Interatrial Shunts I: Corvia

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Evanston Hospital

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NorthShore
University HealthSystem
Evanston Hospital

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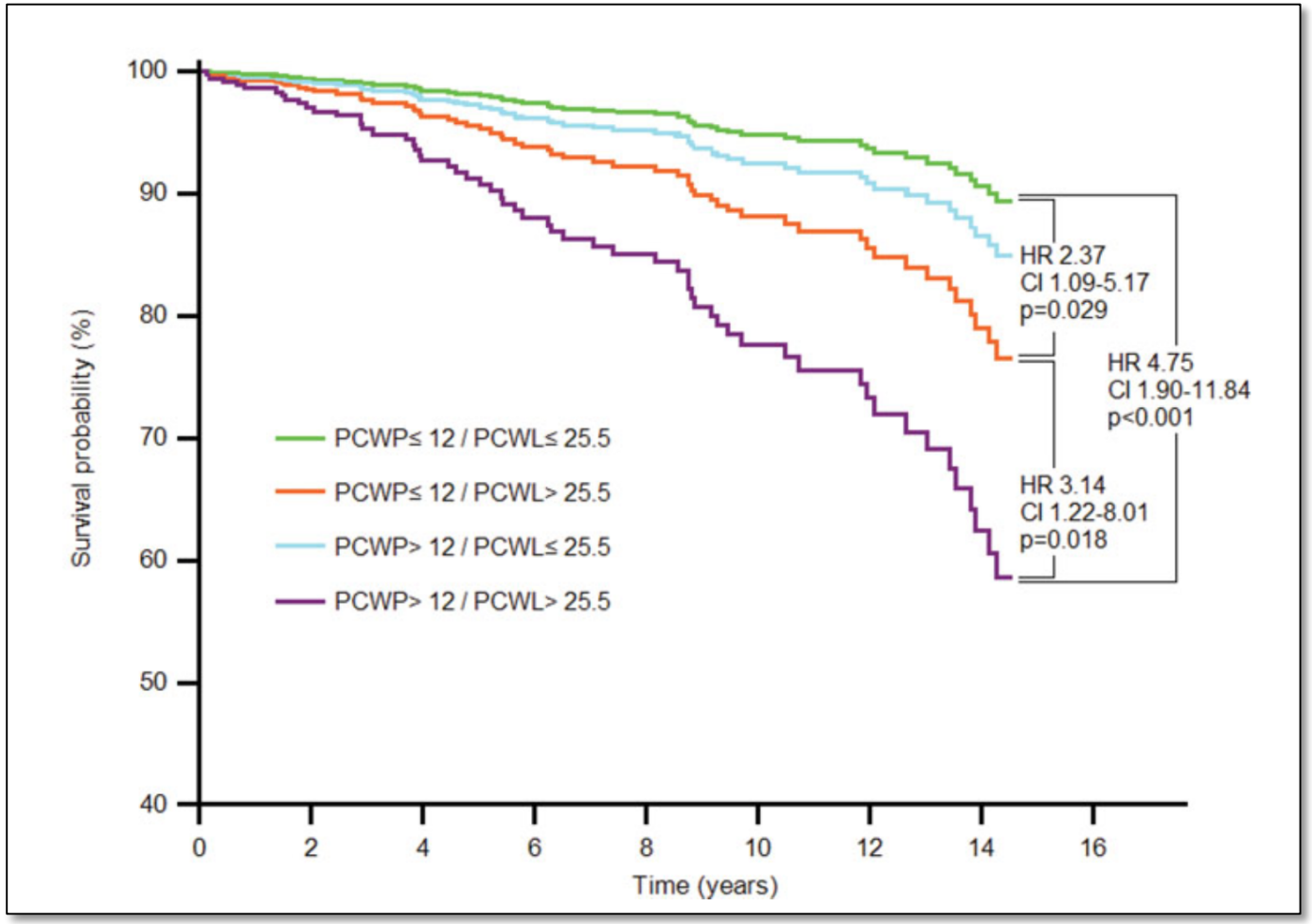
Disclosure Information

The following relationships exist:

Grant support: Abbott, BSC, Corvia, Edwards, WL Gore
Consultant: Abbott, BSC, Edwards, WL Gore
Stock Options: Mitralign, Cardiac Dimensions

Off label use of products and investigational devices will be discussed in this presentation

Pulmonary capillary wedge pressure at rest and during exercise and long-term mortality in patients with dyspnea & suspected HFpEF



European Heart Journal (2014) 35, 3103–3112

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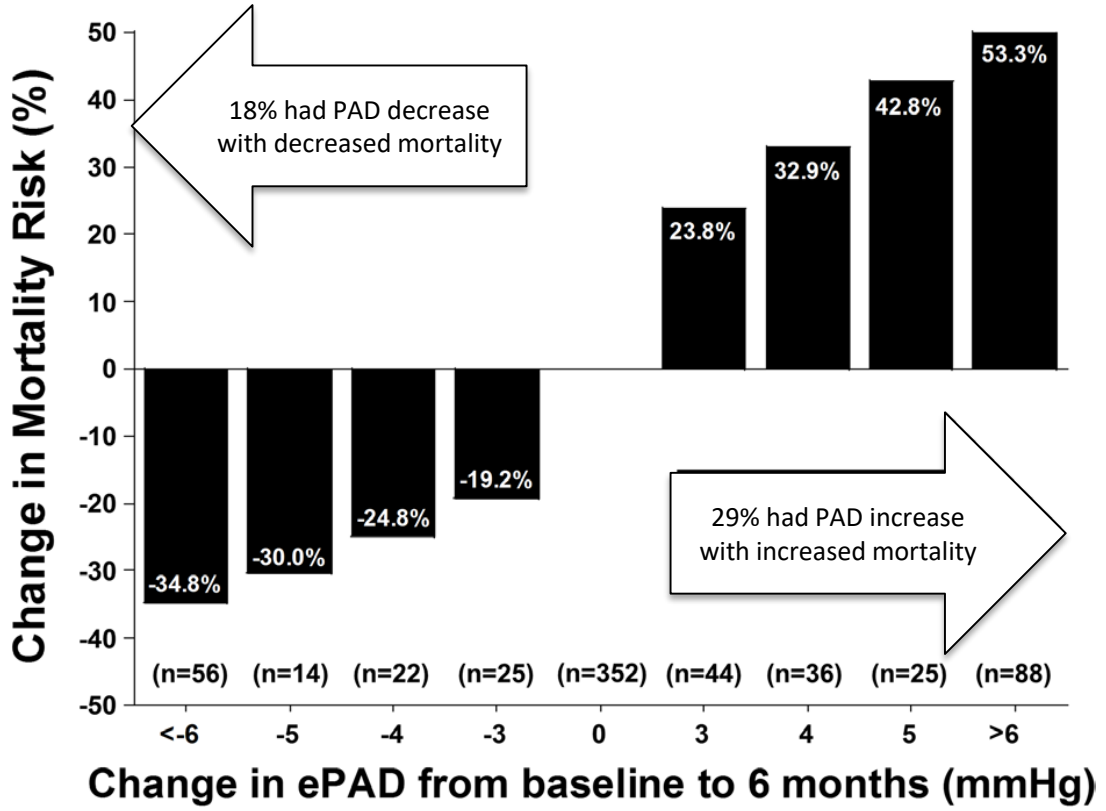
Intracardiac Pressures Measured Using an Implantable Hemodynamic Monitor

