Short-term Atrial Shunt Device Induced Changes in Cardiac Structure/Function and Risk of Subsequent Heart Failure Events:

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on behalf of the REDUCE LAP-HF II Investigators

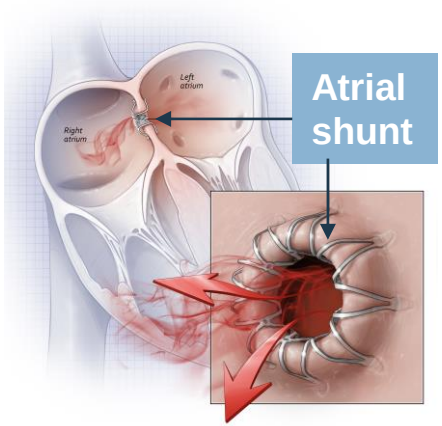
Disclosure of Relevant Financial Relationships

Within the prior 24 months, I have had a financial relationship with a company producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients:

Nature of Financial Relationship	Ineligible Company
Grant/Research Support	Corvia Medical, XVIVO
Consultant Fees/Honoraria	Abbott, Bayer, Boehringer Ingelheim, Novartis
Individual Stock(s)/Stock Options	Cardiac Dimensions

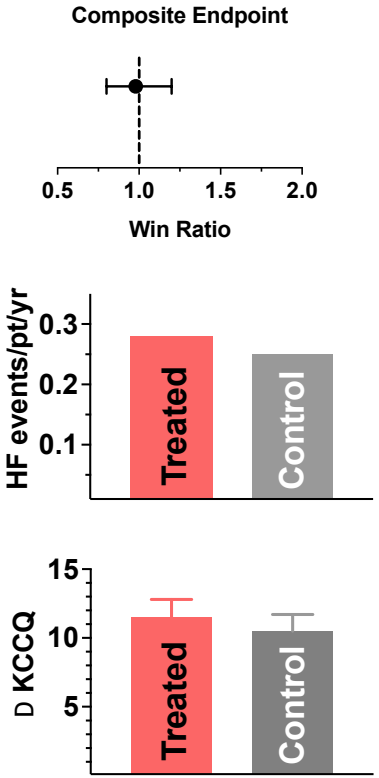
All relevant financial relationships have been mitigated.
Faculty disclosure information can be found on the app

