

Latent Pulmonary Vascular Disease Alters the Response to Atrial Shunt Device Treatment: A Post Hoc Analysis from REDUCE LAP-HF II

Barry A. Borlaug MD,
on behalf of the REDUCE LAP-HF II Investigators
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Disclosure

Financial Relationships

Research Support:

NIH/NHLBI, Axon, AstraZeneca, Corvia, Medtronic, GlaxoSmithKline, Mesoblast, Novartis, Tenax Therapeutics

Consulting/Advisory Board:

Actelion, Amgen, Aria, Boehringer Ingelheim, Edwards, Eli Lilly, Imbria, Janssen, Merck, Novo Nordisk, VADovations

Off-Label/Investigational Uses

Atrial Septal Device

Reduce LAP-HF II study design

Phase III, multi-center, double-blind, Sham-controlled trial

PURPOSE: Evaluate the clinical efficacy and safety of the Corvia Atrial Shunt to improve quality of life and reduce HF related symptoms and events in patients with HFpEF or HFmrEF

POPULATION: Symptomatic HF, ongoing GDMT, age ≥ 40 , LVEF $\geq 40\%$, preserved RV function, elevated PCWP with left-to-right gradient (≥ 5 mmHg)

REDUCE LAP-HF II
626 randomized

93% HFpEF, 7% HFmrEF

Atrial Shunt Treatment
N=314

Sham Control
N=312

PRIMARY ENDPOINT

Hierarchical composite of cardiovascular mortality or non-fatal, ischemic stroke through 12m, rate of total HF admissions or IV diuresis through 24m & time to first HF event, change in KCCQ score between baseline & 12m