Mortality and modest 6 month ePAD changes



n=790

Zile et al. Circ Heart Fail. 2017 Jan;10(1)

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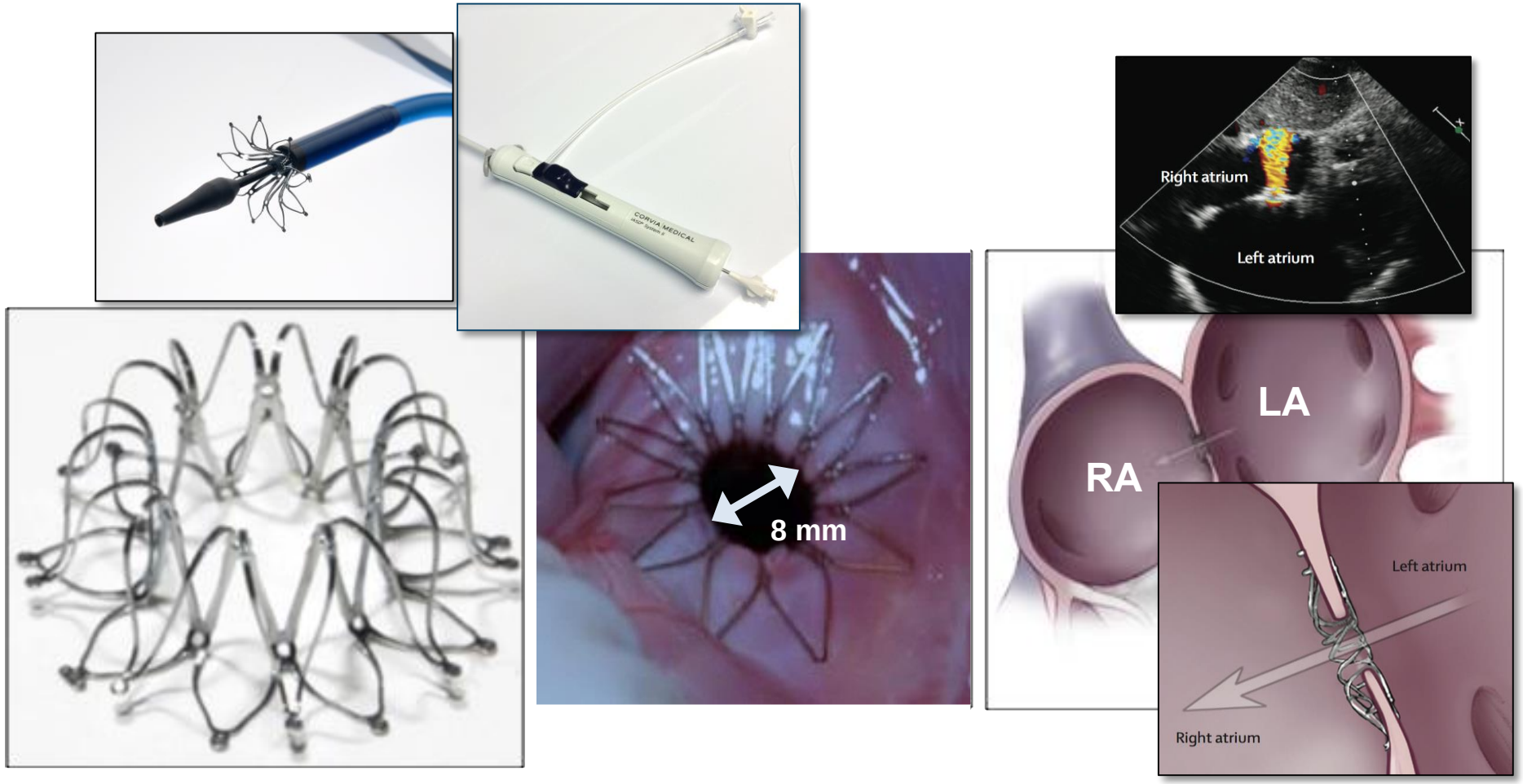
InterAtrial Shunt Device (IASD®) for HFpEF



IASD proposed mode of action: decompresses overloaded LA chamber by shunting blood from LA → RA + systemic veins, particularly during exercise

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Feldman T…Shah SJ: Circ Heart Fail. 2016 Jul;9(7) NCT02600234

Corvia Medical IASD® Clinical Studies

- Pilot study (N=11): non-randomized, single-arm
  - Completed (Søndergaard L, et al. Eur J Heart Fail 2014)
- REDUCE LAP-HF (CE Mark) Study (N=64): non-randomized, single-arm
  - Completed (Hasenfuß Lancet 2016; Kaye Circ. HF 2016)
- REDUCE LAP-HF I (N=44): RCT mechanistic study
  - FDA IDE 30 Day Complete (*Feldman T… Shah SJ. Circulation. 2018;137:364–375)*
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InterAtrial Shunt Device for HFpEF

(REDUCE LAP-HF): multicentre, open-label, single-arm, phase 1 trial

Age, years	69 (8)
Sex	
Men	22
Women	42
NYHA functional class	
II	18
III	46
IV	0
Body-mass index, kg/m²	33 (6)
eGFR, mL/min per 1·73m²	62 (21)
Haemoglobin, g/L	133 (5)
Comorbidities	
Diabetes	21 (33%)
Hypertension	52 (81%)
Atrial fibrillation	23 (36%)
Coronary artery disease	23 (36%)

Echocardiography		
Left ventricular end diastolic volume index, mL/m²	68 (13)	
Left ventricular ejection fraction, %	47 (7)	core lab
Left ventricular mass index, g/m²	119 (36)	
Left arterial diastolic volume index, mL/m²	34 (17)	
Right ventricle diastolic volume index, mL/m²	22 (9)	
Right artery volume index, mL/m²	35 (17)	
E/A ratio	1·3 (0·8)	
E/e' ratio	13·9 (5·9)	
TAPSE, mm	20 (4)	
NT-proBNP, pg/mL	377 (222–925)	
Resting haemodynamics		
Mean right arterial pressure, mm Hg	9 (4)	
Mean pulmonary arterial pressure, mm Hg	25 (7)	
Mean pulmonary capillary wedge pressure, mm Hg	17 (5)	
Cardiac output, L/min	5·5 (1·6)	

