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

Daniel Burkhoff MD PhD

Director CHF, Hemodynamics and MCS Research

Cardiovascular Research Foundation

TEACH

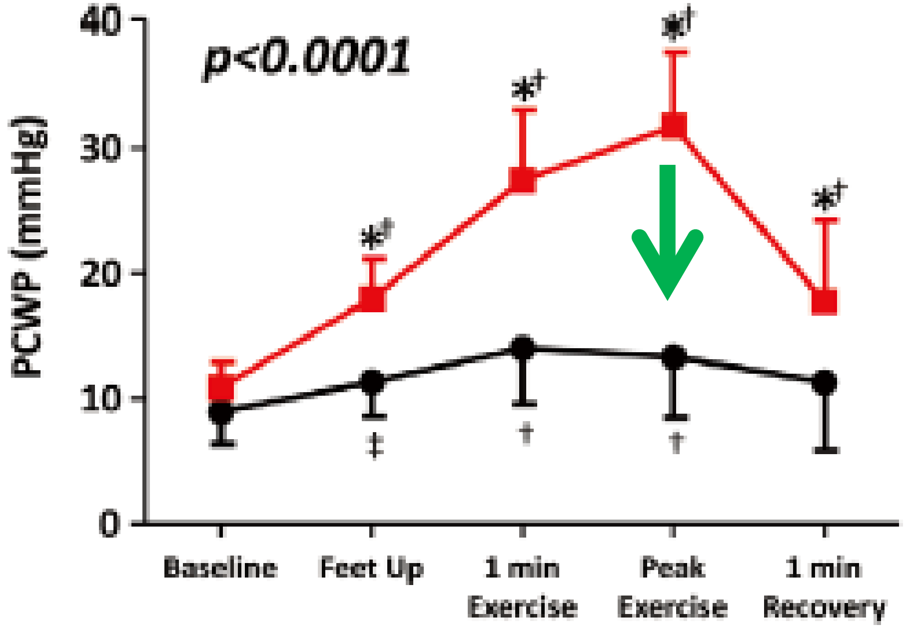
Cardiovascular Research Foundation

Disclosures:

- Consultant to Corvia Medical (Hemodynamic Corel Lab)

InterAtrial Shunts: Rationale

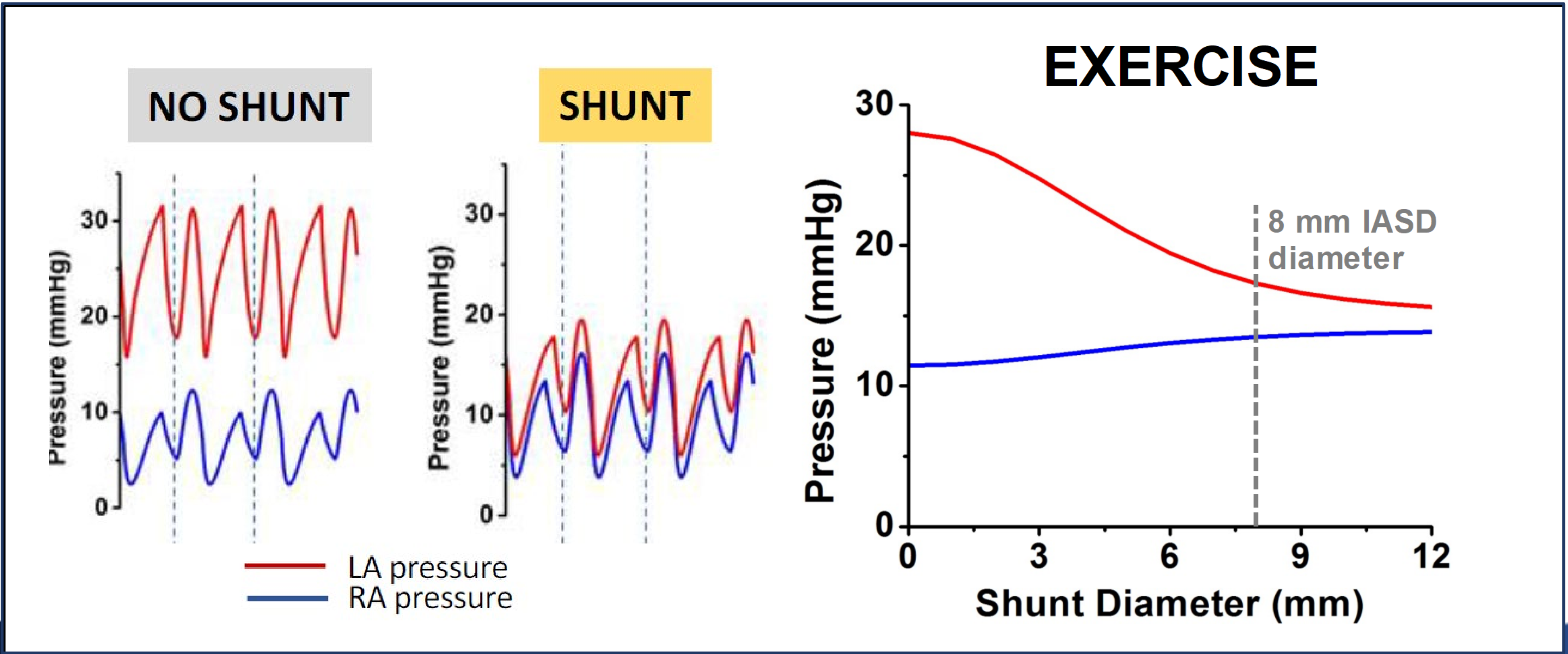
- Common pathophysiologic finding in HF: ↑LA and PCWP pressure at rest or with exertion
- ↑PCWP mechanistically linked with exercise intolerance