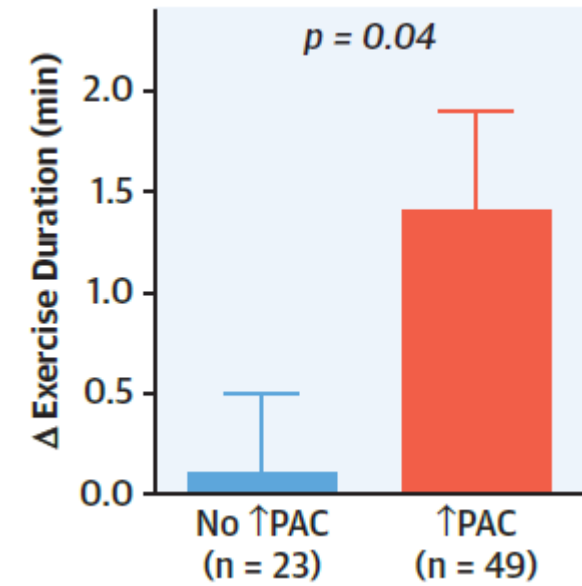
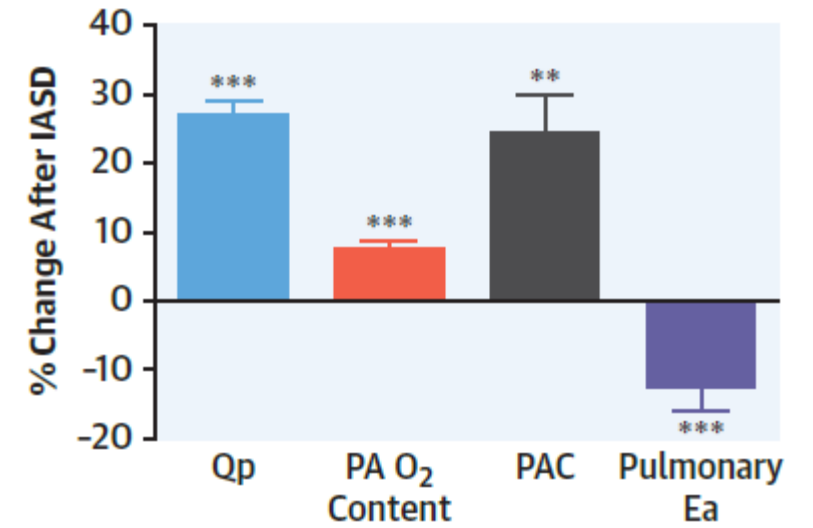
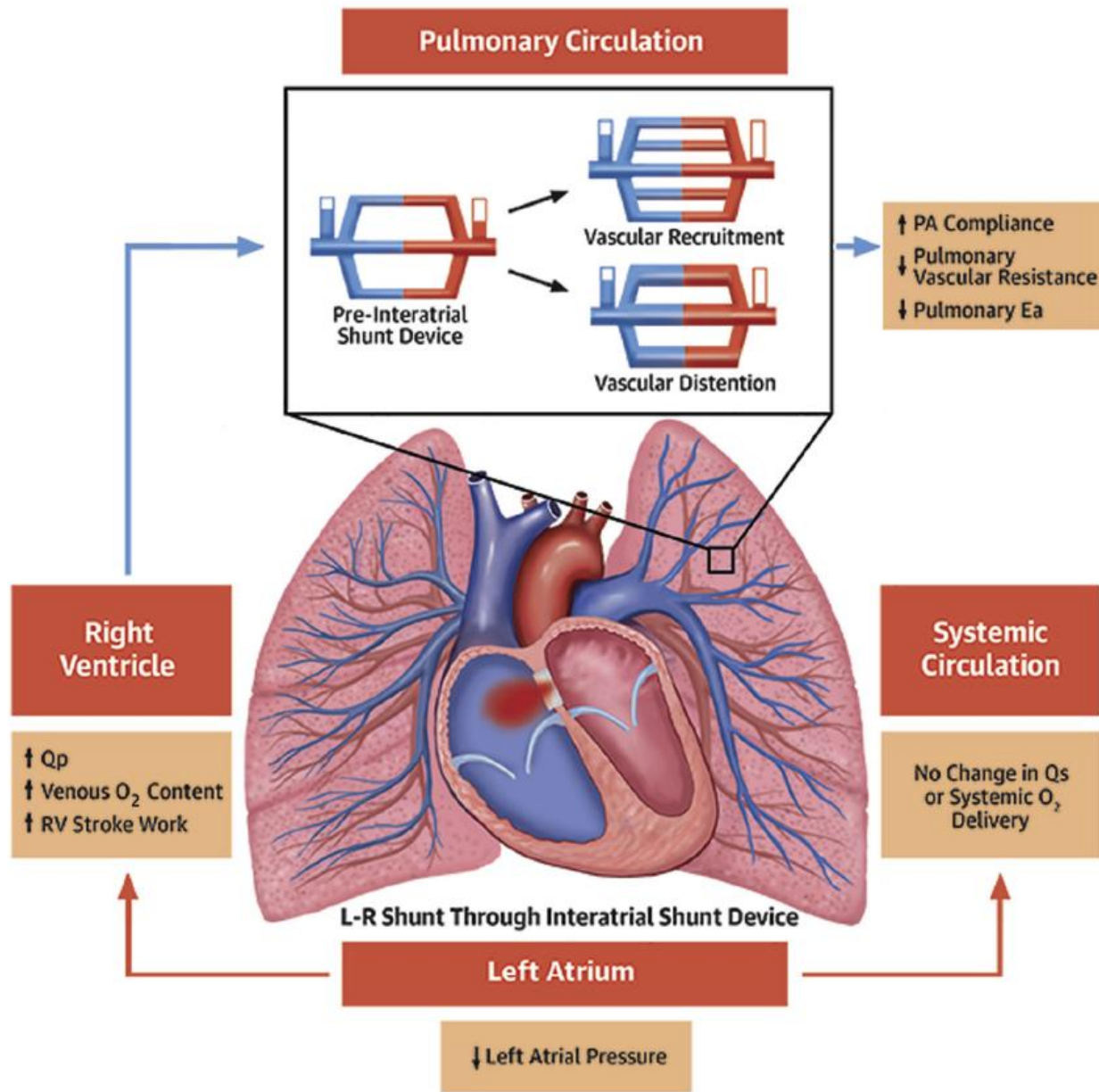
SECONDARY ENDPOINTS

- Composite safety endpoint (MACCRE)
- Rate of HF admissions or IV diuresis, through 24m
- Change in NYHA Class between baseline & 12m
- Change in KCCQ score between baseline & 12m

REDUCE LAP-HF II Trial

	Atrial Shunt Device (N = 309)	Sham Control (N = 312)	P-value
Primary Endpoint			
Finkelstein-Schoenfeld statistic, T/SE	-780/3998	..	0.85
Probability (Better in Treatment) [95% CI] ¹	0.5 (0.46, 0.54)
Win Ratio [95% CI]	0.98 (0.8, 1.2)

