

A photograph of a cable-stayed bridge at sunset. The sun is a bright, glowing orb on the left side of the frame, casting a long, shimmering reflection on the water below. The bridge's structure, including its tall pylon and numerous stay cables, is silhouetted against the orange and yellow sky. The water in the foreground is dark with the golden reflection of the sun.

Obesity and the Response to an Atrial Shunt: Insights from REDUCE LAP-HF II

Sheldon E. Litwin, M.D., F.A.C.C.

Alicia Spaulding-Paolozzi Professor of Cardiology

Medical University of South Carolina

Charleston VA Medical Center

Disclosure Statement of Financial Interest

Within the past 12 months, I have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Grant/Research Support
(paid to institution)

Corvia, V Wave, Axon, Eli Lilly, Astra
Zeneca, Rivus, NIH, Department of
Veterans Affairs

Consulting Fees/Honoraria


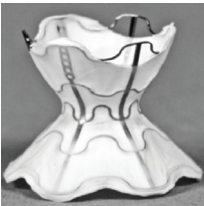



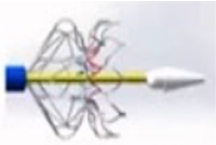
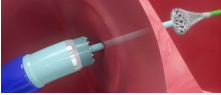
Axon, Eli Lilly, CVRx

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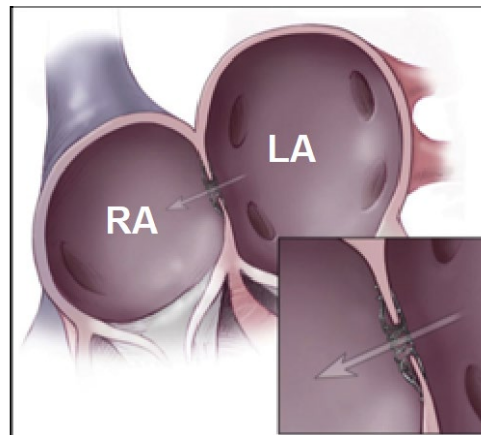
Obesity and HFpEF

- Association between obesity and incident HF
 - Framingham, MESA, CV Health study, ARIC, Heart & Soul, Cooper Center Longitudinal, Cohort of Swedish Men & Swedish Mammography, Jackson Heart Study, WHI
 - ***Graded association***: 41% ↑ in HF/5 unit ↑ BMI (supporting causality)
- **Association much stronger for HFpEF than HFrEF**
- ↑ blood volume, ↑ cardiac output, LVH, OSA
- **Uncertain how obesity may affect the diagnosis of HFpEF and the hemodynamic conditions that govern the potential efficacy of atrial shunts**

Atrial shunt devices/procedures

Device	Corvia	V-Wave	Occlutech	Edwards	Alleviant	NoYA	InterShunt
							
Shunt size	8 mm	5.1 mm	4, 6, 8, 10 mm	7 mm	6 mm	4-12 mm	4 mm

Selective lowering of LA pressure during exercise (LA decompression or unloading)



