Two-year outcomes after implantation of an atrial shunt in patients with heart failure and preserved or mildly reduced ejection fraction: Results from the REDUCE LAP-HF II trial

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Disclosures

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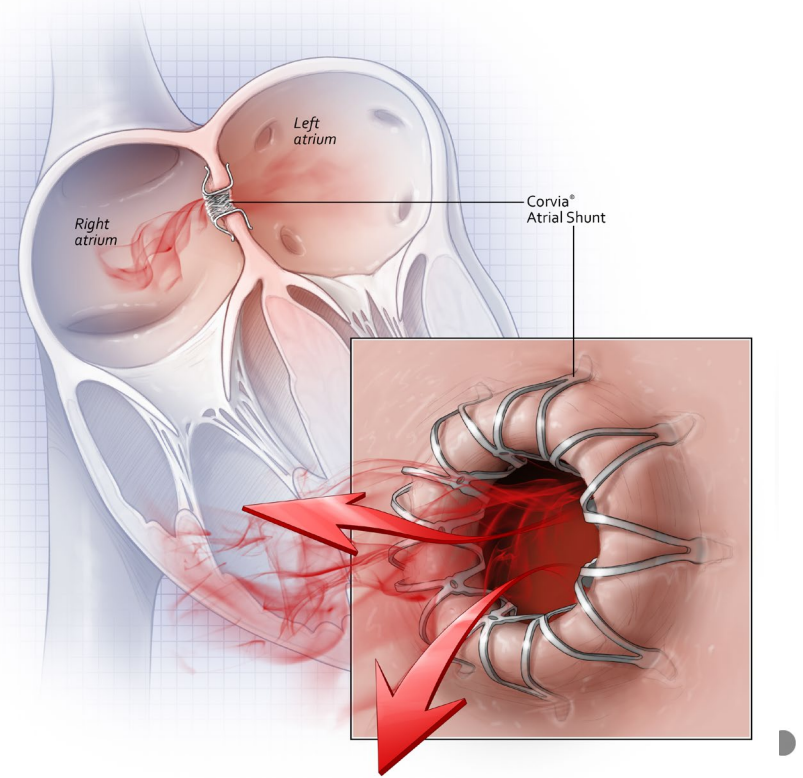
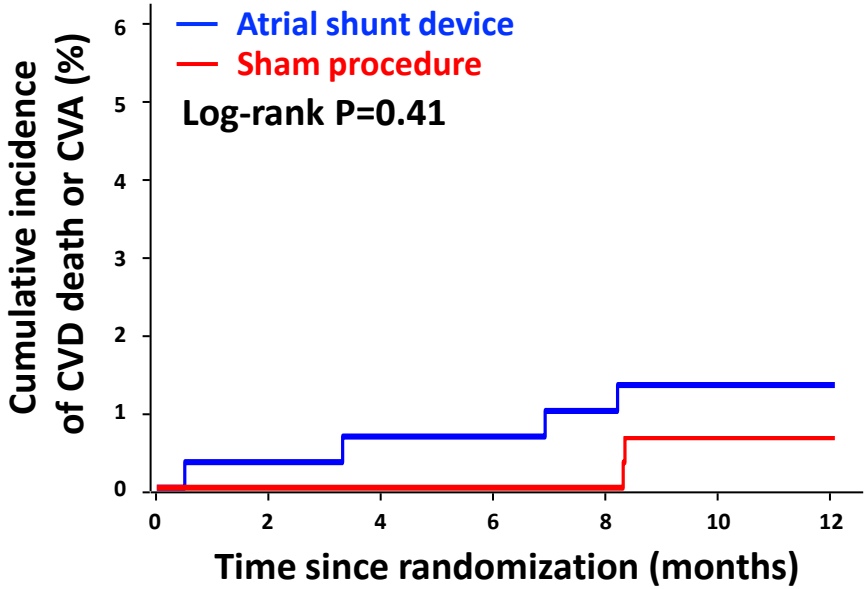
- FG is an unpaid advisor to Corvia Medical