Borlaug et al. Circ. Journal 2013

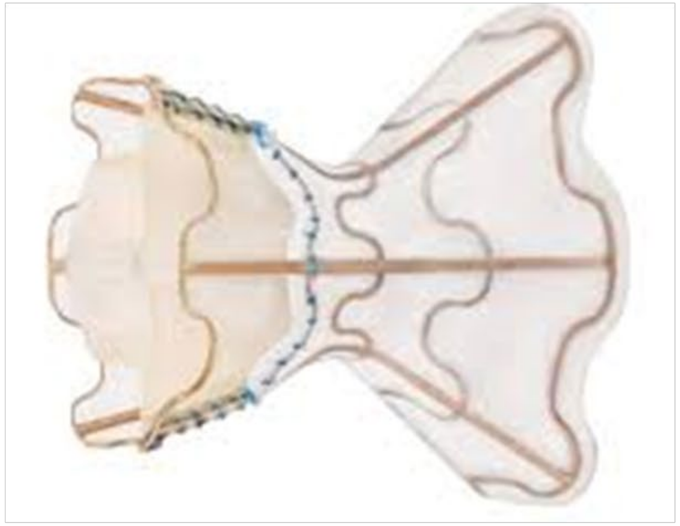
Primary Effects of InterAtrial Shunt

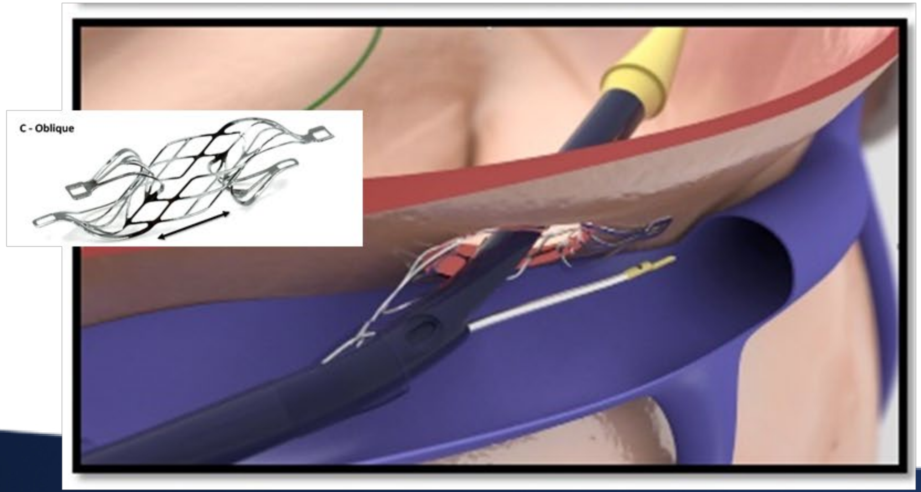
Simulation using exercise hemodynamic data from HFpEF patients

