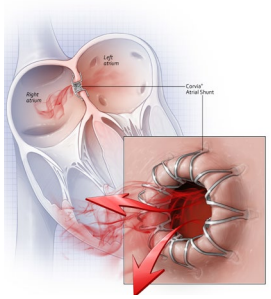
Effects of Atrial Shunt Treatment in Women versus Men with HFpEF and HFmrEF: Results from the REDUCE LAP-HF II Trial

Carolyn Lam; David Kaye; Gerd HasenFuß; John Cleland; Donald Cutlip; Mark Petrie; Dirk van Veldhuisen; Scott Solomon; Elke van Hoendermis; Maja Cikes; Elizabeth Junamon; Bharathi Upadhya; Rhondalyn Forde-McLean; Shelley Hall; Amanda Vest; Sula Mazimba; Melissa Smallfield; Vanessa Van Empel; Michele McGrady; Catherine Demers; Christina Paitazoglou, Jan Komtebedde; Martin Leon, Sanjiv Shah

Purpose

In the REDUCE LAP-HF II trial (n=626 patients with heart failure [HF], ejection fraction [EF] ≥40%, and exercise pulmonary capillary wedge pressure [PCWP] ≥25mm Hg, there was no overall difference in outcomes between patients treated with the Corvia Atrial Shunt vs. sham control.



However, specific subgroups of patients did better with the device, including women and those with smaller right atria, lower pulmonary artery systolic pressure at 20W and lower peak exercise pulmonary vascular resistance (PVR), and those without cardiac rhythm device.

We sought to further examine the differences in baseline characteristics and response to atrial shunt treatment between the sexes among all patients randomized in the REDUCE LAP-HF II trial, and within specific subgroups.

Methods

- Primary endpoint: hierarchical composite of CV death or non-fatal ischemic stroke at 12 months, rate of total HF events up to 24 months, and change in KCCQ overall summary score at 12 months; summarized by win ratio
- Negative binomial regression for recurrent HF events
- Linear regression (adjusting for baseline value) for change in KCCQ

Results

- Despite similar resting & peak exercise PCWP & PVR, women had worse KCCQ, smaller LA, RA & RV volumes (indexed to BSA), and better strain for all 4 cardiac chambers compared to men.

In response to atrial shunt treatment:

- For the primary outcome, the win ratio [95% CI] was similar in women and men (1.03 [0.80, 1.32] vs. 0.95 [0.69, 1.30]).
- For recurrent HF events, women did better than men (0.77 [0.45, 1.31] vs. 2.19 [1.21, 3.95]; interaction P=0.02).
- Within subgroups (peak exercise PVR <1.74 WU, right atrial volume index <29.7 ml/m^2, no cardiac rhythm device), there were no significant sex differences in response to atrial shunt treatment ($P_{interaction}$>0.10 for sex in all subgroups and for all outcomes).

	Baseline Characteristics	Women (n=385)	Men (n=241)	P value
Clinical	Age (years)	71.1±8.8	71.5±8.1	0.496
	Hypertension	85.9% (329/383)	92.1% (222/241)	0.021
	Diabetes	29.9% (115/385)	47.7% (115/241)	<.001
	Ischemic Heart Disease	9.9% (38/383)	26.1% (62/238)	<.001
	Permanent Pacemaker	16.4% (63/385)	22.0% (53/241)	0.078
	Atrial Fibrillation	46.0% (177/385)	61.0% (147/241)	<.001
	HF hospitalization in past 12 mo	25.2% (91/361)	35.2% (80/227)	0.012
Cardiac Structure/Function	LVEF (%)	61±7 (384)	58±8 (240)	<.001
	LA volume index (ml/m^2)	32.5±12.8 (352)	36.6±15.6 (216)	0.001
	RV volume index (ml/m^2)	21.5±8.6 (272)	27.6±11.0 (159)	<.001
	RA volume index (ml/m^2)	25.6±11.8 (311)	31.9±14.1 (195)	<.001
	LV GLS (%)	18.4 (16.1,20.7)	16.8 (14.2,18.8)	<0.001
	LA reservoir strain (%)	20.7 (15.1,27.7)	18.1 (13.0,25.1)	0.002
	RA reservoir strain (%)	25.1 (18.9,33.0)	21.0 (16.5,27.6)	<0.001
	RV free wall strain (%)	23.7 (18.9,26.9)	20.4 (16.5,24.3)	<0.001
	PASP (mmHg)	31.0 (26.0,38.0)	32.0 (26.0,39.0)	0.607
Hemodynamics	Rest PCWP (mmHg)	17.0 (14.0,23.0)	18.0 (14.0,23.0)	0.406
	Rest PVR (Wood units)	1.5 (1.1,2.1)	1.4 (1.1,2.0)	0.403
	Peak exercise PCWP (mmHg)	34.0 (30.0,40.0)	34.0 (28.0,40.2)	0.703
	Peak exercise PVR (Wood units)	1.4 (0.9,2.1)	1.3 (0.8,2.0)	0.237

Conclusions

- In REDUCE LAP-HF II, women had lower comorbidity burden, smaller cardiac chambers, better baseline cardiac function, but similar invasive exercise hemodynamic characteristics and worse baseline quality of life compared to men.
- The sex differences in treatment response were mostly attenuated in key subgroups with lower peak exercise PVR, smaller right atrial volumes and no cardiac rhythm device.