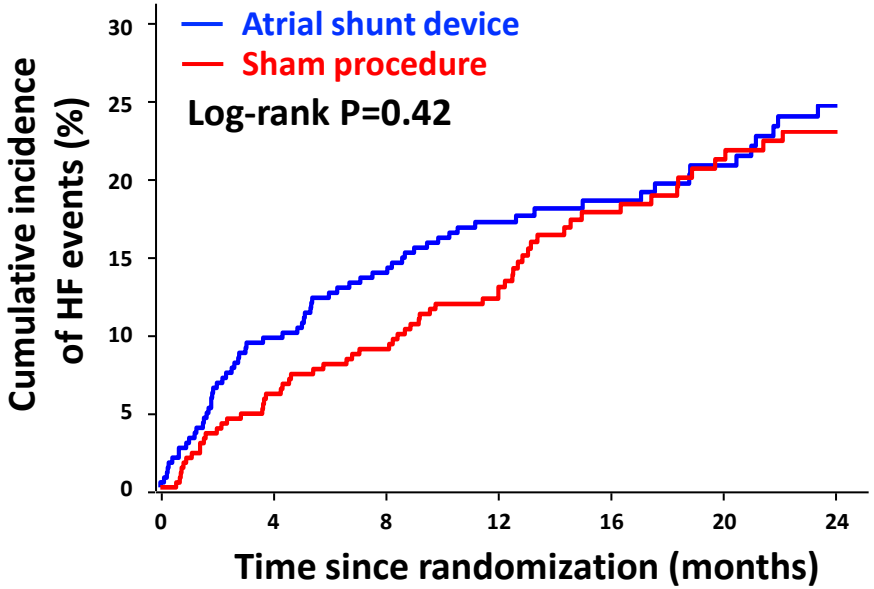
Atrial Shunt device to reduce left atrial hypertension at rest and during exercise in patients with HFpEF/HFmrEF



REDUCE LAP-HF II RCT: Neutral overall result

N=626 with HF, LVEF ≥40%, randomized 1:1 shunt vs. sham. All underwent invasive exercise hemodynamic testing (peak PCWP ≥25 mmHg)





Win ratio: 1.0 (95% 0.8-1.2)

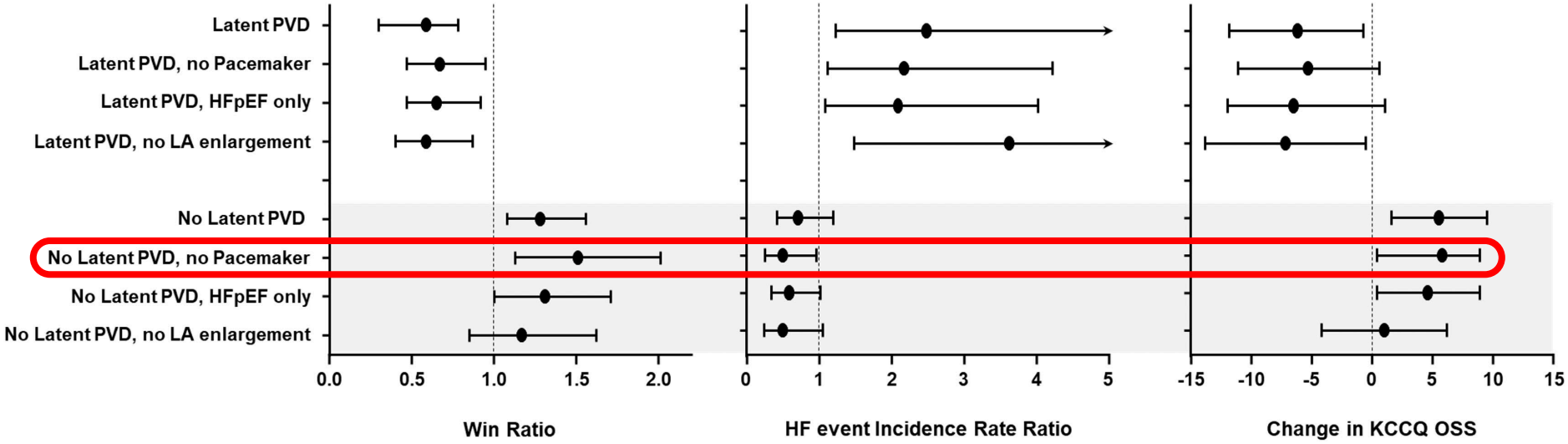
Finkelstein-Schoenfeld p-value=0.85

Shah SJ, et al. Lancet 2022

REDUCE LAP-HF II RCT: Subgroup analysis

N=626 with HF, LVEF ≥40%, randomized 1:1 shunt vs. sham. All underwent invasive exercise hemodynamic testing (peak PCWP ≥25 mmHg)