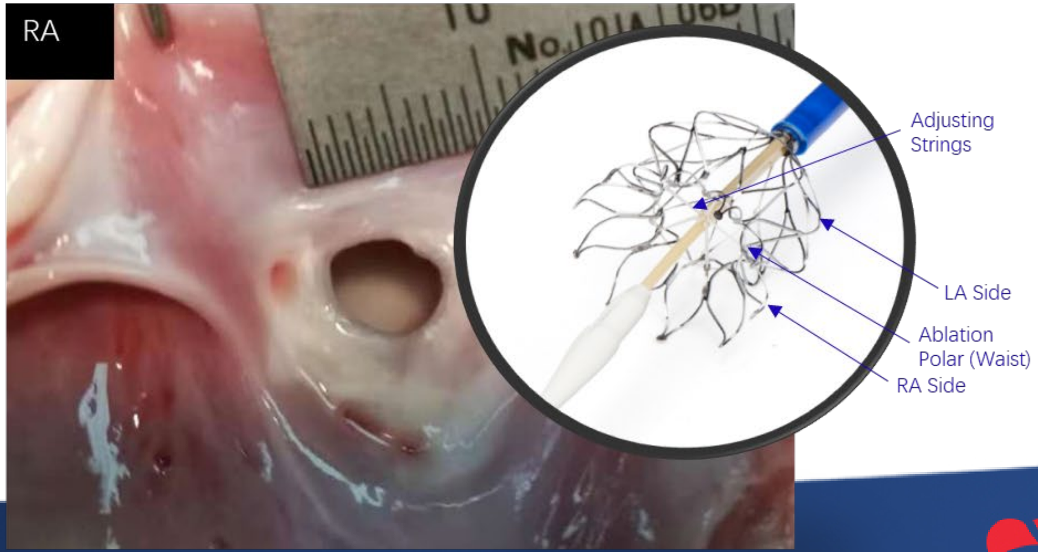


Kaye…Burkhoff. *J Card Fail* 2014

Interatrial Shunt Device Landscape





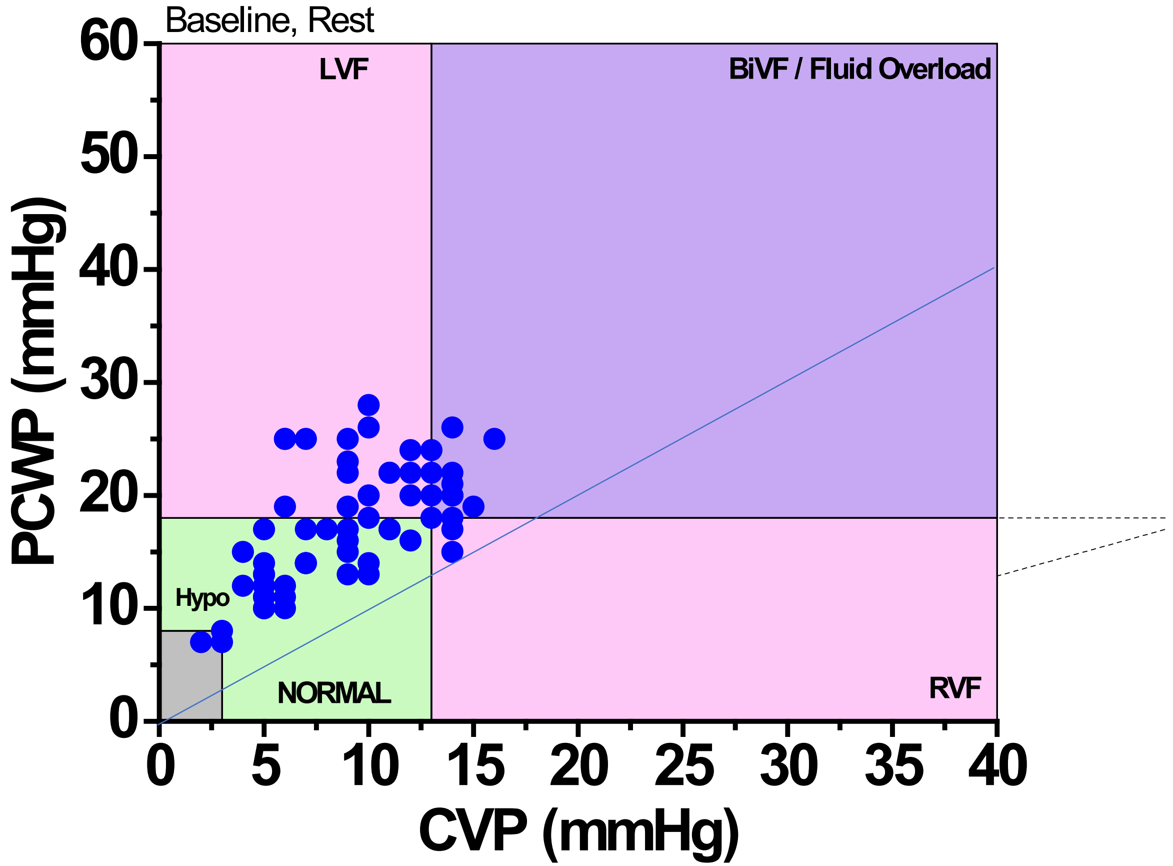


Role of Invasive Hemodynamic Measurements

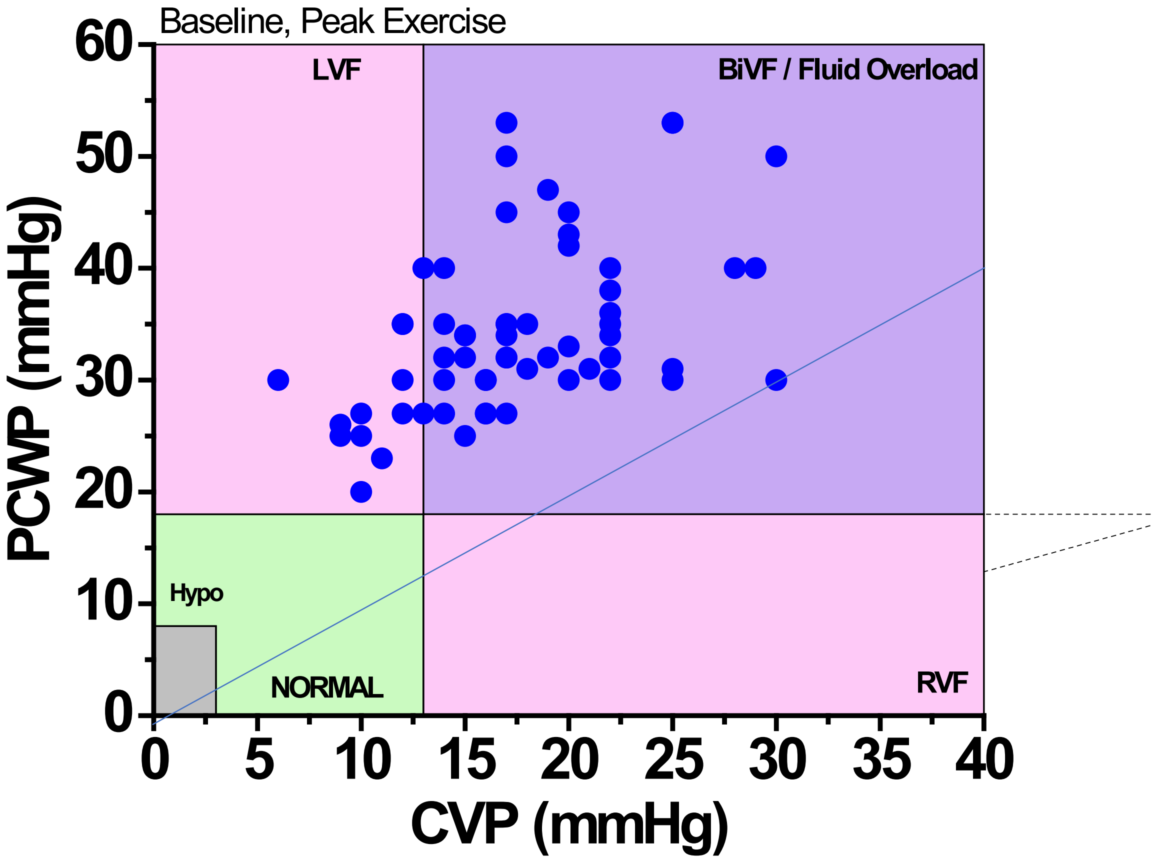
- Characterizing IASD hemodynamic effects (MOA)
- Identifying hemodynamic factors of patients most likely to benefit
  - Inclusion/Exclusion criteria for clinical trials
- Linking beneficial baseline hemodynamic factors to noninvasive surrogates that predict IASD clinical responders

