Corvia Medical InterAtrial Shunt Device (IASD®) for Heart Failure with Preserved Ejection Fraction

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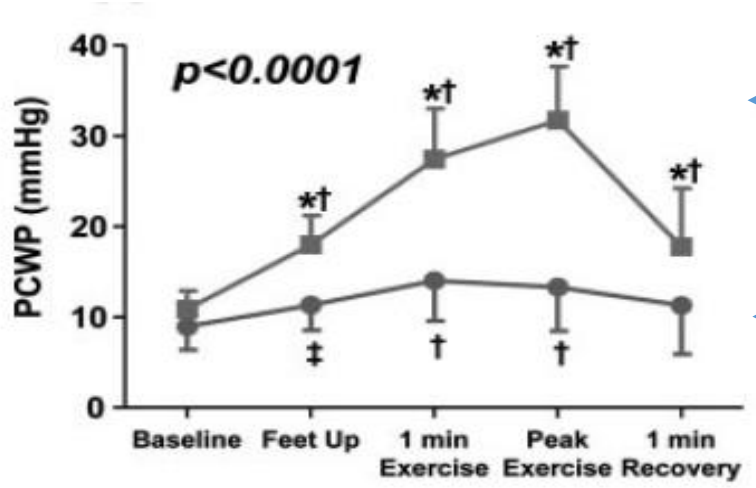
Disclosure Statement of Financial Interest

I, Scott Lilly DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Heart Failure
Preserved Ejection Fraction

DIAGNOSIS: Exercise Hemodynamics



HFpEF

Non-Cardiac

	Resting		Exercise
RA	5 ± 2	→	14 ± 4
PCW	11 ± 2	→	32 ± 6
PASP	31 ± 7	→	59 ± 11
PVR	3.2 ± 1.5	→	2.4 ± 1.2
RA	4 ± 2	→	6 ± 3
PCW	9 ± 3	→	13 ± 5
PASP	24 ± 6	→	35 ± 7
PVR	2.1 ± 1	→	1.9 ± 0.9

Elevated left atrial pressure at rest or with activity, is a near-universal finding in patients with HFpEF

Greater increase in PCW pressure than RA pressure

Borlaug et al. Circ Heart Fail. 2010; 3:588-595.

Heart Failure
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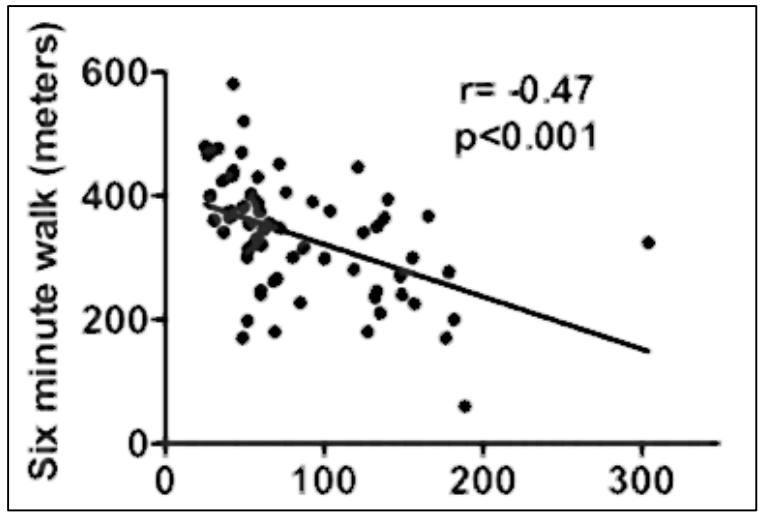
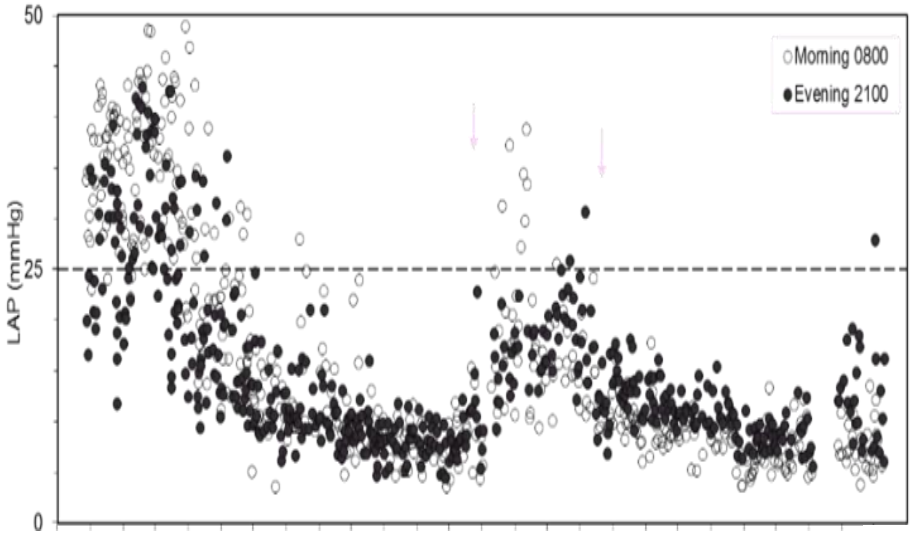
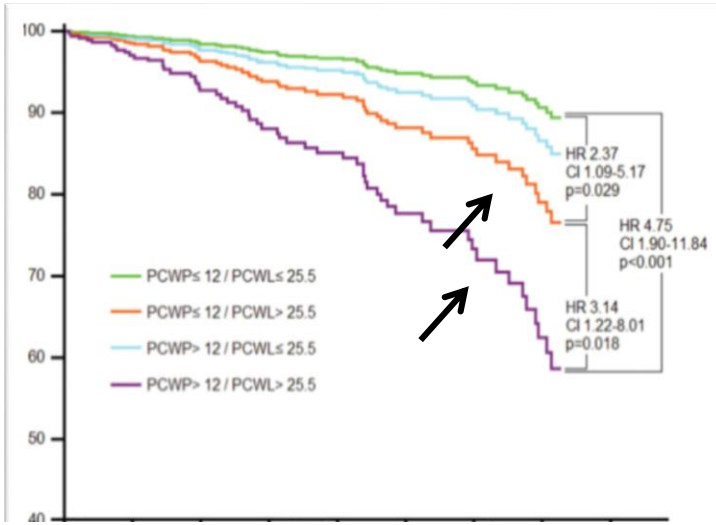
PROGNOSIS: Related to LAP