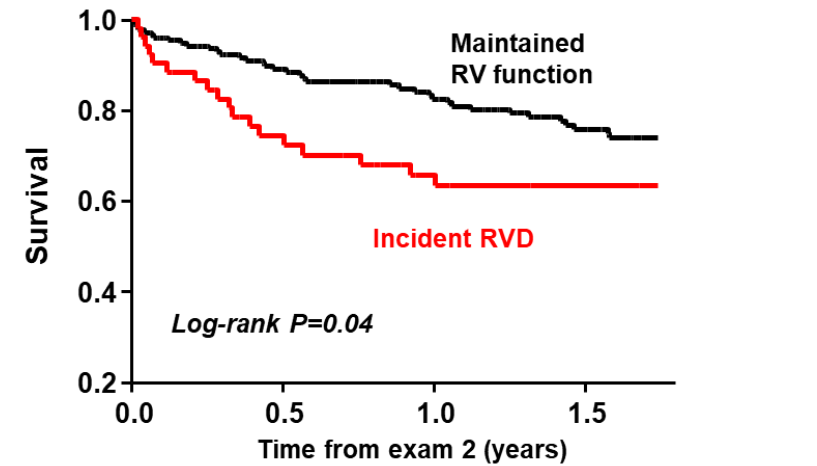
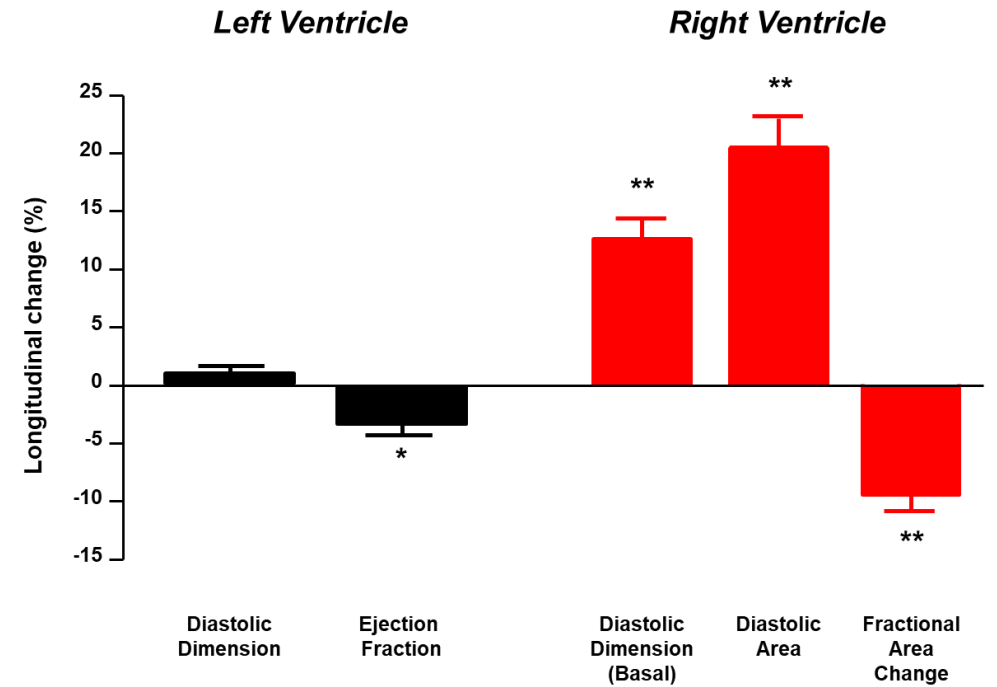
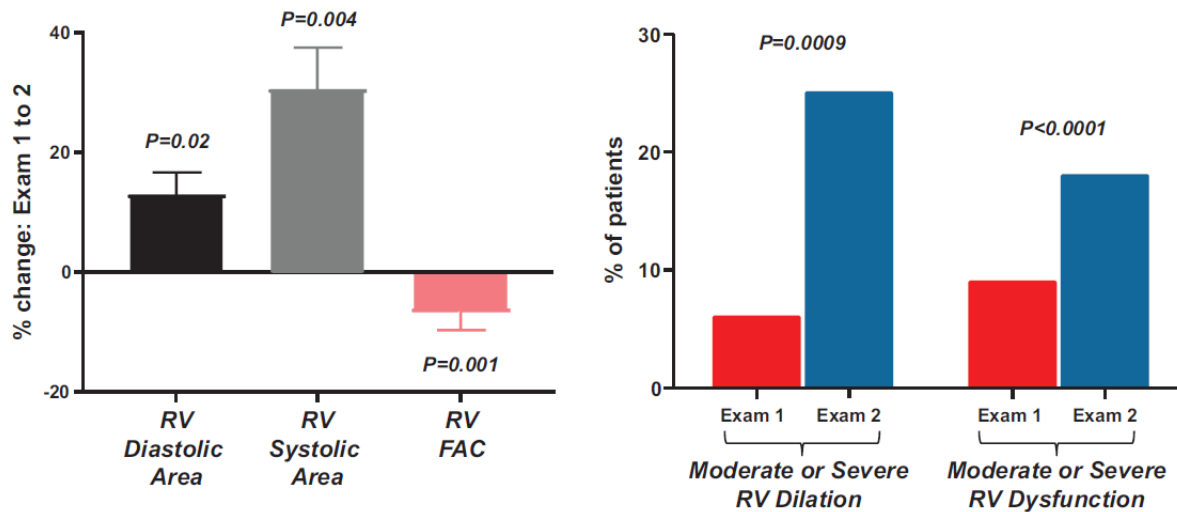
Subgroup	N	Incident Rate Ratio (95% CI)
PA systolic pressure at 20W		
- Tertile 1	192	0.71 (0.46, 1.11)
- Tertile 2	202	0.80 (0.57, 1.12)
- Tertile 3	202	1.40 (1.10, 1.79)