Both CVP and PCWP Increase with Exercise in HFpEF/HFmrEF

REST



EXERCISE



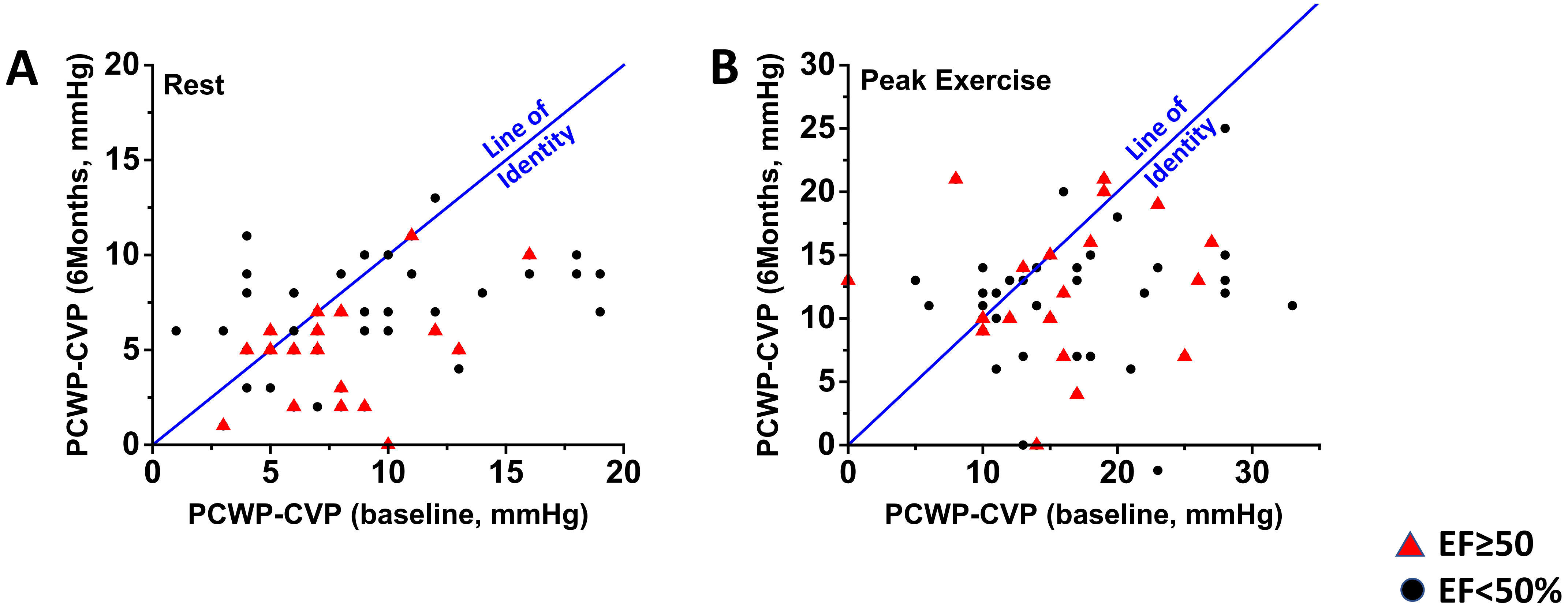
Hemodynamic Effects of Corvia 8mm IASD

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

	At Rest						Peak Exercise					
	Baseline			6Months			Baseline			6Months		
Qp:Qs	1.06	±	0.32	1.27	±	0.24 <0.001	na	±	na	na	±	na
PCWP-CVP	8.3	±	4.1	6.1	±	2.7 <0.001	16.8	±	6.9	11.4	±	5.5 <0.001
PCWP	17.4	±	5.2	16.5	±	6.7	34.1	±	7.6	31.6	±	8.0 0.025
CVP	9.0	±	3.7	10.6	±	5.1 0.027	17.5	±	5.4	20.3	±	7.9 0.041
CO (TD)	5.5	±	1.6	6.7	±	1.5 <0.001	8.7	±	2.6	10.2	±	2.7 <0.001
CO (Fick)	4.6	±	1.2	4.8	±	1.3	na	±	na	na	±	na
Peak Watts	na	±	na	na	±	na	42.5	±	18.3	49.0	±	20.3 0.002
PCWP/(Watts/Kg)	na	±	na	na	±	na	89.1	±	53.5	70.5	±	42.8 <0.001