Background: REDUCE LAP-HF II Trial

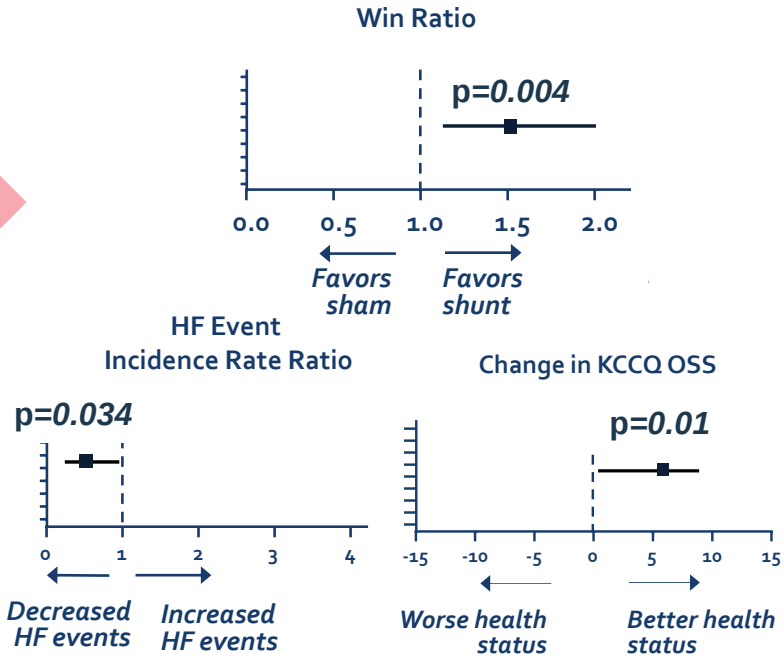


- Sham-controlled, blinded RCT (n=626)
- HF, LVEF ≥40%
- exPCWP≥25mmHg

Shah et al Lancet 2022
Borlaug et al Circulation 2022



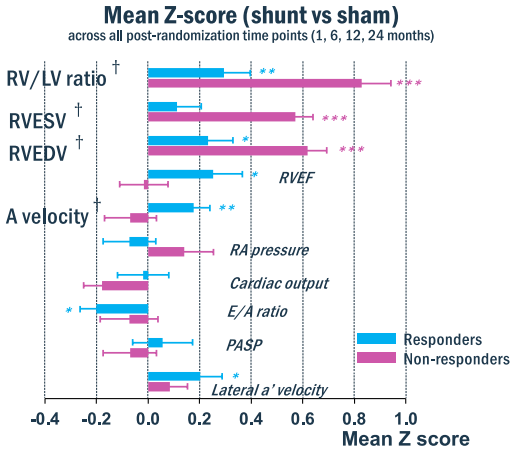
Responder Group: 50% of trial patients
(exPVR <1.74WU, no pacemaker/ICD)



Atrial Shunting, Responder Status and "Remodeling"

1. Atrial Shunting: ↑right heart volumes and ↓left heart volumes

2. Remodeling x Responder Status interaction



- ***<u>Over 2 years:</u> 4 echo parameter treatment effects were significantly different between responders vs. non-responders*** ($P_{interaction}$ <0.05):
  - **Lower RV/LV volume ratio**
  - **Lower RVESV, RVEDV**
  - **Higher transmitral A velocity**

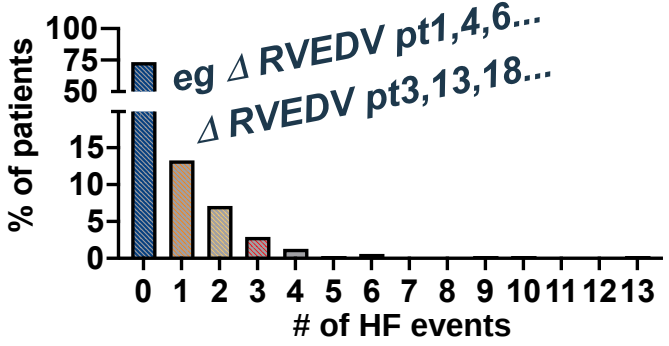
Patel RB…Shah SJ. JAMA Cardiology 2024 (in press)

Remodeling in REDUCE LAP-HF II

Question:

Is there a relationship between degree of remodeling observed at 6 months and the number of HF events through 24 months of follow-up?

Methodology: Negative binomial regression (to account for recurrent HF events)



Atrial Shunt Associated “Remodeling” at 6 months

Overall results in all trial patients

	Sham	Shunt	p value
RAV (mL)	0.5±1.2	11.3±1.5 ↑	<0.001
RVEDV (mL)	2.6±1.4	13.5±1.6 ↑	<0.001
LAV	2.5±0.9	-0.7±0.8 ↓	0.009
LVEDV	-4.7±1.5	-11.4±1.4 ↓	0.001
Lateral s'	-0.1±0.1	0.6±0.1 ↑	<0.001
Mitral E	1.2±1.2	-3.1±1.2 ↓	0.012
Av. E/e'	0.2±0.3	-1.0±0.3 ↓	0.006

Mean±SEM. n=158-262 paired measures per parameter/group

How do responders and non-responders differ?

Right heart changes are exaggerated in NON-RESPONDERS

	Sham	Shunt	p value
RAV (mL)	-2.7±1.9	12.6±2.8 ↑	<0.001
RVEDV (mL)	2.8±2.4	16.4±2.7 ↑	<0.001
LAV	3.8±1.3	-0.7±1.5 ↓	0.021
LVEDV	-3.9±2.1	-12.6±2.3 ↓	0.006
Lateral s'	-0.2±0.2	0.6±0.2 ↑	0.012
Mitral E	2.4±1.9	-3.5±2.0 ↓	0.03
Av. E/e'	-0.1±0.5	-1.2±0.3	0.10

Mean±SEM. n=62-114 paired measures per parameter/group

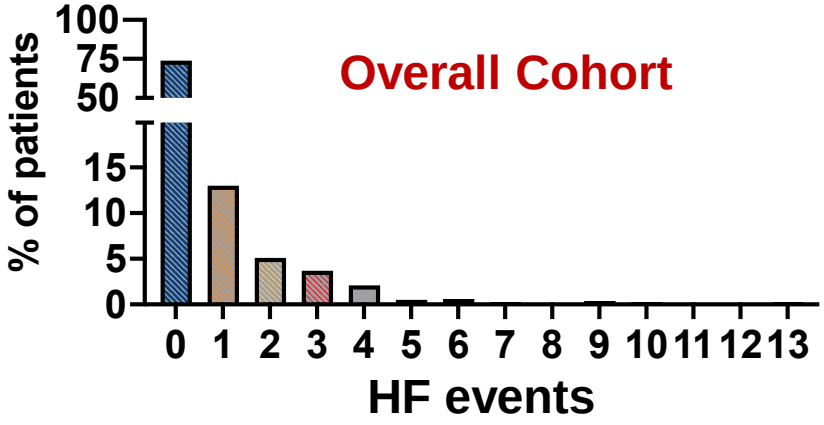
How do responders and non-responders differ?