33% of patients >40 yo with ASD present with PH + normal LAP

26% of patients with AV Shunt-related HOHF present with PH + normal LAP

Changes in RV Structure and Function Following AV Fistula



Konstantinidis, Kasper *NEJM* 1995

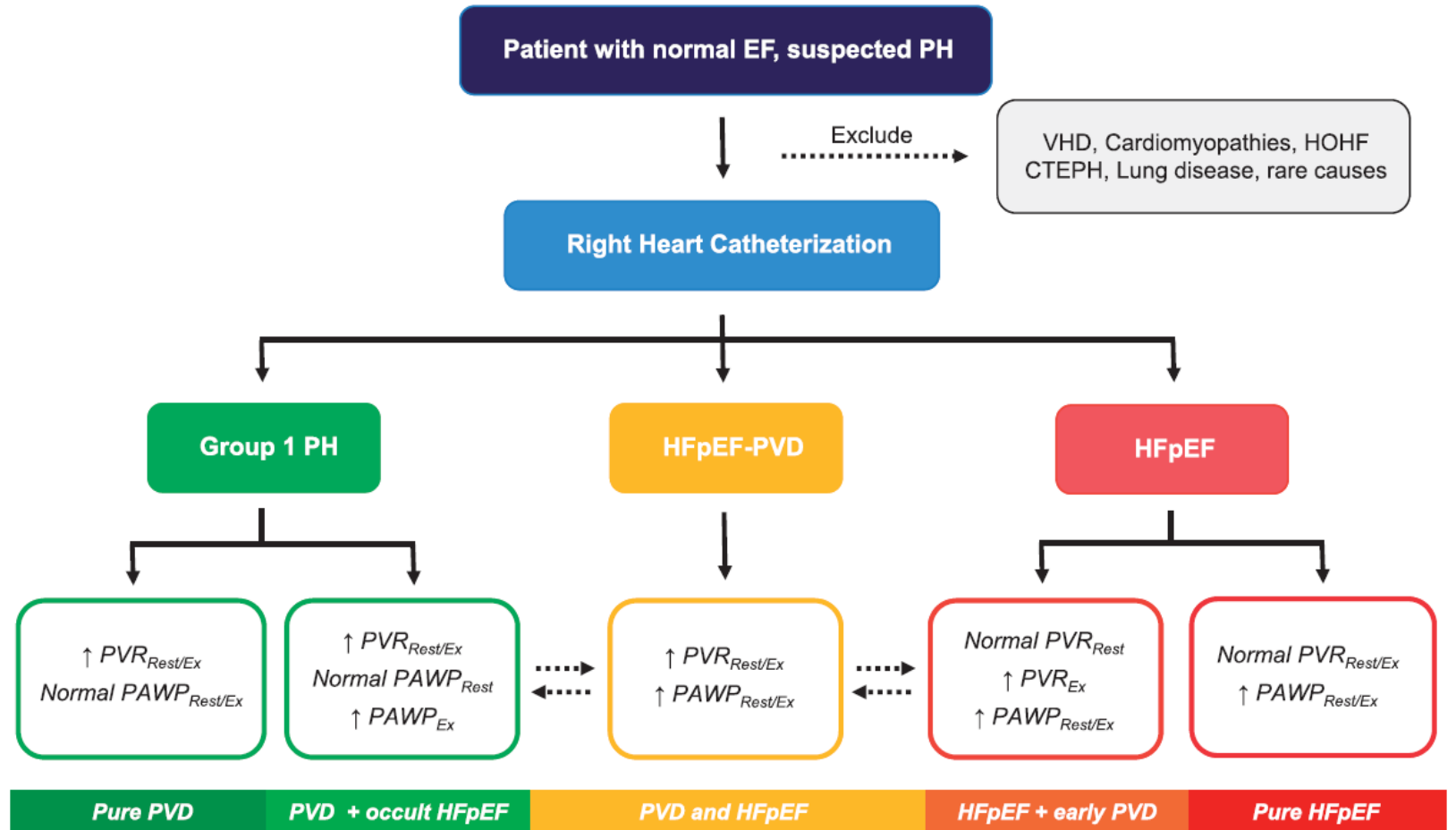
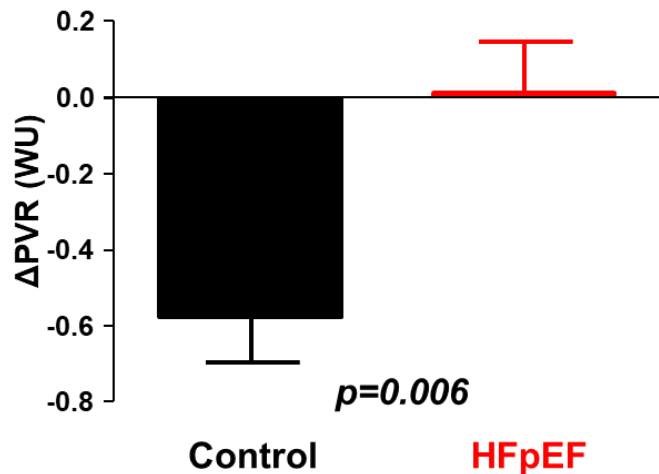
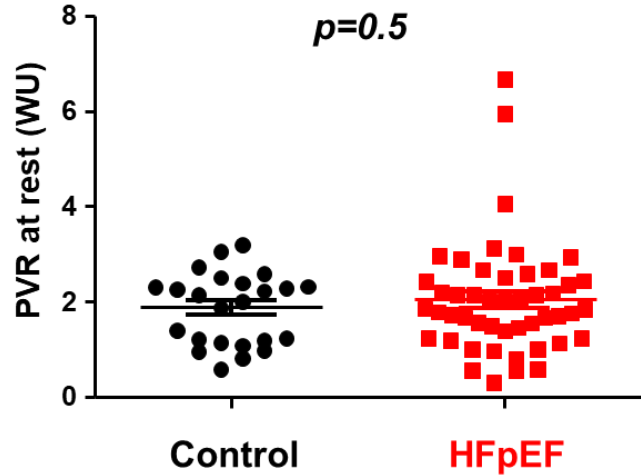
Reddy, Borlaug *J Am Coll Cardiol* 2016

Reddy, Borlaug *Eur Heart J* 2017

Obokata, Borlaug *Eur Heart J* 2019

$$mPA = PVR * Qp + PAWP$$

~~**PVR > 3.5 WU**~~



Hypothesis: Patients with HFpEF/HFmrEF and latent PVD ($\uparrow PVR_{ex}$), might be harmed by shunt implantation, while patients without latent PVD might benefit.