N=64

Hasenfuß G: Lancet 2016; 387: 1298–304

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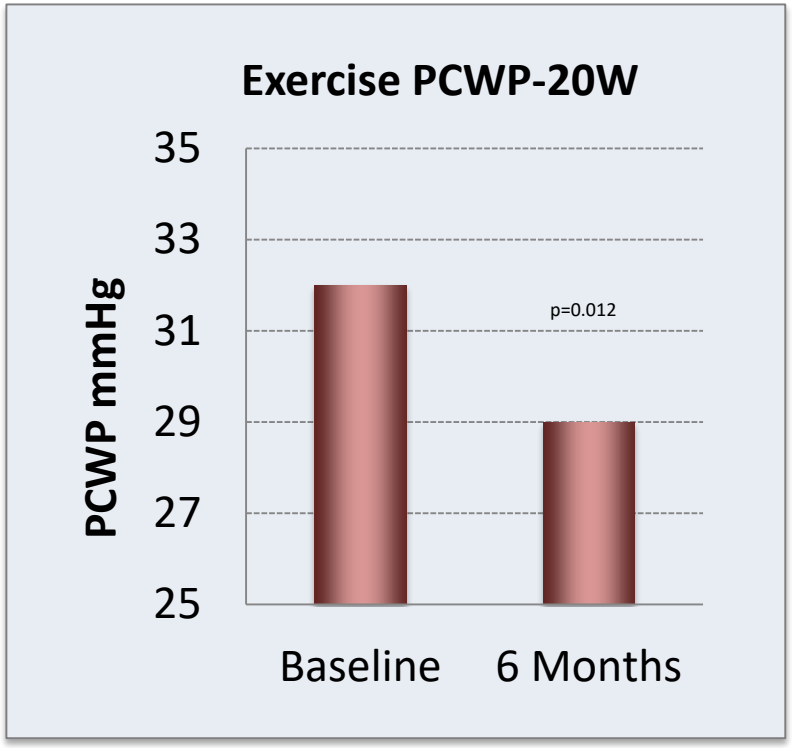
InterAtrial Shunt Device for HFpEF (REDUCE LAP-HF)

multicentre, open-label, single-arm, phase 1 trial



N=64

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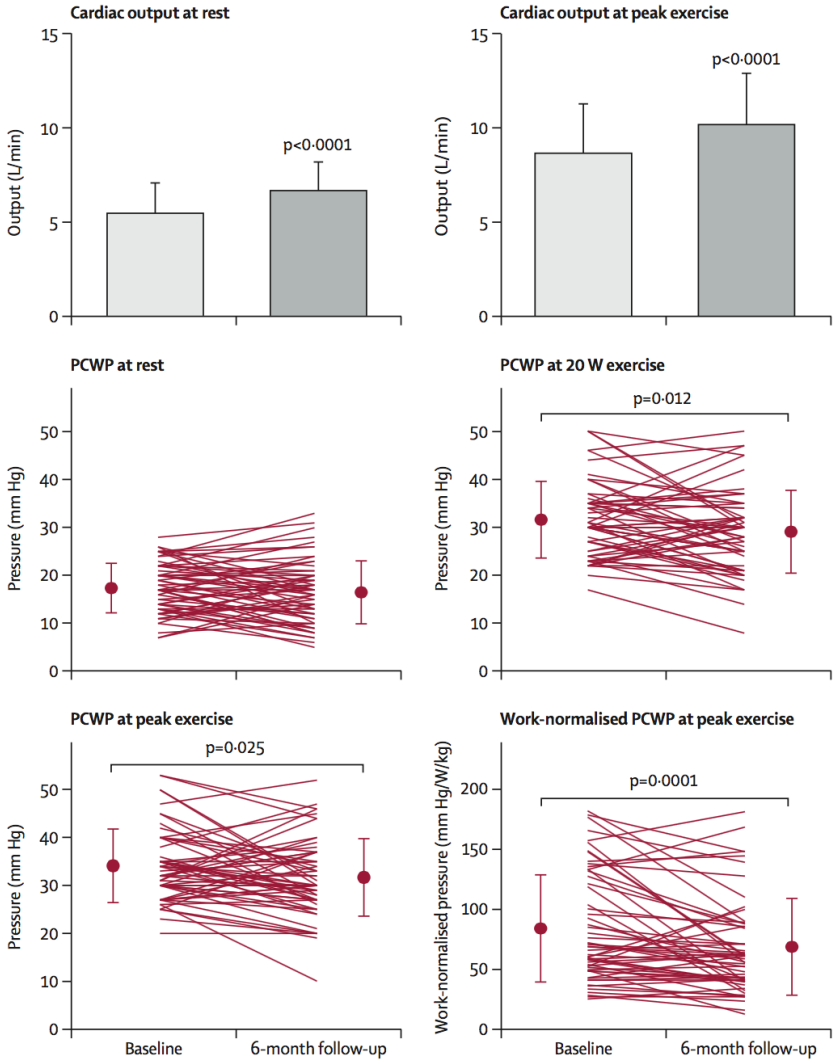

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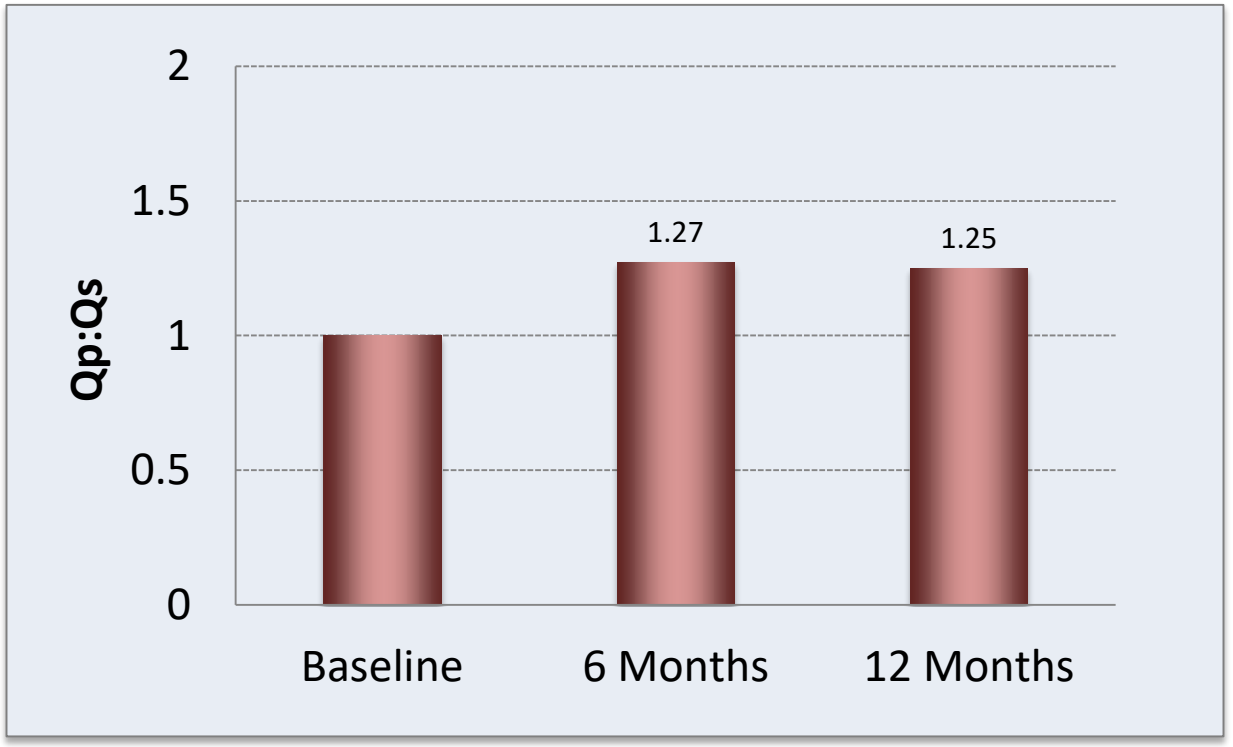
1-Year Outcomes After InterAtrial Shunt Device for HFpEF