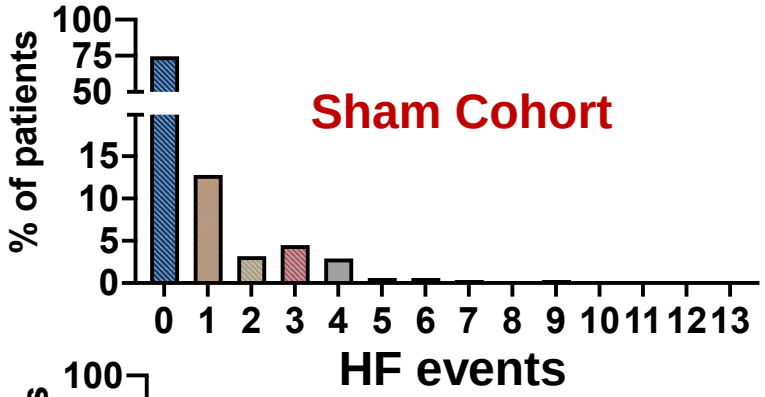
These changes are less exaggerated in RESPONDERS randomized to shunt

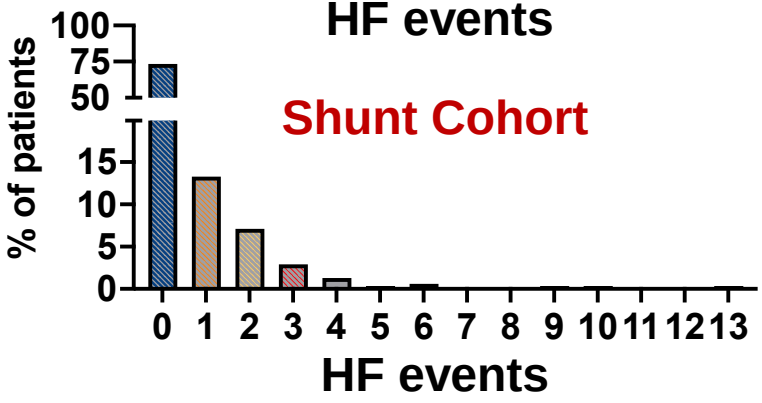
	Sham	Shunt	p value
RAV (mL)	3.7±1.7	10.9±1.4 ↑	0.001
RVEDV (mL)	2.8±1.8	12.3±2.0 ↑	<0.001
LAV	2.2±1.3	-0.8±1.0 ↓	0.07
LVEDV	-4.9±2.2	-10.8±1.8 ↓	0.04
Lateral s'	-0.2±0.2	0.6±0.2 ↑	0.012
Mitral E	-0.3±1.7	-3.1±1.2	ns
Av. E/e'	0.5±0.4	-0.9±0.4 ↓	0.01

