort
KCCQ Shows Clinically Meaningful Improvement Similar to Feasibility Study

**Overall Scores**

- Baseline (n=57)
- 1 Mo (n=53)
- 3 Mos (n=44)
- 6 Mos (n=32)

**Responder Analysis**

- Improved or Worsened requires a 5-point change from Baseline

* P<0.01 vs. Baseline
Conclusions

• Interatrial shunting is feasible, safe, and associated with promising effectiveness results, in pilot studies of HFrEF and HFpEF patients
  • Improved quality of life, functional status, and exercise ability
  • Low rates of morbidity and mortality suggesting potential for improved clinical outcomes

• Ongoing randomized controlled pivotal trials designed to confirm the safety and effectiveness of interatrial shunting may further support the use of these devices in the treatment of heart failure
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