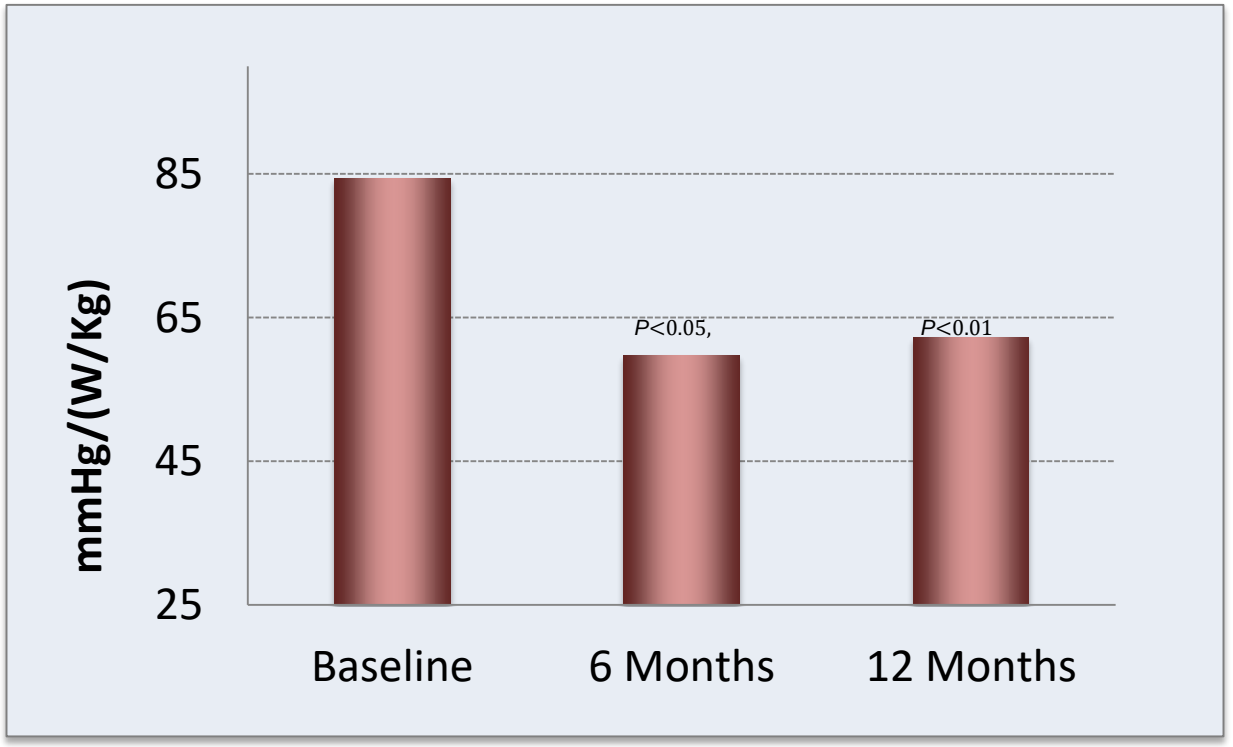
Qp:Qs



REDUCE LAP-HF *Kaye Circ Heart Fail. 2016 Dec;9(12). pii: e003662*

1-Year Outcomes After InterAtrial Shunt Device for HFpEF

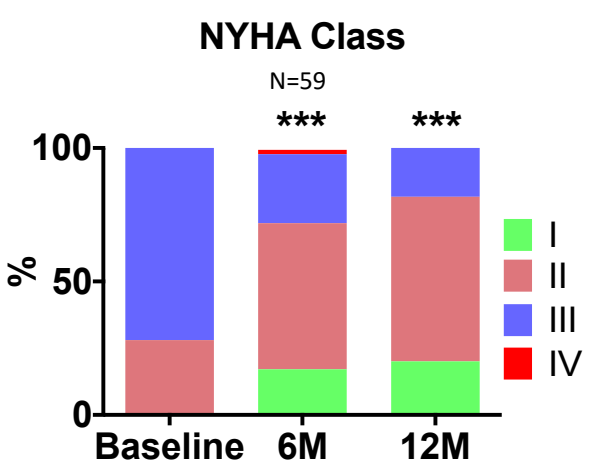
Workload indexed peak exertion wedge pressure



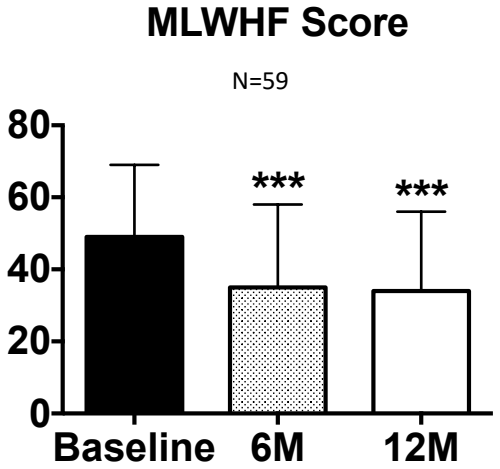
REDUCE LAP-HF *Kaye Circ Heart Fail. 2016 Dec;9(12). pii: e003662*

