Atrial fibrillation and cardiac rhythm device therapy and therapeutic efficacy of atrial shunt treatment in HFpEF and HFmrEF: Results from the REDUCE LAP-HF II Trial

Mark C Petrie, Barry Borlaug, Don Cutlip, Jan Komtebedde, Dirk van Veldhuisen, Scott Solomon, Marty Leon, Thomas Gorter, Finn Gustafsson, Vivek Reddy, Vijay Swarup, Sanjiv Shah on behalf of the REDUCE LAP II Investigators

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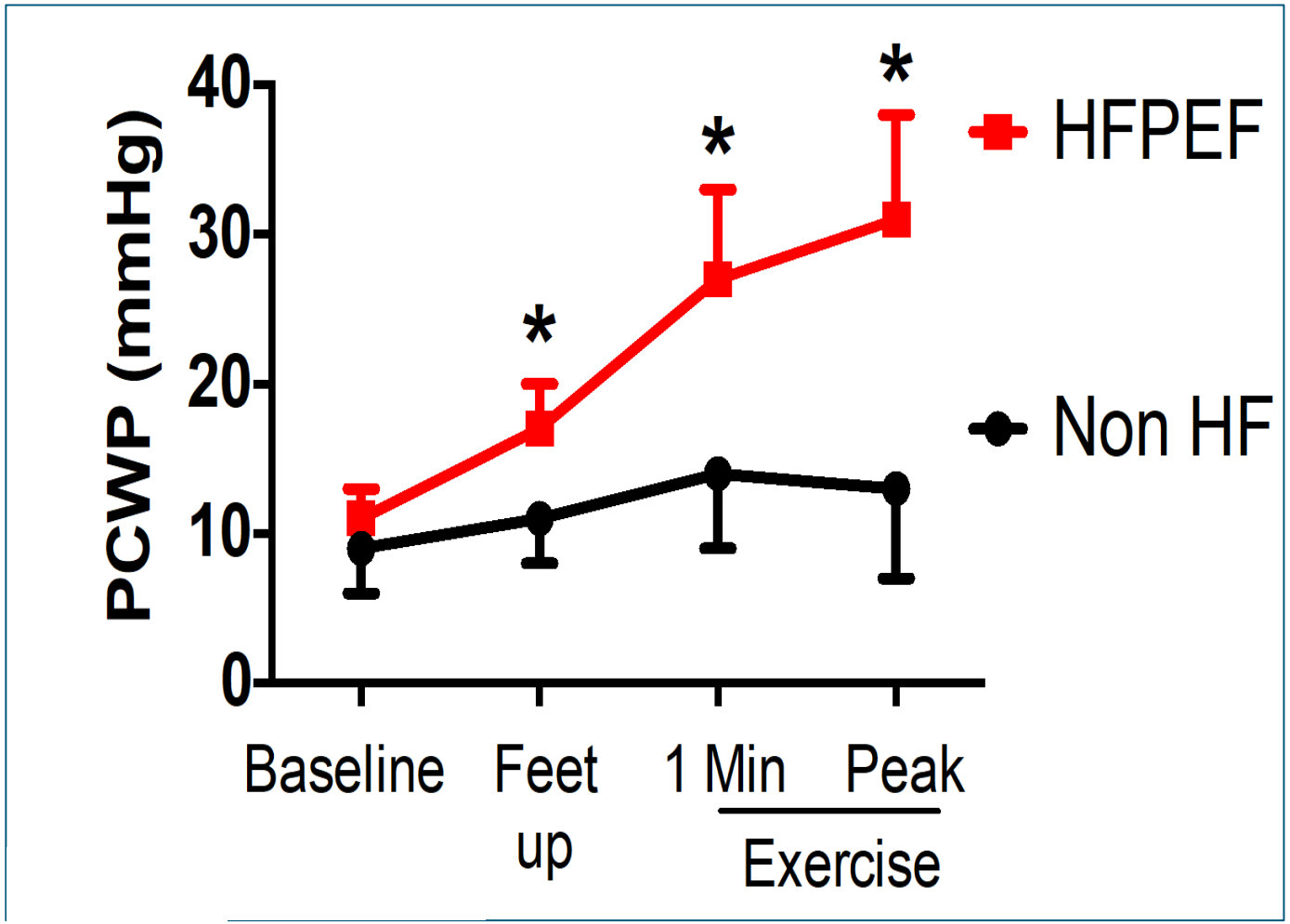
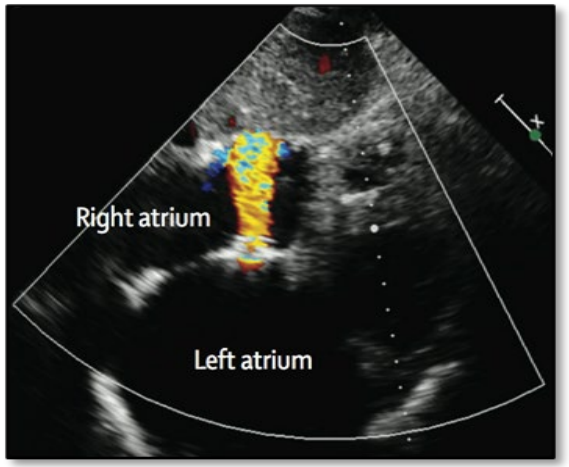
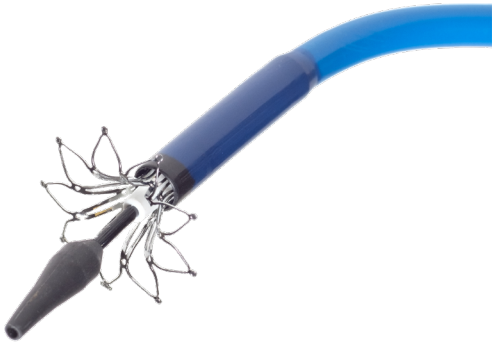
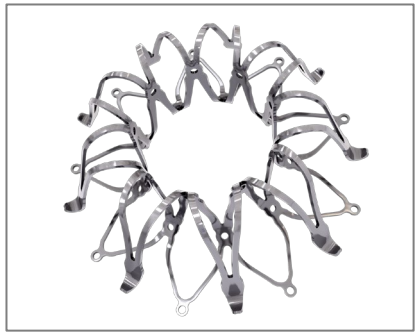
University of Glasgow