Mean±SEM. n=84-135 paired measures per parameter/group

24 Month HF Event Profiles and Remodelling

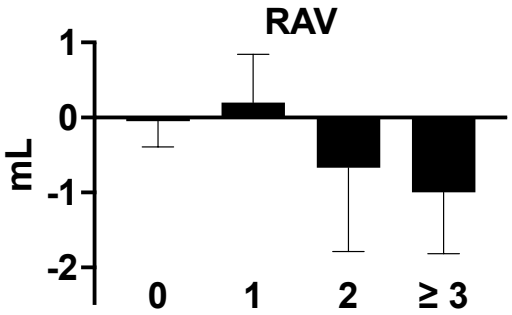


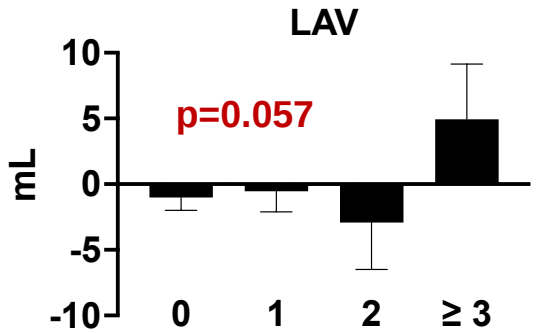


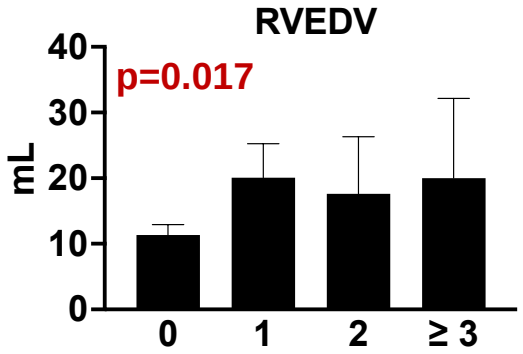


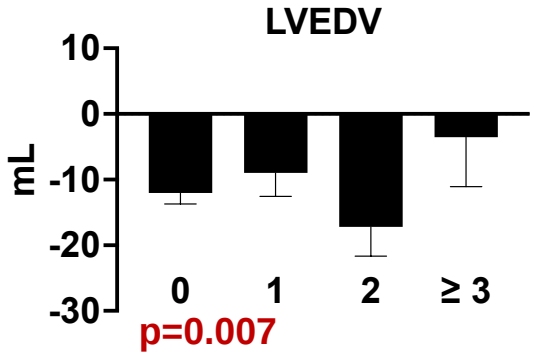
HF Events & Remodeling

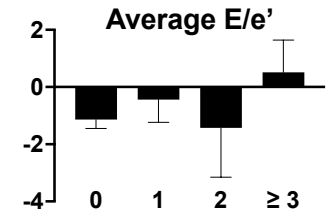
24 Month HFE vs 6 months echo change: Shunt Cohort.