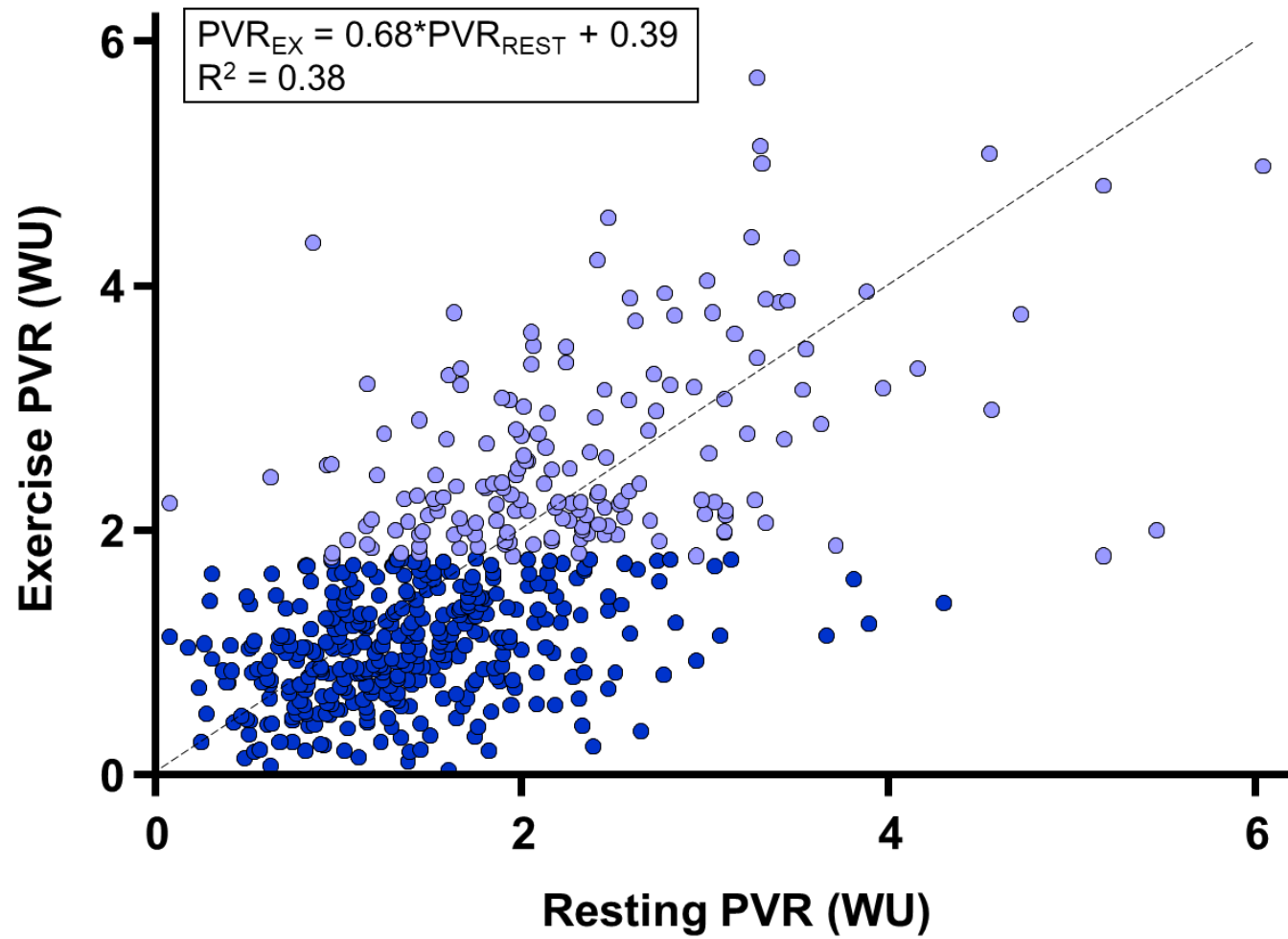
Latent PVD = exercise $PVR \geq 1.74$ WU (third tertile)

Baseline Characteristics

Cardiac Structure and Function	No PVD (n=382)	Latent PVD (n=188)	p
LVEF (%)	60±8	59±8	0.200
LA volume index (ml/m ²)	34±13 (347)	35±17 (172)	0.270