Sustained Clinical Efficacy

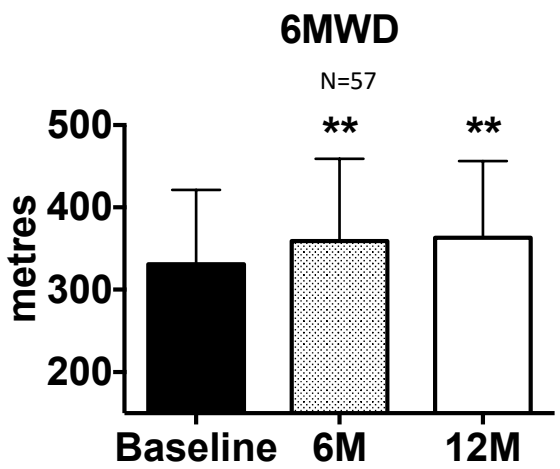
At one year IASD therapy was associated with sustained improvements in NYHA class, quality of life score and six minute walk distance



RM-Friedman's test:
**p<0.01, ***p<0.001



Mean Δ at 1 year: 15 points



Mean Δ at 1 year: 33m

REDUCE LAP-HF *Kaye Circ Heart Fail. 2016 Dec;9(12). pii: e003662*

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REDUCE LAP HF 2 year Outcomes

Outcome measure	@6M	@12M	@24M
Survival	100%	95.3% (61/64)	92.2% (59/64)
All cause mortality	0%	4.7% (3/64)	7.8% (5/64)
HF related mortality	0%	0%	3.1% (2/64)

Total follow up: Median 739 days, 177.2 pt years f/u:

- **6 deaths: = 3.4 deaths/100 yrs (3 HF, 2 non HF, 1 CVA)**
- **42 HFH events in 19 patients**

Kaye D et al: ESC Heart Failure 2018 (in press)

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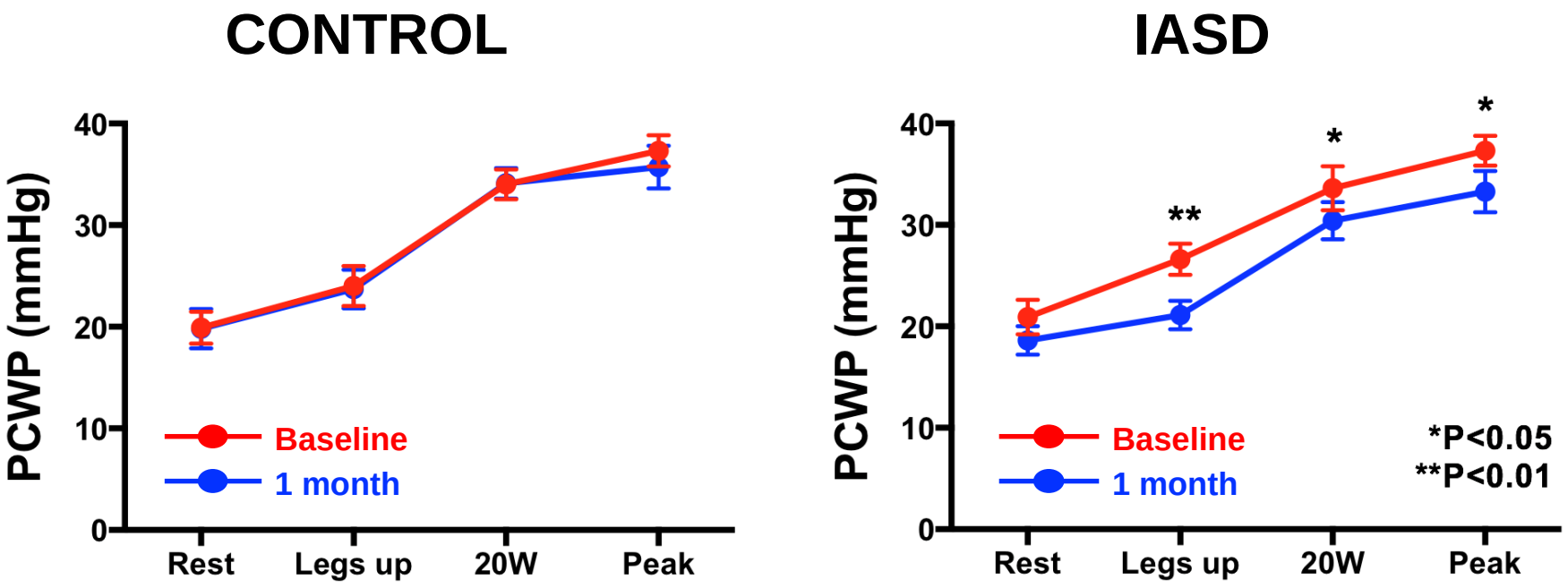
Results: Baseline characteristics (3)

Baseline hemodynamics	IASD	Control	P-value
RA pressure (mmHg)	10.1±2.3	9.1±3.7	0.27
Mean PA pressure (mmHg)	30.2±9.5	28.4±8.6	0.52
Cardiac output (L/min/m^2)	5.4±1.6	5.7±2.7	0.66
Pulmonary vascular resistance (WU)	2.19±1.52	1.74±1.45	0.32
PCWP, legs down (mmHg)	20.9±7.9	19.9±7.5	0.67
PCWP, legs up (mmHg)	26.6±7.1	24.0±9.3	0.32
PCWP, peak exercise (mmHg)	37.3±6.5	37.3±6.7	1.00
PCWP-RAP gradient at rest (mmHg)	10.8±5.6	10.9±7.3	0.95
Exercise duration (minutes)	7.4±3.1	8.9±4.0	0.18
Peak exercise workload (W)	42.3±19.5	41.8±16.2	0.93

REDUCE LAP HF I: Mechanistic RCT

Change in PCWP: Baseline to 1M



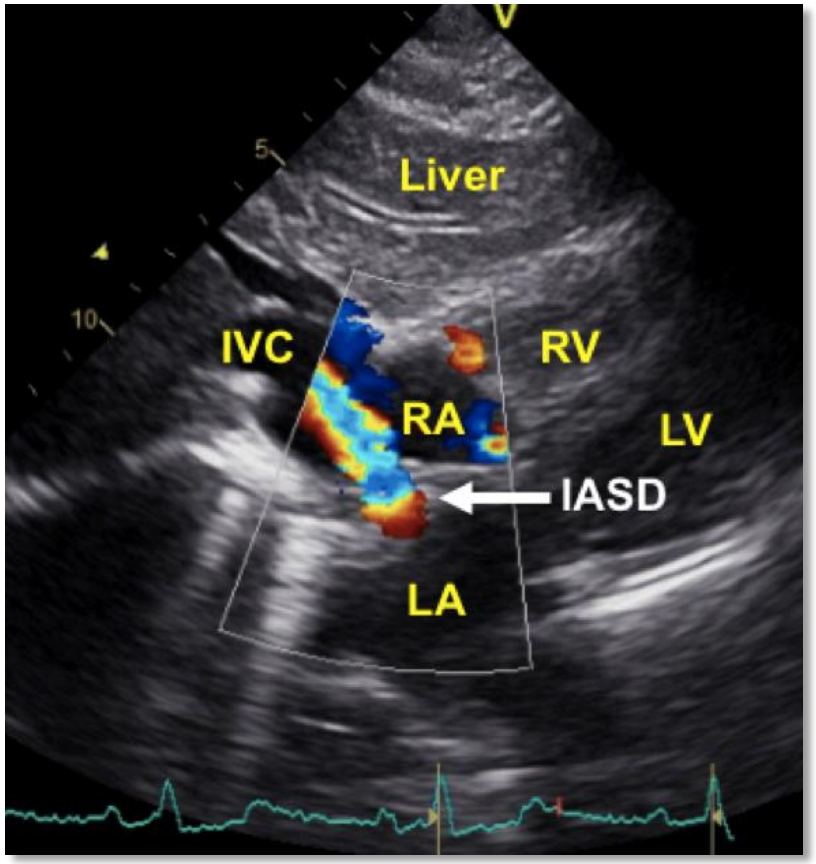
Feldman T… Shah SJ. Circulation. 2018;137:364–375