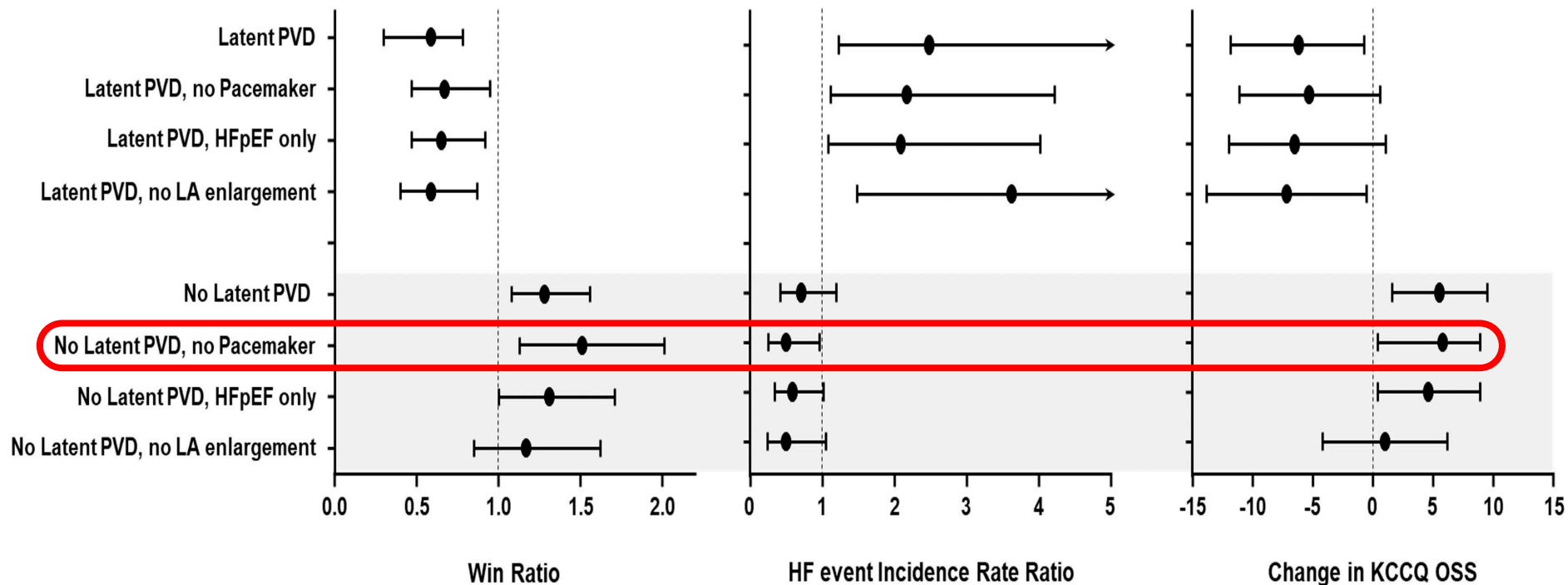
Atrial shunt device for heart failure with preserved and mildly reduced ejection fraction (REDUCE LAP-HF II): a randomised, multicentre, blinded, sham-controlled trial

*Sanjiv J Shah, Barry A Borlaug, Eugene S Chung, Donald E Cutlip, Philippe Debonnaire, Peter S Fail, Qi Gao, Gerd Hasenfuß, Rami Kahwash, David M Kaye, Sheldon E Litwin, Philipp Lurz, Joseph M Massaro, Rajeev C Mohan, Mark J Ricciardi, Scott D Solomon, Aaron L Sverdllov, Vijendra Swarup, Dirk J van Veldhuisen, Sebastian Winkler, Martin B Leon, on behalf of the REDUCE LAP-HF II investigators**

- N=608, multicenter, double blind, sham controlled RCT
- Pivotal study of Corvia Atrial Shunt device
- Primary endpoint (hierarchical composite of)
 - 1) incidence of and time to CV mortality or first nonfatal ischemic stroke through 12 months,
 - 2) total rate of HF admissions, HF visit for iv diuresis or urgent intensification of oral diuresis up to 24 months,
 - 3) change in KCCQ score at 12 months
- **Overall result and individual components were neutral**

Responder analysis

Latent PVD = peak exercise PVR ≥ 1.74 WU



~ 50% of patients fall into responder group

Borlaug BA...Shah SJ.
Circulation 2022

Obesity in HFpEF:

Patient characteristics

- Obesity defined based on WHO categories (normal, overweight, class 1-3 obesity)
- 60.9% had BMI ≥ 30 kg/m²
- With increasing obesity (normal \rightarrow class 3):
 - Younger: 76 \rightarrow 68 years
 - Black: 2.2% \rightarrow 14%
 - \uparrow HTN, DM
 - \uparrow HF hospitalizations in prior year: 20% \rightarrow 38%
 - More use of loop diuretics: 67% \rightarrow 95%
 - Less atrial fibrillation: 66% \rightarrow 41%