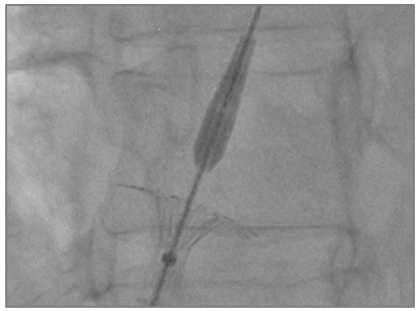
Atrial shunts in HFpEF - the concept

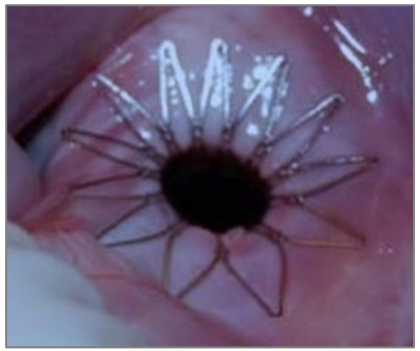












Circ Heart Failure 2010 Sep;3(5):588-95

Studies and trials with the Corvia Atrial Shunt

- Pilot study (N=11)
- Observational study: REDUCE-LAP-HF (N=64)
- Feasibility RCT: REDUCE LAP-HF I (N=44)
- Pivotal RCT: REDUCE LAP-HF II (N=626)

2012

2020

Lancet 2016 Mar 26;387(10025):1298-304

Circulation 2018 Jan 23;137(4):364-375

REDUCE LAP-HF II – design

626 patients

Inclusion criteria

- LVEF ≥40%
- Exercise PCWP ≥25mmHg (and ≥RAP by 5mmHg)

Major exclusion criteria

- Resting RAP >14 mmHg
- PVR >3.5 (rest or peak exercise)
- Mild or more RVSD
- Moderate or more TR
- Previous stroke, TIA, DVT or PE

Randomized to Corvia Atrial Shunt (n=314) or Sham Control (n=312)

Hierarchical primary efficacy endpoint:

- CV death or non-fatal ischemic stroke at 12 months
- Rate of total heart failure events up to 24 months
- Change in KCCQ OSS at 12 months

Patients and assessors masked to randomized therapy for 24 months

Lancet. 2022 Mar 19;399(10330):1130-1140

REDUCE LAP-HF II – main results

No difference in the primary endpoint (or its components)