Functional Status, Exercise Capacity

HF Hospitalization

Survival

Left atrial pressure is related to exercise capacity, heart failure hospitalizations, and survival

Exercise-associated pressures can better discriminate

Wolsk et al. Eur J Heart Failure 2018; 20:715-722.
Ritzema et al. Circ. 2010; 121:1086-1095.
Dorfs et al. Eur J Heart Failure 2014; 35:3103-3112.

Heart Failure
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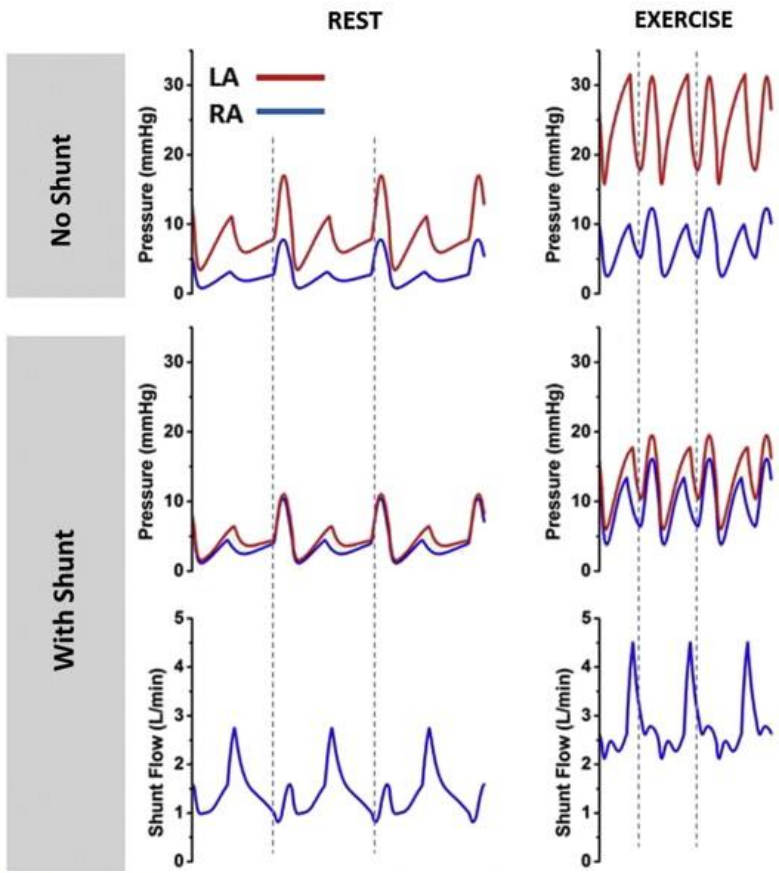
Can an Interatrial Shunt be Therapeutic?