1 Year Results

Shunt Patency

- At 1 year, shunt patency was documented in all participants who received the IASD and were still alive (n=20)

- There was no evidence through 1 year in the IASD arm vs. control of:
  - Greater increases in number of diuretic medications (p=0.83)
  - Total daily loop diuretic dose (p=0.20)



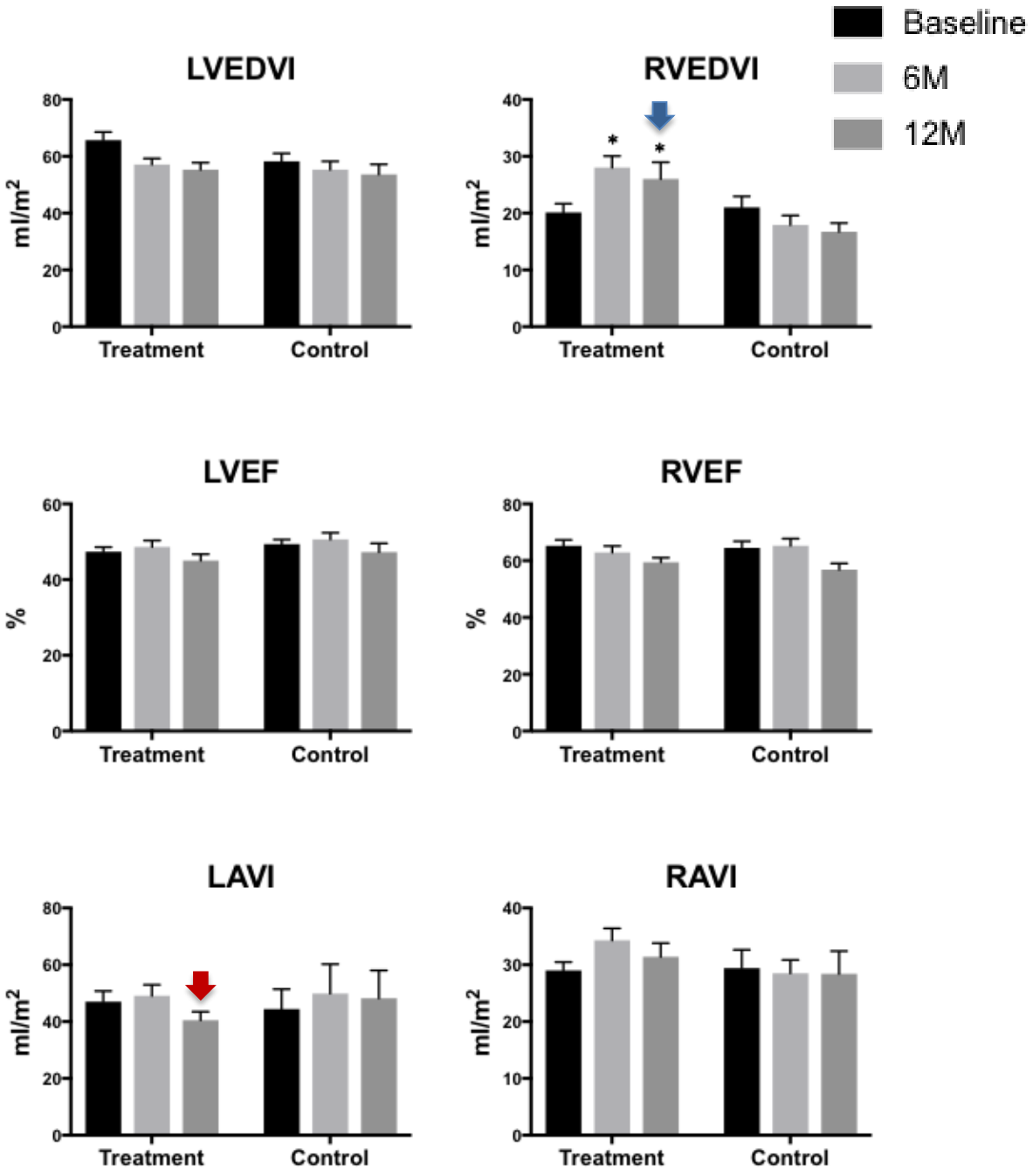
Left-to-Right Shunting Through a Patent IASD at 12 Months in a Study Participant

Baseline, 6-, and 12-Month Echocardiographic Parameters of Cardiac Structure and Function

- No significant change in left heart structure/function

- Trend towards greater reduction in LA volume index in IASD vs. control at 12 months (6.3±10.7 vs. 1.5±14.2 ml/m^2; p=0.078).

- Increase in RVEDV (p=0.01) without any change in RVEF in the IASD arm.