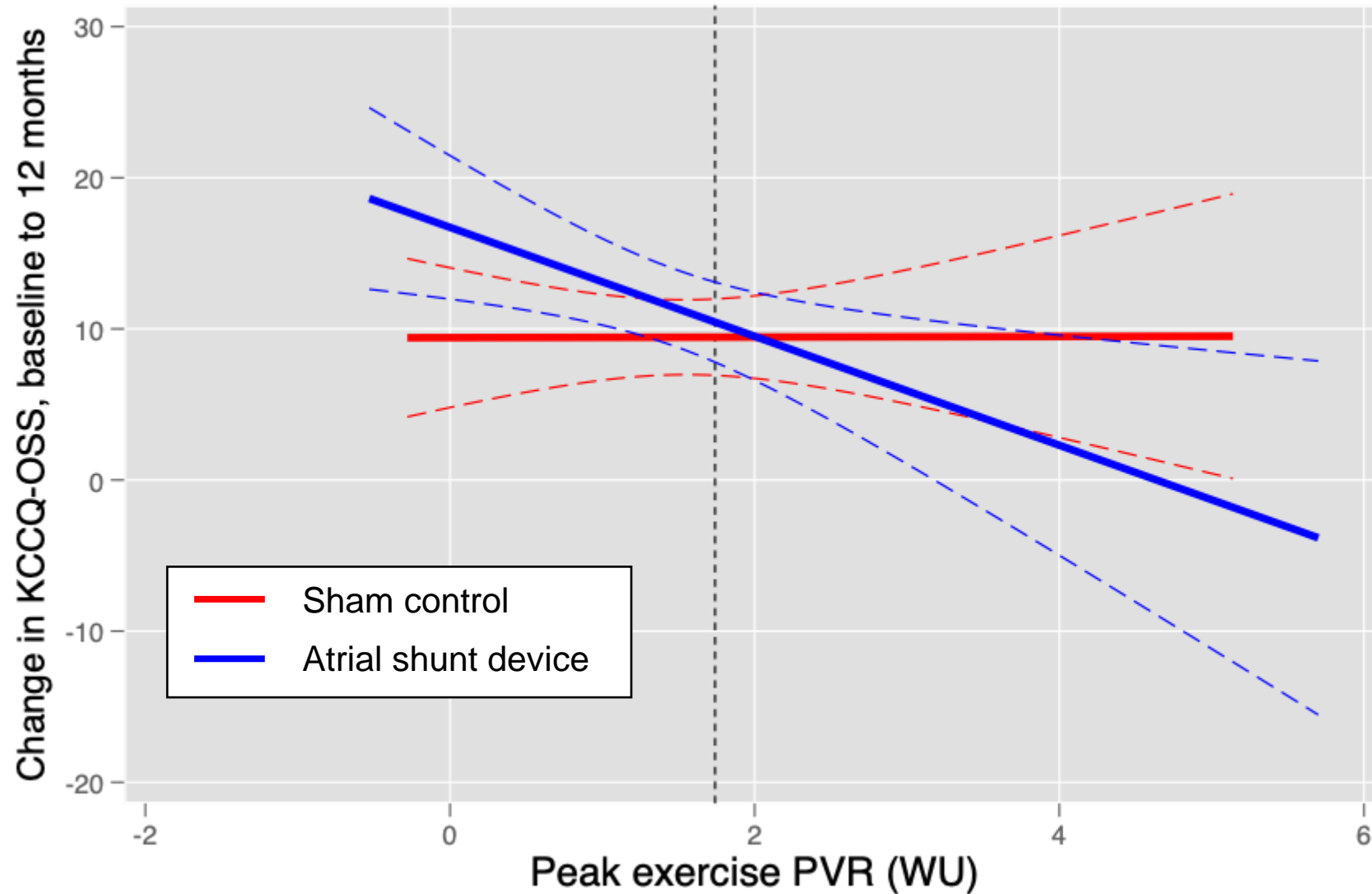
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LVEF (%)	60±8	59±8	0.200
LA volume index (ml/m²)	34±13 (347)	35±17 (172)	0.270
TAPSE (cm)	2.1±0.4 (339)	1.9±0.4 (157)	<.001
RV volume index (ml/m²)	23±9 (276)	25±11 (117)	0.063
RA volume index (ml/m²)	27±12 (314)	31±15 (145)	0.003

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RA volume index (ml/m²)	27±12 (314)	31±15 (145)	0.003
RA pressure (mmHg)	9±4 (378)	10±4 (187)	0.026
PA mean pressure (mmHg)	25±7 (375)	31±8 (187)	<.001
PA wedge pressure (mmHg)	18±7 (375)	20±6 (187)	0.001
Cardiac output (l/min)	5.7±2.2 (366)	5.0±1.3 (185)	<.001

