Transcatheter Intracardiac Shunt Device Provides Sustained Clinical Benefit at One Year in Heart Failure with Preserved or Mildly Reduced Ejection Fraction: The REDUCE LAP Heart Failure Trial

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PGY-5
Disclosures

None
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Introduction

Heart failure with preserved ejection fraction (HFPEF) has a complex pathophysiology and remains a therapeutic challenge.

Elevated left atrial pressure, especially during exercise, is a near-universal finding in patients with HFPEF.

Increased LV passive stiffness
Reduced active LV relaxation
Reduced LA compliance
The magnitude of the exercise-mediated rise in PCWP in HFPEF is related to both symptoms and outcome.

**SYMPTOMS**

![Graph showing correlation between six minute walk (meters) and workload corrected PCWP (mmHg/W/kg)].

- \( r = -0.47 \)
- \( p < 0.001 \)

**SURVIVAL**

![Graph showing survival analysis with different PCWP categories].

- Work corrected PCWP < 25.5 mmHg/W/kg
- Work corrected PCWP > 25.5 mmHg/W/kg

- \( p = 0.03 \)

REDUCE LAP-HF Unpublished data

Dorfs EHJ 2014
Computer simulation demonstrated that an 8mm interatrial shunt device (IASD®) would provide acute LA decompression during exercise.

Kaye et al JCardFail 2014
InterAtrial Shunt Device - Mode of Action

Elevated LV filling pressures (Elevated LAP)

Pulmonary Venous hypertension

Pulmonary Congestion & Dyspnea (rest/exercise)

Transcatheter interatrial shunt device
Inclusion Criteria (n=64):

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

6 month outcomes:

- NYHA Class
  - No. of patients
  - Baseline: [Chart]
  - Follow-up: [Chart]
  - p < 0.001

- MLWHF
  - Score
  - Baseline: [Chart]
  - Follow-up: [Chart]
  - p < 0.001

- 6 MWT
  - Metres
  - Baseline: [Chart]
  - Follow-up: [Chart]
  - p = 0.003

- Exercise time
  - Minutes
  - Baseline: [Chart]
  - Follow-up: [Chart]
  - p = 0.03

& reduced exercise PCWP

Objective & Methods

To assess **device safety** (major adverse cardiac, cerebrovascular and systemic embolic events -MACCE), and **device performance** one year post implant.

- **device performance: shunting (echocardiography)**

To evaluate **persistence of clinical benefit:**

- clinical efficacy: NYHA class, quality of life (MLWHFQ), 6MW distance
- cardiac structure and function (echocardiography)
- rest and exercise hemodynamics (**optional sub-study**, n=18)
  - oximetry to assess Qp:Qs (n=13)

Study monitored by independent CEC and DSMB
## Baseline Characteristics (n=64)

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Age (Y)</td>
<td>69±8</td>
</tr>
<tr>
<td>Gender (% Female/Male)</td>
<td>66 / 34</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>47 ± 7</td>
</tr>
<tr>
<td>NYHA Class (n, II/III/IV)</td>
<td>18/46/0</td>
</tr>
<tr>
<td>Minnesota Living with HF Score</td>
<td>49 ± 20</td>
</tr>
<tr>
<td>BMI kg/m²</td>
<td>33 ± 6</td>
</tr>
<tr>
<td>Permanent AF (%)</td>
<td>36</td>
</tr>
<tr>
<td>NT-Pro BNP (median, IQR pg./ml)</td>
<td>377 (222-925)</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>81</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>33</td>
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<tr>
<td>Coronary artery disease (%)</td>
<td>36</td>
</tr>
<tr>
<td>Diuretics at baseline (%)</td>
<td>91</td>
</tr>
<tr>
<td>Resting CVP (mm Hg)</td>
<td>9 ± 4</td>
</tr>
<tr>
<td>Resting PCWP (mm Hg)</td>
<td>17 ± 5</td>
</tr>
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## Safety (MACCE) and Device Performance

<table>
<thead>
<tr>
<th>MACCE event</th>
<th>Six months %</th>
<th>One year %</th>
</tr>
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<tbody>
<tr>
<td>Death</td>
<td>0</td>
<td>4.7 (3/64)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0</td>
<td>1.5 (1/64)* (pt died)</td>
</tr>
<tr>
<td>MI</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Systemic embolic event</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Implant removal</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Effectiveness</th>
<th>Six months %</th>
<th>One year %</th>
</tr>
</thead>
<tbody>
<tr>
<td>L→ R Shunt flow (Echo)</td>
<td>100 (49/49)</td>
<td>100 (48/48)</td>
</tr>
<tr>
<td>R→ L Shunt flow (Echo)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Qp:Qs</td>
<td>1.27 ± 0.24</td>
<td>1.28 ± 0.25</td>
</tr>
</tbody>
</table>

Device patency confirmed in 54 subjects (by echo or oximetry)
Sustained Clinical Efficacy

Patients with data at all 3 time points.

**p<0.01, ***p<0.001 vs baseline

Mean Δ at 1 year: 15 points

Mean Δ at 1 year: 33m

**p<0.01, ***p<0.001 vs baseline
Echocardiographic Results

- **LVEF**
  - Baseline 6M 12M
  - **No change in atrial volumes**

- **RVEF**
  - Baseline 6M 12M
  - *p<0.05, **p<0.01, ***p<0.001

- **LVEDVI**
  - Baseline 6M 12M
  - **No change in atrial volumes**

- **RVEDVI**
  - Baseline 6M 12M
  - **No change in atrial volumes**

**Note:** *p<0.05, **p<0.01, ***p<0.001
Invasive Hemodynamic Results (rest)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Six months</th>
<th>One year</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA pressure</td>
<td>8 ± 3</td>
<td>11 ± 6</td>
<td>10 ± 4</td>
</tr>
<tr>
<td>PA$_{\text{mean}}$ pressure</td>
<td>25 ± 8</td>
<td>23 ± 7</td>
<td>26 ± 8</td>
</tr>
<tr>
<td>Wedge pressure</td>
<td>19 ± 6</td>
<td>16 ± 8</td>
<td>17 ± 6</td>
</tr>
<tr>
<td>Cardiac output</td>
<td>5.2 ± 1.3</td>
<td>6.3 ± 1.4**</td>
<td>6.7 ± 1.8**</td>
</tr>
</tbody>
</table>

Patients with data at all 3 time points.  

** p<0.01 vs baseline
Exercise Hemodynamic Results

Exercise time

- Baseline
- 6M
- 12M

PCWP

- Baseline
- 6M
- 12M

Workload

- Baseline
- 6M
- 12M

Cardiac Output

- Baseline
- 6M
- 12M

* p<0.05, ** p<0.01 vs baseline
Exercise Hemodynamic Results

IASD therapy provides increased work capacity for a given LA pressure.

*p < 0.05, **p < 0.01 vs baseline
Summary and Conclusions

Implantation of an interatrial shunt device appears to be safe with an acceptable MACCE rate through one year of follow-up.

Interatrial shunt device patency was maintained through one year.

The clinical and hemodynamic benefit observed 6 months after implant was sustained through one year, with no evidence of adverse sequelae:
- Meaningful improvements in NHYA class, exercise capacity and QOL
- Clinically meaningful reduction in normalized PCWP

Randomised trials are required and ongoing to determine the value of this novel strategy for the management of HFPEF.