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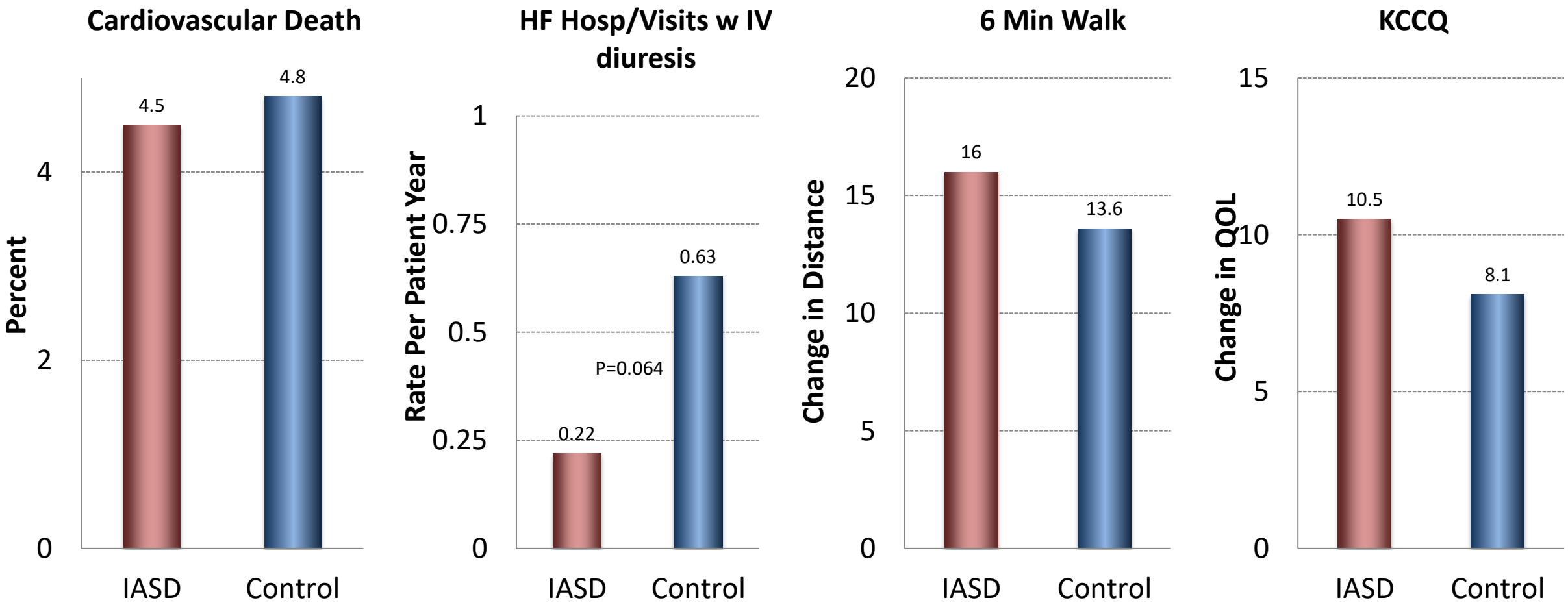
Key Secondary Outcome Measures at 12 Months*



*powered for primary and not for secondary outcome measures

N=39

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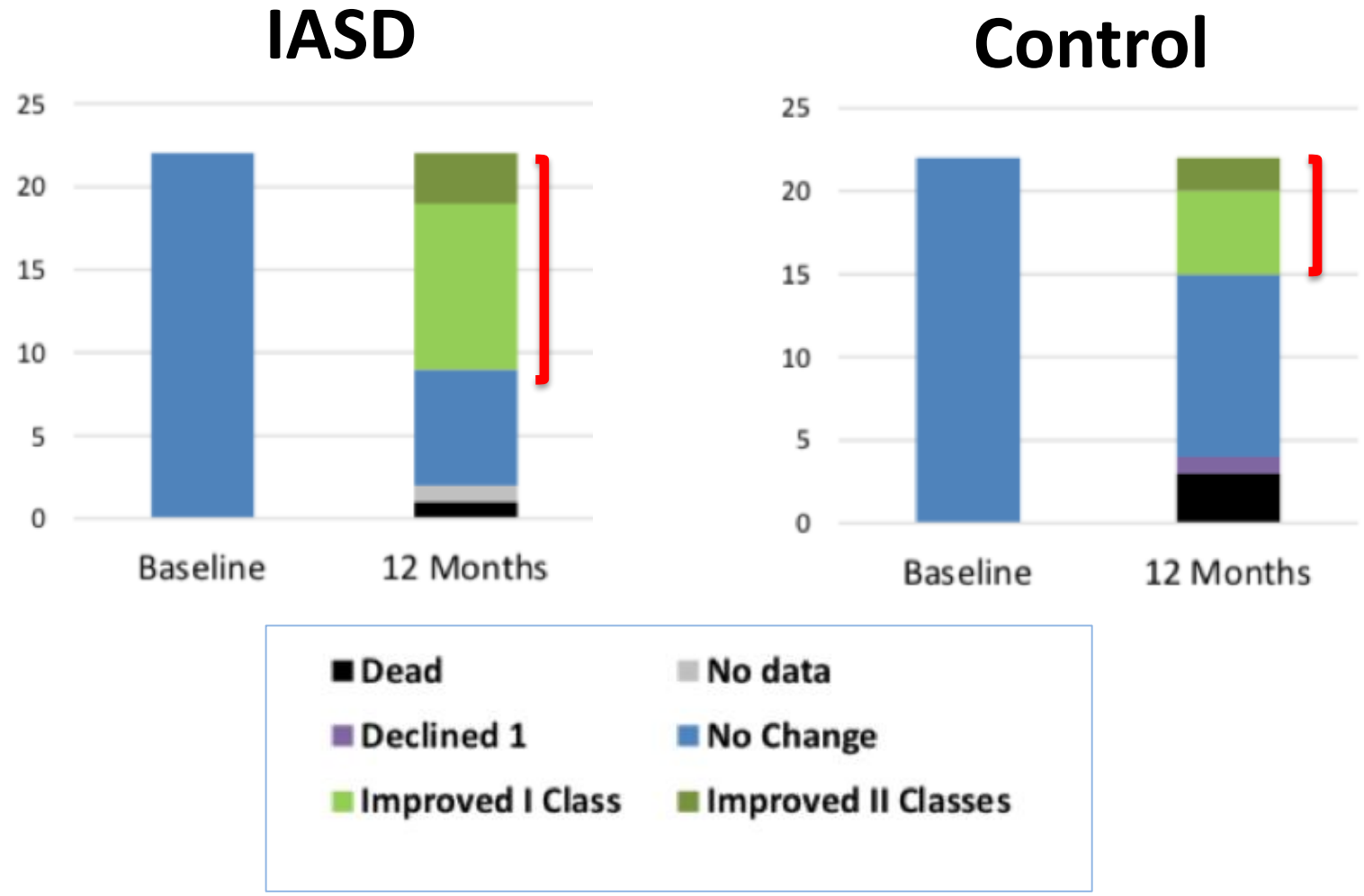
Change in NYHA Functional Class: InterAtrial Shunt Device vs. Sham Control