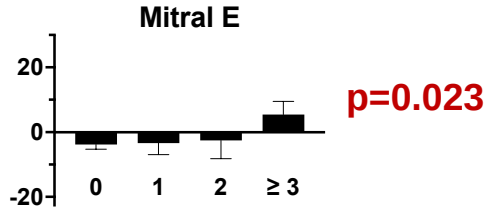


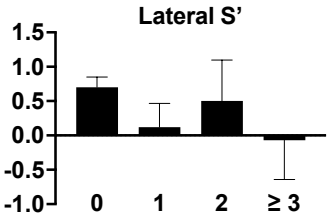






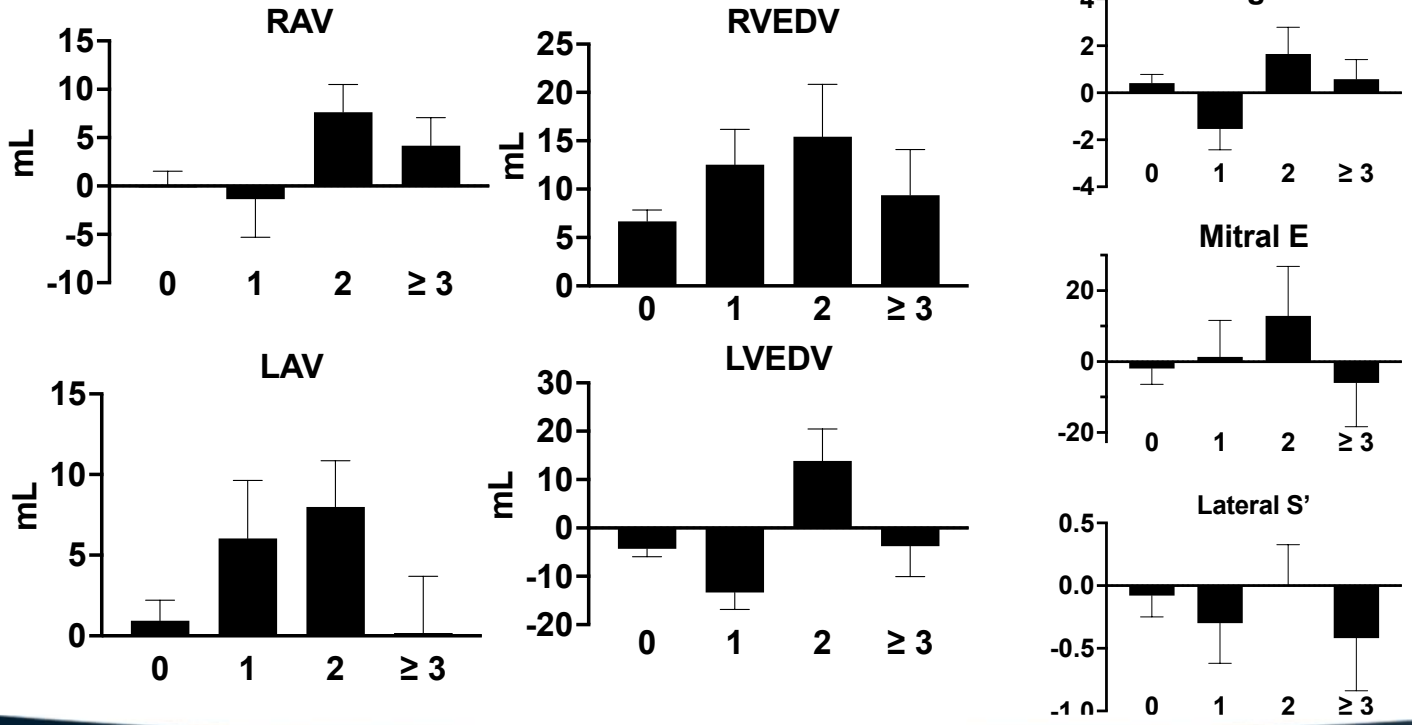






HF Events & Remodeling

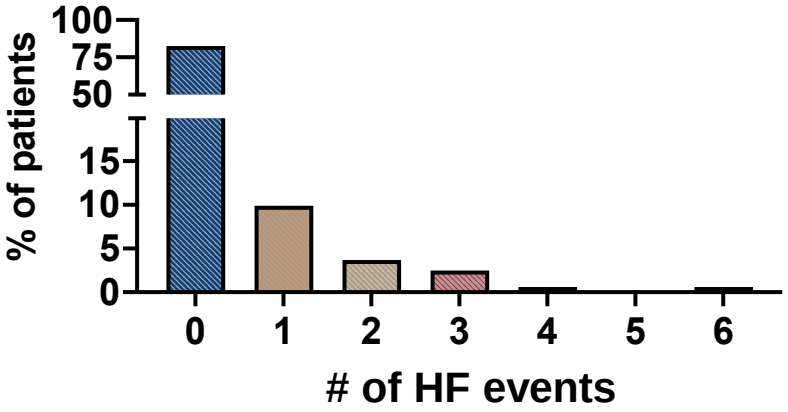
24 Month HFE vs 6 months echo change: Sham Cohort



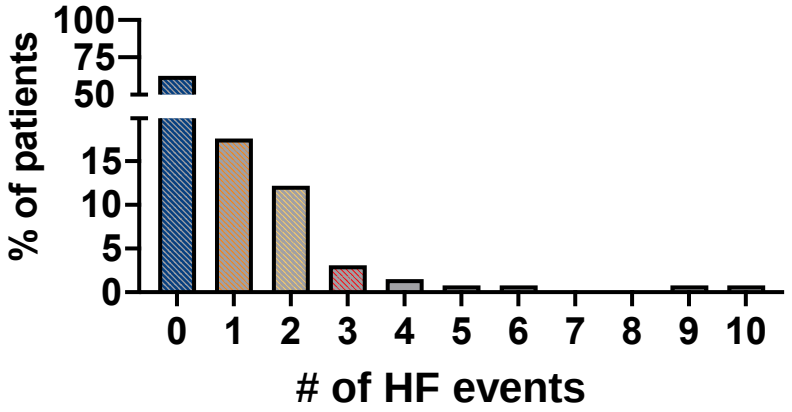
No significant associations (P=NS for all comparisons)

HF Events and Echo by Responder Status

Responder Group



Non-Responder Group



At 6Months:

- **Bigger LA (p<0.001)**
- **Bigger RA (p<0.001)**
- **Bigger RV (p<0.001)**
- **Higher E/e' p=0.002**

Conclusions

- Specific patterns of right and left heart remodeling occur in response to atrial shunting
- Optimal levels of remodeling (**less prominent RA and RV dilation, and less LV underfilling**) in response to atrial shunting are associated with favorable HFH profiles and are evident in the responder cohort of shunt patients
- The ongoing RESPONDER-HF trial will provide further insights into the characterization of patients most likely to benefit from atrial shunting