Symptoms & labs

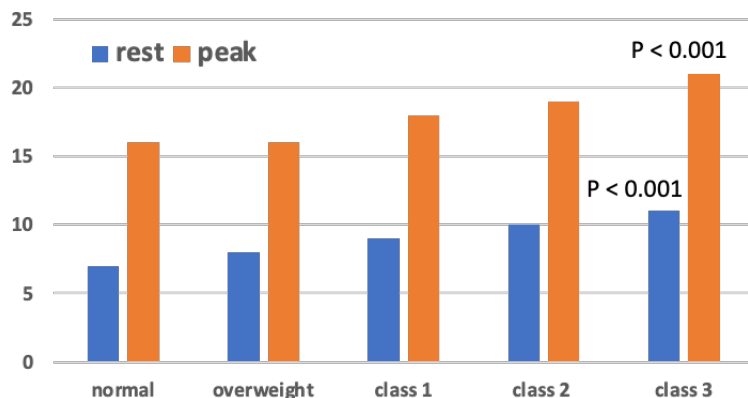
- With increasing category of obesity:
- Worse KCCQ OSS: 51.7 \rightarrow 39.8
- Lower 6 MWD: 334 \rightarrow 254 m
- Lower natriuretic peptide levels (\sim \downarrow 70%)

Echocardiography

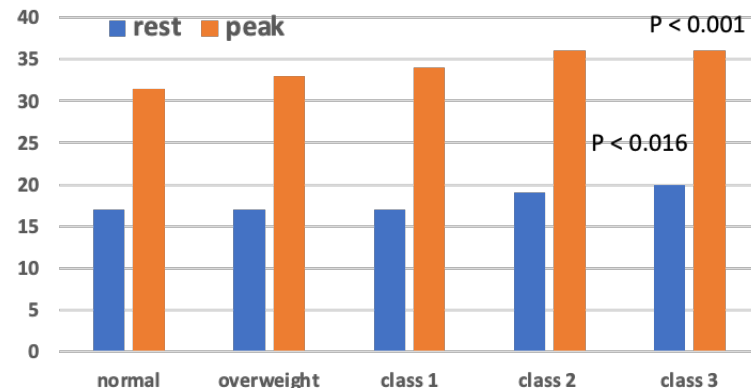
- ↑ LV diastolic volume: 93 → 120 ml
- ↑ LV mass: 148 → 175 g
- ↑ LA volume: 54 → 66 ml
- ↔ RV dimension: 3.8 → 3.7 cm
- ↔ RA volume: 48 → 48 ml
- ↔ Est RA pressure: 3 → 3 mmHg
- ↓ E/e': 13.6 → 11.5
- ↑ CO: 3.9 → 5.2 L/min

Invasive Hemodynamics

RA pressure (mmHg)



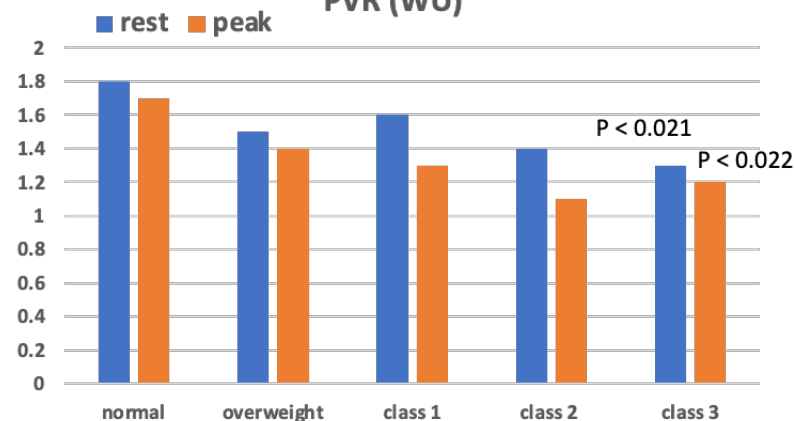
PCWP (mmHg)



