The importance of exercise hemodynamics in HF patient selection/device evaluation

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Disclosures:

• Consultant to Corvia Medical (Hemodynamic Corel Lab)
InterAtrial Shunts: Rationale

- Common pathophysiologic finding in HF: ↑LA and PCWP pressure at rest or with exertion
- ↑PCWP mechanistically linked with exercise intolerance

Borlaug et al. Circ. Journal 2013
Primary Effects of InterAtrial Shunt Simulation using exercise hemodynamic data from HFpEF patients

Kaye...Burkhoff. J Card Fail 2014
Interatrial Shunt Device Landscape
Role of Invasive Hemodynamic Measurements

- Characterizing IASD hemodynamic effects (MOA)
- Identifying hemodynamic factors of patients most likely to benefit
  - Inclusion/Exclusion criteria for clinical trials
- Linking beneficial baseline hemodynamic factors to noninvasive surrogates that predict IASD clinical responders
Both CVP and PCWP Increase with Exercise in HFpEF/HFmrEF

Wessler et al, Circ HF 2018
### Hemodynamic Effects of Corvia 8mm IASD

Hasenfuss et al, Lancet 2016  
Wessler et al, CircHF 2018

<table>
<thead>
<tr>
<th></th>
<th>At Rest</th>
<th>Peak Exercise</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>6Months</td>
<td>Baseline</td>
<td>6Months</td>
</tr>
<tr>
<td>Qp:Qs</td>
<td>1.06 ± 0.32</td>
<td>1.27 ± 0.24</td>
<td>&lt;0.001</td>
<td>na ± na</td>
</tr>
<tr>
<td></td>
<td>16.8 ± 6.9</td>
<td>11.4 ± 5.5</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>PCWP-CVP</td>
<td>8.3 ± 4.1</td>
<td>6.1 ± 2.7</td>
<td>&lt;0.001</td>
<td>16.8 ± 6.9</td>
</tr>
<tr>
<td>PCWP</td>
<td>17.4 ± 5.2</td>
<td>16.5 ± 6.7</td>
<td>34.1 ± 7.6</td>
<td>31.6 ± 8.0</td>
</tr>
<tr>
<td>CVP</td>
<td>9.0 ± 3.7</td>
<td>10.6 ± 5.1</td>
<td>0.027</td>
<td>17.5 ± 5.4</td>
</tr>
<tr>
<td>CO (TD)</td>
<td>5.5 ± 1.6</td>
<td>6.7 ± 1.5</td>
<td>&lt;0.001</td>
<td>8.7 ± 2.6</td>
</tr>
<tr>
<td>CO (Fick)</td>
<td>4.6 ± 1.2</td>
<td>4.8 ± 1.3</td>
<td>na ± na</td>
<td>na ± na</td>
</tr>
<tr>
<td>Peak Watts</td>
<td>na ± na</td>
<td>na ± na</td>
<td>42.5 ± 18.3</td>
<td>49.0 ± 20.3</td>
</tr>
<tr>
<td>PCWP/(Watts/Kg)</td>
<td>na ± na</td>
<td>na ± na</td>
<td>89.1 ± 53.5</td>
<td>70.5 ± 42.8</td>
</tr>
</tbody>
</table>

Differences are larger during exercise than at rest.
Left-to-Right Pressure Gradient is Reduced by 8mm IASD

A

B

Rest

Peak Exercise

PCWP-CVP (6Months, mmHg)

PCWP-CVP (baseline, mmHg)

PCWP-CVP (6Months, mmHg)

PCWP-CVP (baseline, mmHg)

EF≥50

EF<50%

Wessler et al. CircHF 2018
Hemodynamic Effectiveness

IASD Premise:
• Shunt flow depends on shunt size and pressure gradient

Hypothesis:
• Hemodynamic effects depend on baseline pressure gradient
Corvia IASD: Baseline PCWP-CVP Pressure Gradient Correlates with Decrease in PCWP at 6 Months

Peak Exercise

Does this provide clue as to who would benefit most from an IASD?

Wessler et al. CircHF 2018
The greater the Shunt, the greater the reduction in the L-to-R Gradient

Peak Exercise

\[ \Delta (PCWP-CVP) \text{ (6 Months - Baseline)} \]

Qp:Qs

EF \geq 50%
EF < 50%

Wessler et al. CircHF 2018
IASD Study Entry Criteria

- Vary for different ongoing protocols
- Wide range of EF being included
- Hemodynamic Criteria (Corvia IASD Pivotal Study; EF>40%):
  - PCWP > 25 during exercise
  - PCWP-RA pressure gradient >5 during exercise
  - PVR < 3.5 WU
  - CI > 2.0
Corvia IASD Screen Failures

~15% of patients who enter screening drop out due to hemodynamic criteria:

- ~40% due to exercise PCWP < 25 mmHg
- ~20% due to CVP > 14
- ~20% due to PVR > 3.5 WU
- ~20% due to CI < 2.0
Major Questions being Addressed in Ongoing Pivotal Trails

- Does clinical effectiveness correlate with baseline L→R pressure gradient during exercise?
- Diameter of IASD
- If so, are there noninvasive measures that provide equivalent information as invasive exercise hemodynamic testing?
Summary

- Diameter of IASD matter
- Hemodynamic measurements have provided the foundation for understanding the physiological effects of IASDs
- Initial indications are that patients with larger R→L pressure gradients have more profound reductions of PCWP during exercise
- Hemodynamic assessments at baseline can exclude patients in whom conditions are not physiologically favorable for IASD
  - Not possible to identify these patients based on non-invasive clinical assessment
- The link between hemodynamic effects and clinical response remains to be clarified
- If link is made between baseline hemodynamic and clinical response, data will be available to assess whether and which noninvasive measures can serve as surrogates for invasive monitoring