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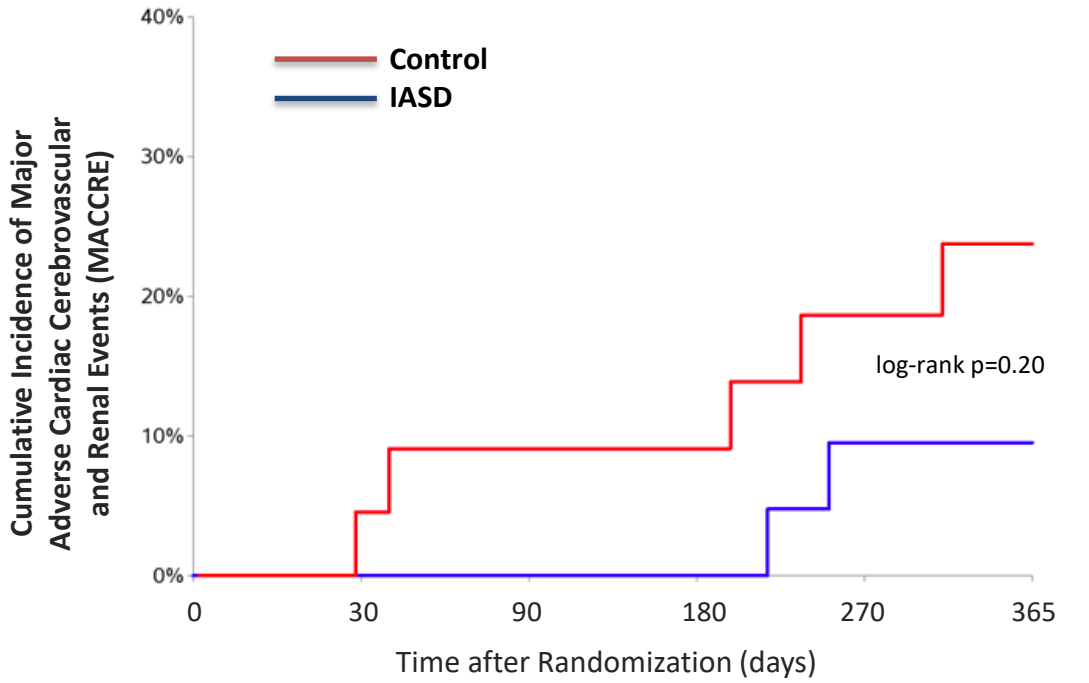
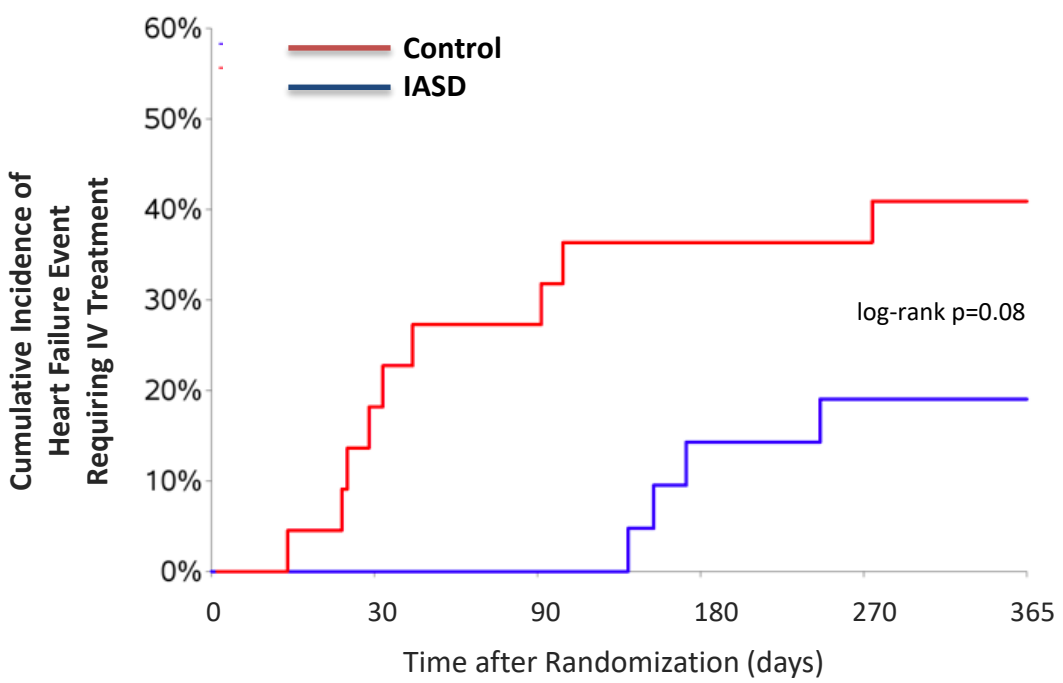
Cumulative Incidence of MACCRE and Heart Failure Events Requiring Intravenous Diuretic Treatment Through 12 Months

MACCRE



No. at risk						
Treatment:	22	21	21	21	21	14
Control:	22	22	21	20	19	12

Heart Failure Events



No. at risk						
Treatment:	22	21	21	21	18	12
Control:	22	22	18	16	14	11

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Consistent Safety Profile across 3 studies

	Pilot study (N=11)	REDUCE LAP-HF (N=64)	REDUCE LAP-HF I (N=22)	Combined (N=97)
1 Year Survival	100%	95.4%	95.2%	95.8%
2 Year Survival	91%	92%	TBD	
3 Year Survival	82%	89%	TBD	
1 Year Freedom from CVA	100%	98.5%	100%	99%
2 Year Freedom from CVA	100%	98.5%	TBD	
3 Year Freedom from CVA	100%	98.5%	TBD	
IASD thrombosis/removal/closure	0%	0%	0%	0%

Consistent & Durable Efficacy across 3 studies

	Pilot study (N=11)	REDUCE LAP-HF (N=64)	REDUCE LAP-HF I (N=22)	Combined (N=97)
1Y % NYHA I/II vs. baseline	55% vs. 0%	82% vs. 29%	63% vs. 0%	74% (vs.19%)
2Y % NYHA I/II vs. baseline	NA	69% vs. 29%	TBD	
1Y QOL improvement	-20[1]	-15[1]	+12[2]	
2Y QOL improvement	-26[1]	-16[1]	TBD	
1Y Freedom from IV HFH	82%	80%[3]	81%	80%
1Y Freedom from IV HFH in patients with prior year HFH	67%	88%	75%	79%
1 Y Patency with L→ R flow	100%[4]	100%[4]	100%	100%

[1] MLWHF; [2] KCCQ; [3] 2Y: 71%, 3Y: 69%; [4] Echo CL unable to assess in 1 patient

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- **REDUCE LAP-HF** CE Mark Study (N=64): non-randomized, single-arm Hasenfuß Lancet 2016; Kaye Circ. HF 2016
  - Safety
  - Improved PCWP with exercise, patent shunts, Qp/Qs 1.25 at one year
  - Improved NYHA, MLWHF, 6MWT at one year
- **REDUCE LAP-HF I** (N=44): RCT mechanistic study *Feldman T… Shah SJ. Circulation. 2018;137:364–375, Shah SJ online August 27, 2018 at jama.com*
  - Decreased PCWP with exercise established as mechanism
  - No change in left heart structure/function; increase in RVEDV without change in RVEF, decrease in LAVI
  - Clinical outcomes improved at 1 year, all shunts patent
- **REDUCE LAP-HF II** (N=608): RCT pivotal IDE study **recruiting**
- *HFrEF Feasibility study FDA approved IDE; recruiting*
- *REDUCE LAP-HF III (N=100): Post-market Registry Germany Recruiting*