Latent PVD = peak exercise PVR ≥1.74 WU



Borlaug BA, …Shah SJ. Circulation 2022

Aims and methods (1)

- **To determine** if safety and efficacy signals seen at 1 year of follow-up were maintained during longer-term follow-up (2 years)
- **To test** the hypothesis that the efficacy of the Corvia Atrial Shunt observed in the previously identified ”responder group” was maintained after two years
- Unchanged **primary endpoint**: hierarchical composite of CV death or non-fatal ischemic stroke, rate of total heart failure events, time to first event, and change in Kansas City Cardiomyopathy Questionnaire (KCCQ) overall summary score.
  - ⇢ Finkelstein-Schoenfeld hierarchical analysis with win ratio calculation
- Stratified by “**responder group**” (50% of the of the overall population), defined as:
  - ⇢ Baseline peak exercise PVR < 1.74 WU
  - ⇢ Absence of cardiac rhythm management device

Aims and methods (2)

- **Key inclusion criteria:**
  - ⇢ Age >40 years
  - ⇢ Symptomatic HF with LVEF ≥40%
  - ⇢ PCWP during exercise of ≥25 mmHg and PCWP-RA pressure ≥5 mmHg
- **Key inclusion criteria:**
  - ⇢ Stage D HF or cardiac index <2.0 L/min/m²
  - ⇢ Previous documented LVEF <30%
  - ⇢ Greater than mild RV dysfunction
  - ⇢ Resting RA pressure >14 mm Hg
  - ⇢ Pulmonary vascular resistance (PVR) >3.5 Wood units at rest

Baseline characteristics

Patient Characteristics	Atrial shunt (N=309 Patients)	Sham control (N=312 Patients)
Age (years)	71.3±8.4	71.1±8.7
Male	36%	41%
BMI (kg/m^2)	32.3±6.5	32.5±6.0
Hypertension	89%	87%
Diabetes	37%	37%
COPD	20%	17%
Ischemic Heart Disease	13%	19%
Atrial Fibrillation	50%	53%
Stroke	7%	8%
NYHA II/III/IV (%)	22% / 77% / 1%	20% / 78% / 2%
LVEF (%)	53.4±5.8	52.7±6.0
Loop Diuretics	83%	81%
HF hospitalization/ER visit within prior 12 mo.	44%	43%

Efficacy results: Overall cohort

Primary endpoint at 2 years: Win ratio 1.01 (0.82-1.24); p=0.930

Components of the primary endpoint	Atrial shunt (N=309 Patients)	Sham control (N=312 Patients)	P-value
CV death	13 (4.4%)	7 (2.3%)	0.18
Non-fatal ischemic stroke	5 (1.7%)	1 (0.3%)	0.10
HF events	0.24	0.22	0.63
Change in KCCQ overall summary score (baseline to 24 months)	12.1±22.9	9.0±21.2	0.078