Differences are larger during exercise than at rest

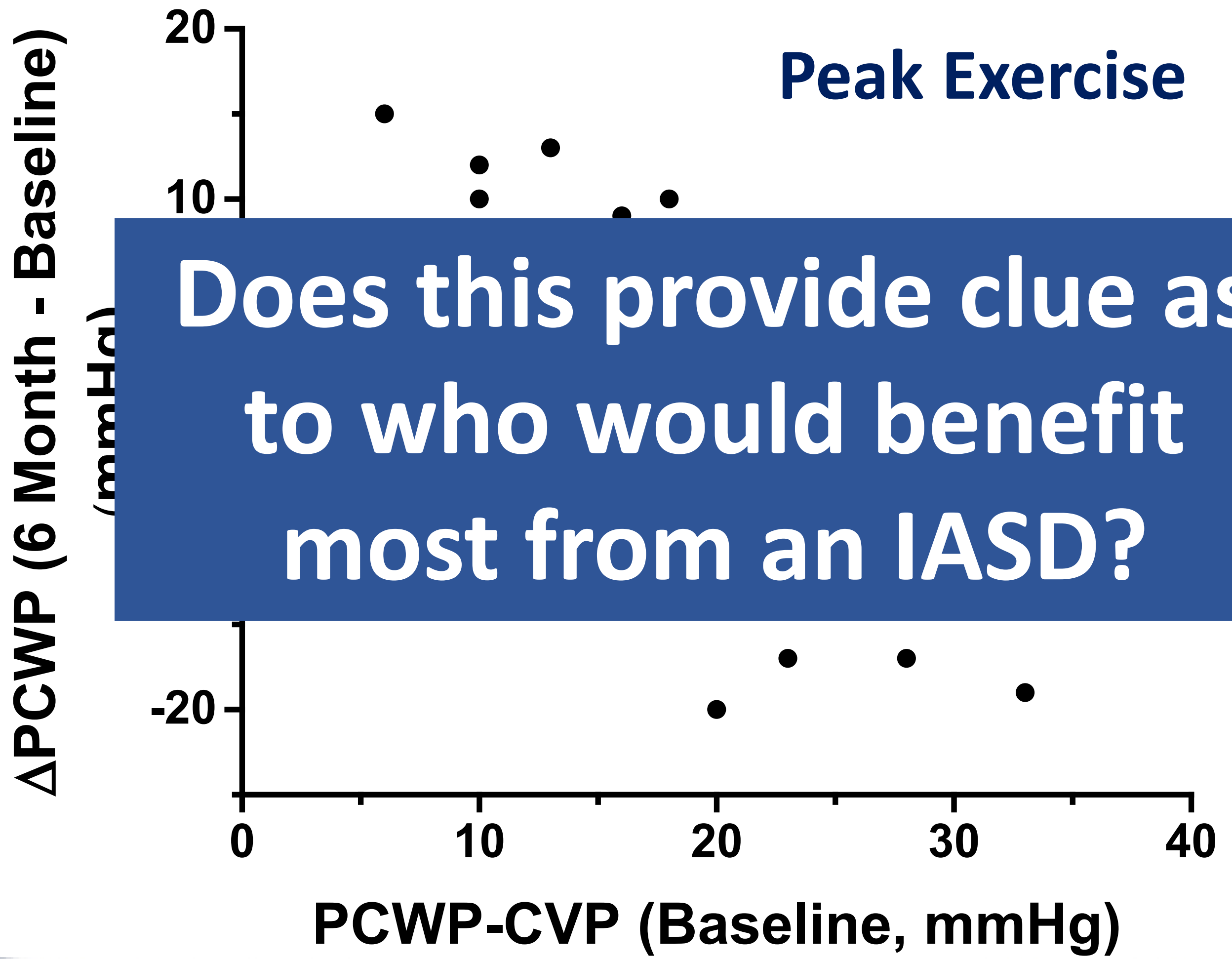
Left-to-Right Pressure Gradient is Reduced by 8mm IASD