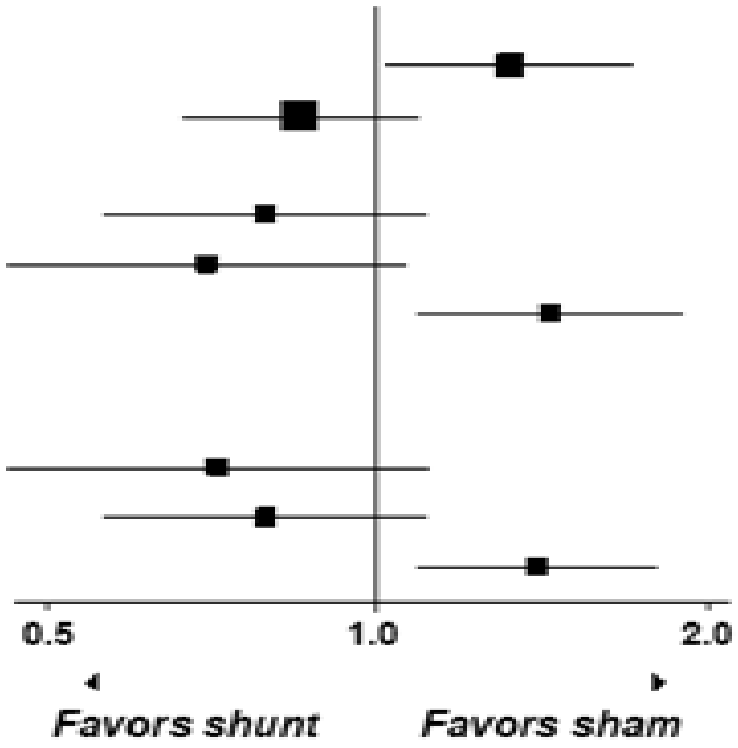
	Atrial Shunt Device (n=309)	**Sham Control** (n=312)	**p-Value**
Primary Endpoint			
Finkelstein-Schoenfeld statistic, T (SE)	-780 (3998)	-	0.85
Probability of favourable distribution (95% CI)	0.50 (0.46 to 0.54)	-	-
Win ratio (95% CI)	1.0 (0.8 to 1.2)	-	-
Components of the primary endpoint or secondary endpoints			
Incidence of time-to-cardiovascular death or non-fatal ischaemic stroke at 12 months	1% (4 events)	1% (2 events)	0.41
Cardiovascular Death	1% (3 events)	1% (2 events)	0.65
Non-fatal Ischaemic Stroke	<1% (1 event)	0	0.32
Total rate (first plus recurrent) per patient-year of heart failure events	0.28	0.25	0.45
Median change in KCCQ-OSS from baseline to 12 months (IQR)	10.2 (-1.8 to 26.8)	9.4 (-2.1 to 22.9)	0.73

Lancet. 2022 Mar 19;399(10330):1130-1140

REDUCE LAP-HF II – main results

Patients in highest tertile for both PAP at 20W and RAVI, and men appeared to have more total HF events with IASD v sham

Subgroup	N	IRR (95% CI)	$P_{interaction}$
Sex			0.020
• **Male**	**239**	**1.32 (1.01-1.71)**	
• Female	382	0.85 (0.55-1.09)	
RA volume index			0.012
• Tertile 1	167	0.79 (0.57-1.11)	
• Tertile 2	168	0.70 (0.46-1.07)	
• **Tertile 3**	**168**	**1.43 (1.08-1.90)**	
PA systolic pressure at 20W			0.002
• 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)**	



Lancet. 2022 Mar 19;399(10330):1130-1140

REDUCE LAP-HF II – outcomes by latent PVD (post hoc)

Subgroup	Variable	Statistic	Atrial Shunt	Sham Control	Win ratio	P-value
No latent PVD (exercise PVR<1.74) N=381	Primary efficacy endpoint	Win ratio	-	-	Favours IASD 1.31 (1.02, 1.68)	0.038
	HF event	Rate per person year	0.17	0.23	-	0.103
	Change in KCCQ OSS at 12 months	Mean+/-SD	14.6 ± 21.4	9.2 ± 20.7	-	0.010
Latent PVD (exercise PVR≥1.74) N=187	Primary efficacy endpoint	Win ratio	-	-	Favours Sham 0.60 (0.42, 0.86)	0.005
	HF event	Rate per person year	0.47	0.25	-	0.02
	Change in KCCQ OSS at 12 months	Mean+/-SD	4.1 ± 20.4	9.9 ± 19.8	-	0.027

Circulation. 2022 Mar 31. doi: 10.1161/CIRCULATIONAHA.122.059486

REDUCE LAP-HF II – CRD/ no CRD

Baseline characteristics

CRD = Cardiac rhythm device (PPM or CRTP/D)