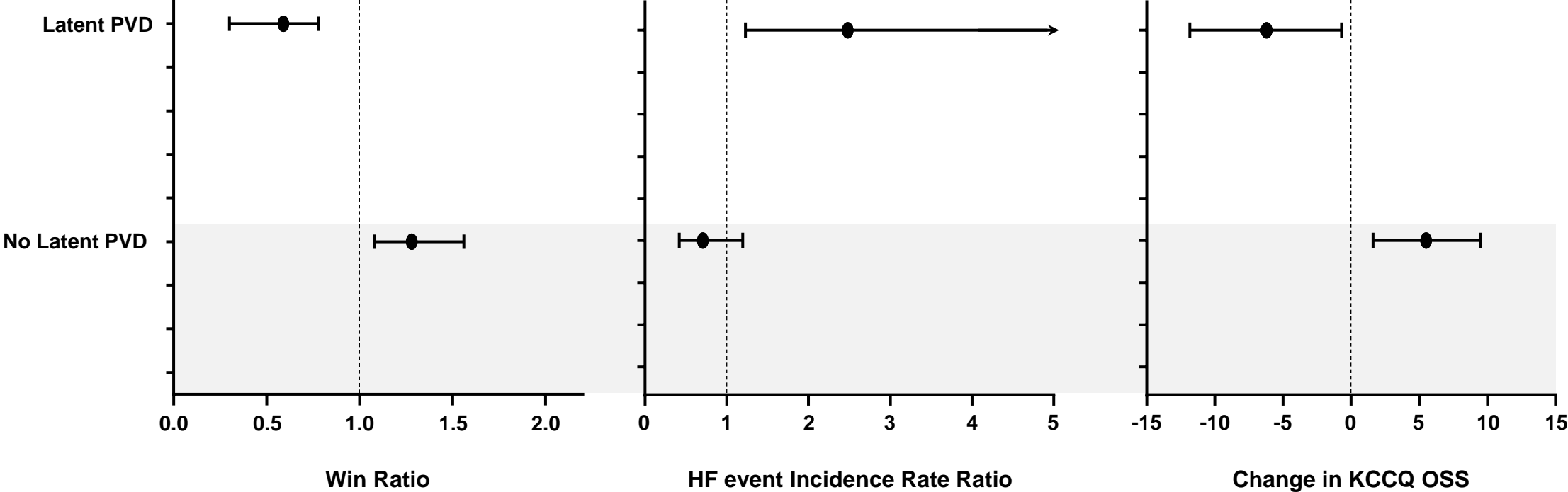


● *No Latent PVD* ● *Latent PVD*

Effect on Health Status with Shunt by PVD



Effect of Latent PVD on the Response to Shunt

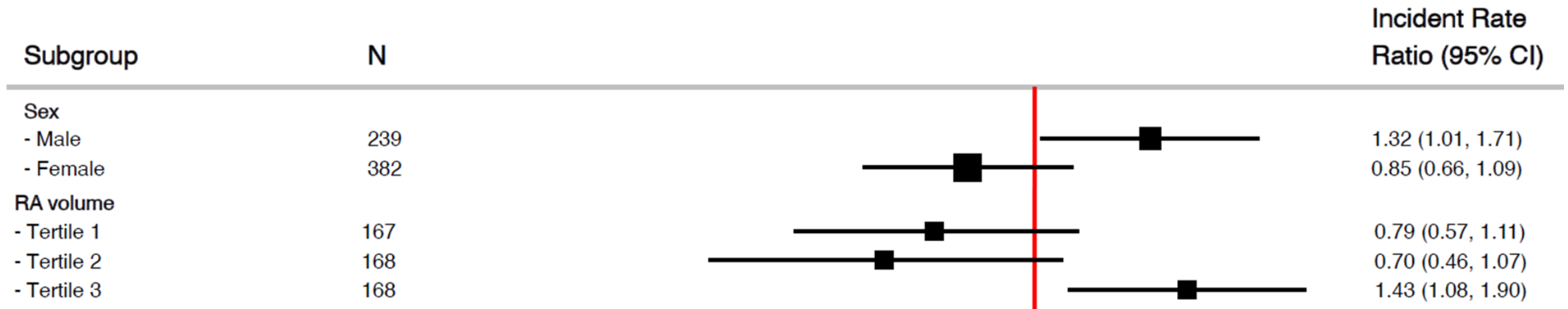


No significant relationship with resting PVR

Conclusions

- This post hoc analysis shows that latent PVD critically modifies the response to atrial shunt therapy in HFpEF/HFmrEF
 - Potential harm in latent PVD
 - Potential benefit in patients without latent PVD
- These data have important implications for devices and procedures relying on atrial shunt creation
- Emphasize the importance of PVD in HFpEF/HFmrEF
- Reinforce the importance of invasive exercise phenotyping to individualize treatment

Thank you



Baseline Characteristics Common to women & ↓RA volume:
 More likely HFpEF (vs HFmrEF), smaller LAV,
Lower prevalence of PM use