Hemodynamic Effectiveness

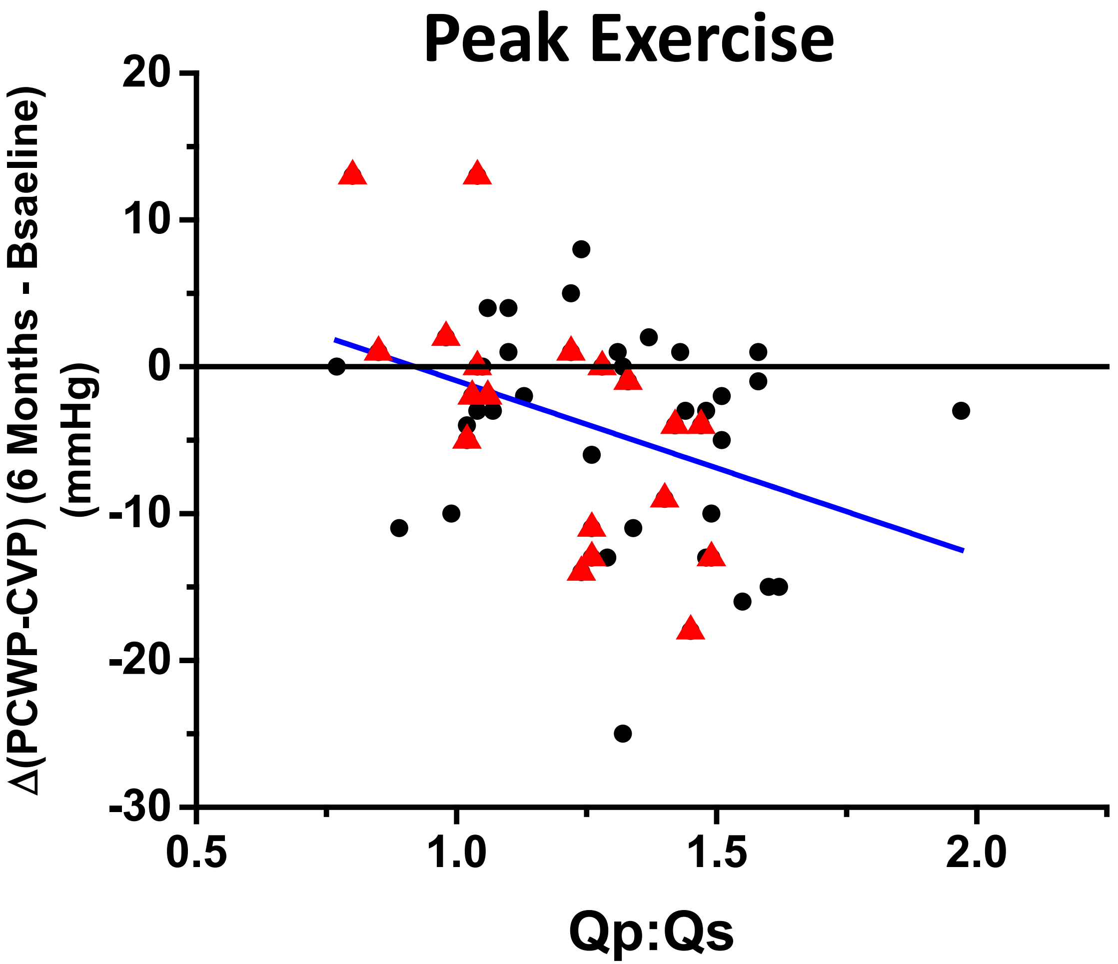
- **IASD Premise:**
  - Shunt flow depends on shunt size and pressure gradient
- **Hypothesis:**
  - Hemodynamic effects depend on baseline pressure gradient

Corvia IASD: Baseline PCWP-CVP Pressure Gradient Correlates with Decrease in PCWP at 6 Months



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

The greater the Shunt, the greater the reduction in the L-to-R Gradient



EF≥50%

EF<50%

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