Safety results: Overall cohort

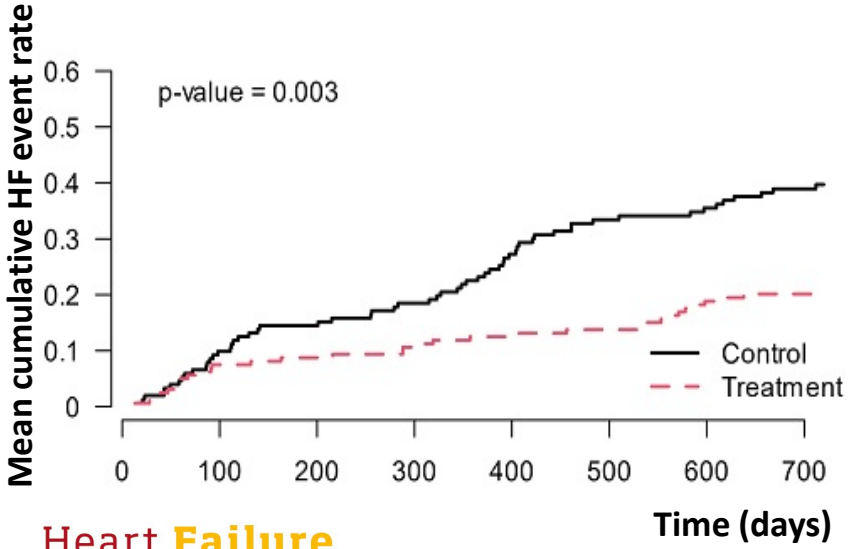
Safety endpoint	Atrial shunt (N=309 Patients)	Sham control (N=312 Patients)	P-value
Cardiovascular Death	4.3%	2.3%	0.19
Non-fatal Ischemic Stroke	1.6%	0.3%	0.14
Major Vascular or Bleeding Complication	4.3%	0.0%	—
New Onset or Worsening of Kidney Dysfunction	9.2%	11.6%	0.33
MACE	6.9%	2.7%	0.018
Cardiac Death	3.9%	2.0%	0.17
Myocardial Infarction	2.0%	1.0%	0.33
Thrombo-embolic Complications	1.0%	0.3%	0.34
TIA	1.0%	0.3%	0.34
Systemic Embolic Events	0.0%	0.0%	—
Newly Acquired Persistent or Permanent Atrial Fibrillation or Atrial Flutter	2.3%	2.7%	0.78
≥30% Increase in RV Size/Decrease in TAPSE	38.7%	27.8%	0.005
≥30% Increase in RV Size	37.1%	23.2%	<0.001
≥30% Decrease in TAPSE	2.0%	5.0%	0.051

Outcomes at 2 years stratified by responders vs. non-responders

Responder group

Peak exercise PVR <1.74 WU, *and* no cardiac rhythm management device

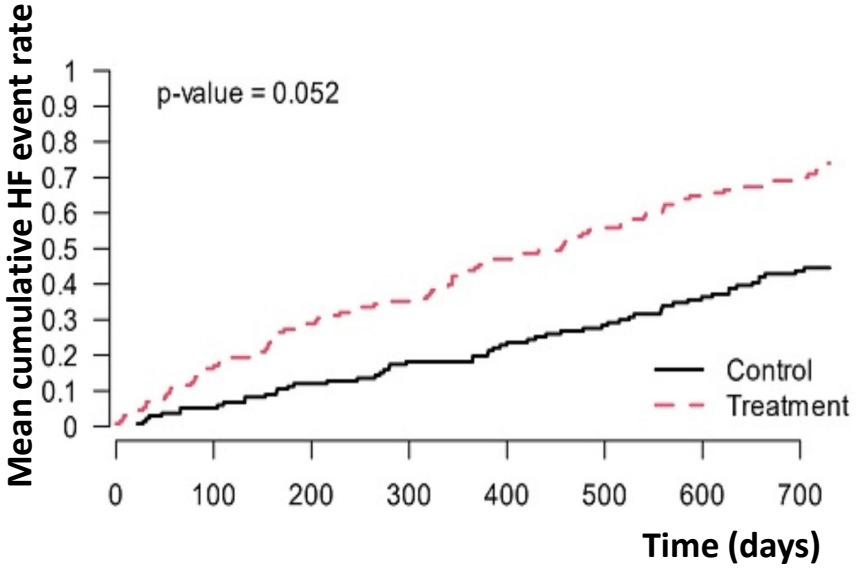
Win ratio: 1.36 (95% CI 1.02-1.83)
P=0.039



Non-responder group

(Peak exercise PVR ≥1.74 WU, *or* cardiac rhythm management device)

Win ratio: 0.73 (95% CI 0.53-1.01)
P=0.055



Conclusions

- In the REDUCE LAP-HF II trial the effect of the Corvia Atrial Shunt on the composite of CV death, non-fatal ischemic stroke and HF events remained neutral in the overall population
- Overall safety of the Corvia atrial shunt at 2 years was demonstrated
- At 2 years the positive effect of the shunt on the primary endpoint in the previously described “responder-group” persisted as did the trend towards worse outcome in the non-responder group.
- These findings support that future trials should examine the effect of atrial shunting in HF patients free from latent pulmonary vascular disease (exercise PVR ≥1.74 WU) and cardiac rhythm management devices (RESPONDER-HF trial, NCT05425459)