	No CRD (n=510)	CRD (n=116)	p
Age (years)	72	74	0.03
Men (%)	37	46	0.08
Obesity (%)	63	52	0.02
Diabetes (%)	39	28	0.04
AF or flutter (%)	47	81	<0.001
Loop diuretics (%)	82	84	0.64
LVEF (%)	55	50	<0.001
LV mass (g)	158	181	0.004
Moderate or more TR (%)	11	24	<0.001
RAVI (ml/m^2)	24	33	<0.001
RAP rest	9	10	0.004
PVR (peak exercise)	1.3	1.4	0.76

REDUCE LAP HF-II – outcomes by CRD/ no CRD

Subgroup	Variable	Statistic	Atrial Shunt	Sham Control	Rate Ratio	Win Ratio	P-value
No CRD N=504	Primary efficacy endpoint	Win ratio	-	-	-	1.13 (0.91, 1.40)	0.23
	HF event	Rate per person year	0.26	0.27	1.06 (0.66, 1.71)	-	0.81
	Change in KCCQ OSS at 12 months	Mean+/-SD	11.3 (-2.3, 27.3)	8.3 (-2.6, 22.1)	-	-	0.32
CRD N=115	Primary efficacy endpoint	Win ratio	-	-	-	0.63 (0.40, 1.01)	0.05
	HF event	Rate per person year	0.40	0.23	2.19 (1.00, 4.75)	-	0.05
	Change in KCCQ OSS at 12 months	Mean+/-SD	7.7 (-0.4, 20.3)	10.7 (-1.8, 23.2)	-	-	0.71

REDUCE LAP-HF II – SR v AF/AFL (without CRD)

Baseline characteristics

	SR (n=270)	AF/ AFL (n=240)	p
Age (years)	70	74	<0.001
Men (%)	31	43	0.008
Obesity (%)	66	59	0.10
Diabetes (%)	41	36	0.30
Loop diuretics (%)	82	82	0.86
LVEF (%)	55	55	0.09
LV mass (g)	153	164	0.002
Moderate or more TR (%)	5	15	<0.001
RAVI (ml/m^2)	21	29	<0.001
RAP rest	9	9	0.15
PVR (peak exercise)	1.1	1.5	<0.001

REDUCE LAP-HF II – outcomes by SR v AF/AFL (without CRD)

Subgroup	Variable	Statistic	Atrial Shunt	Sham Control	Rate Ratio	Win Ratio	P-value
SR N=266	Primary efficacy endpoint	Win ratio	-	-	-	1.27 (0.93, 1.72)	0.10
	HF event	Rate per person year	0.17	0.22	0.77 (0.36, 1.65)	-	0.51
	Change in KCCQ OSS at 12 months	Mean+/-SD	14.3 (0.2, 31.3)	10.2 (-0.5, 26.6)	-	-	0.44
AF or AFL N=238	Primary efficacy endpoint	Win ratio	-	-	-	0.95 (0.70, 1.29)	0.74
	HF event	Rate per person year	0.33	0.29	1.33 (0.72, 2.45)	-	0.36
	Change in KCCQ OSS at 12 months	Mean+/-SD	7.0 (-4.9, 22.9)	6.5 (-6.3, 18.5)	-	-	0.65

REDUCE LAP-HF II – outcomes by SR v AF/AFL (without CRD)

In those with PVR<1.74

Subgroup	Variable	Statistic	Atrial Shunt	Sham Control	Rate Ratio	Win Ratio	P-value
SR N=180	Primary efficacy endpoint	Win ratio	-	-	-	1.45 (1.00, 2.11)	0.036
	HF event	Rate per person year	0.10	0.20	0.46 (0.19, 1.11)	-	0.084
	Change in KCCQ OSS at 12 months	Mean+/-SD	16.4 (2.5, 35.2)	10.0 (1.4, 25.5)	-	-	0.14
AF or AFL N=132	Primary efficacy endpoint	Win ratio	-	-	-	1.50 (0.98, 2.31)	0.064
	HF event	Rate per person year	0.16	0.25	0.54 (0.20, 1.48)	-	0.24
	Change in KCCQ OSS at 12 months	Mean+/-SD	11.4 (-1.2, 26.8)	4.7 (-7.8, 16.1)		-	0.033

Conclusion

- In the overall REDUCE LAP-HF II trial there was no benefit of the Corvia Atrial Shunt
- Patients with a peak exercise PVR <1.74 without cardiac rhythm devices (about 50% of patients enrolled in the trial) appeared to benefit from the Corvia Atrial Shunt.
- Further trials are planned to investigate the role of the Corvia Atrial Shunt in this population