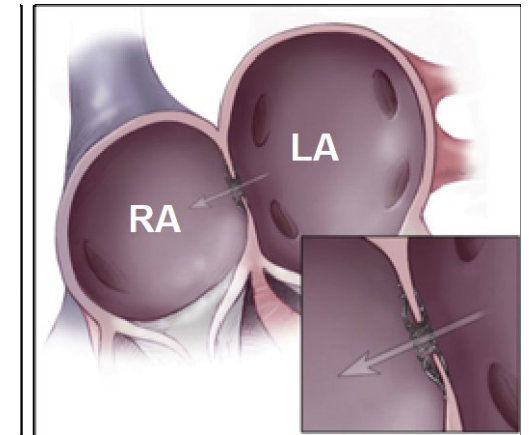
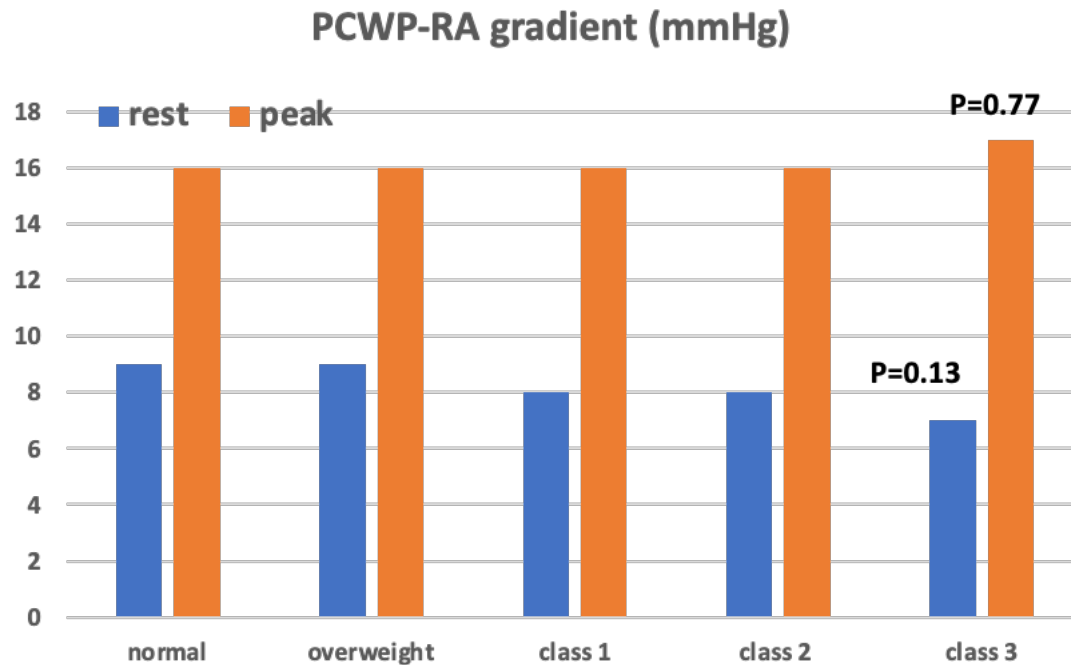
Cardiac Output (L/min)



PVR (WU)



Driving force for left to right shunting



Even severely obese patients maintain hemodynamic conditions that favor less shunting at rest but favoring LA unloading with exertion

Responder Characteristics & Outcomes

- Fewer Pacemakers: 25% → 11%
- Lower Exercise PVR: 1.7 → 1.2 WU
- Outcomes:
 - More first and recurrent HF hospitalizations as obesity worsened (HR 1.26 per 1 SD increase in BMI, 95% CI 1.06-1.51, $p = 0.01$)
 - **No interaction between obesity and treatment effects** (time to first HF event by BMI ≤ 30 vs. > 30) in overall population (p interaction = 0.77) or in those with responder characteristics (p interaction = 0.2)

In patients with HFpEF, more severe obesity was associated with:

- Worse symptoms and lower 6MWD
- Progressive left heart remodeling
- No right heart remodeling (selection criteria)
- Elevated right and left sided filling pressures & CO
- Echo not reliable for filling pressures but good for stroke volume and CO
- Obese frequently have responder characteristics
 - Fewer PM, lower exercise PVR, less AF
- Increased HF events with worsening obesity
- No interaction between obesity and response to atrial shunt
- Obesity alone is not a reason to exclude patients from atrial shunt therapies