Elevated LV filling pressures (Elevated LAP)

Shunt Device

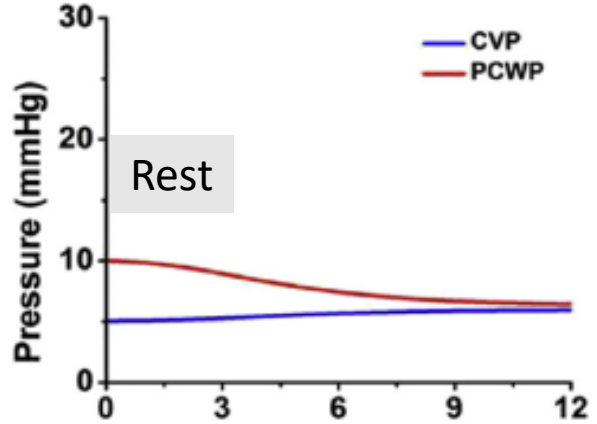
Pulmonary Venous hypertension

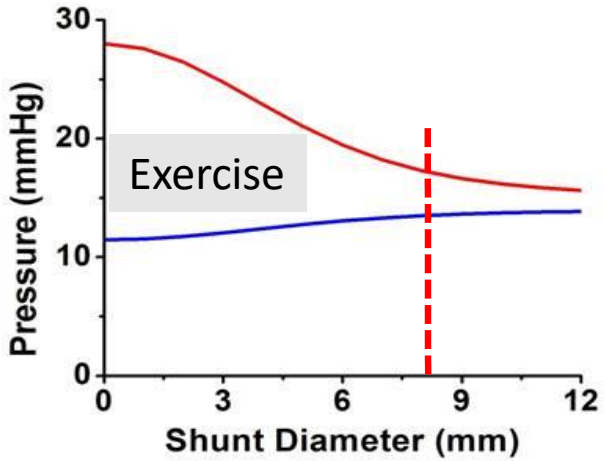
Pulmonary Congestion Dyspnea

↓LAP

RA → LA Flow

Sustained Patency





Kaye et al. J Card Fail. 2014; 20:212-221

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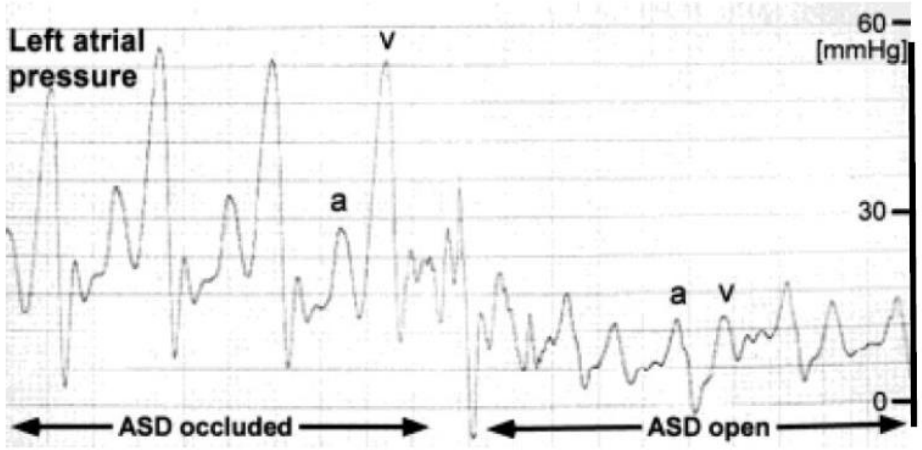
Observational Basis for Interatrial Shunt Therapy



Ewert et al. Cath Cardiovasc Interv. 2001; 52:177-180

LONGEVITY IN EXTENSIVE ORGANIC HEART LESIONS: A CASE OF LUTEMBACHER'S SYNDROME IN A MAN AGED 72 *

By JOHN MARTIN ASKEY, M.D., F.A.C.P., and JAMES E. KAHLER, M.D.,
Los Angeles, California

AN astounding feature of Lutembacher's syndrome is the ability of many patients to endure the marked lesion for many decades. One woman lived to the age of 74 [1] and passed successfully through 11 pregnancies and three abortions. In Bonnabel's report,[2] two patients lived to be over 70. It is difficult to document precisely the instances of Lutembacher's syndrome [3] in the literature. Many are included in reports upon interatrial septal defect without definite designation of the mitral lesion. An approximate enumeration would be as follows:

McGinn and White [4] reported 24; Roesler [5] mentioned 6 more; Tinney [6] in 1940 found 11 instances reported since 1934. A few additional case reports in the literature were not noted. Since then a number of individual reports have appeared.[7, 8, 9, 10, 11, 12, 13, 14] There are now in the literature probably between 50 and 60 cases proved by autopsy. In the absence of a central medical registry where cases may be assembled and analyzed, it is important that all cases encountered be available in the literature.

CASE REPORT

Catheterization and Cardiovascular Interventions 46:179–186 (1999)

Blade and Balloon Atrial Septostomy for Left Heart Decompression in Patients With Severe Ventricular Dysfunction on Extracorporeal Membrane Oxygenation

Paul M. Seib,[1]* MD, Sherry C. Faulkner,[2] CCP, Christopher C. Erickson,[1] MD, Stephen H. Van Devanter,[2] MD, James E. Harrell,[2] MD, James W. Fasules,[1] MD, Elizabeth A. Frazier,[1] MD, and W. Robert Morrow,[1] MD

Atrial Septostomy for Left Atrial Decompression During Extracorporeal Membrane Oxygenation by Inoue Balloon Catheter

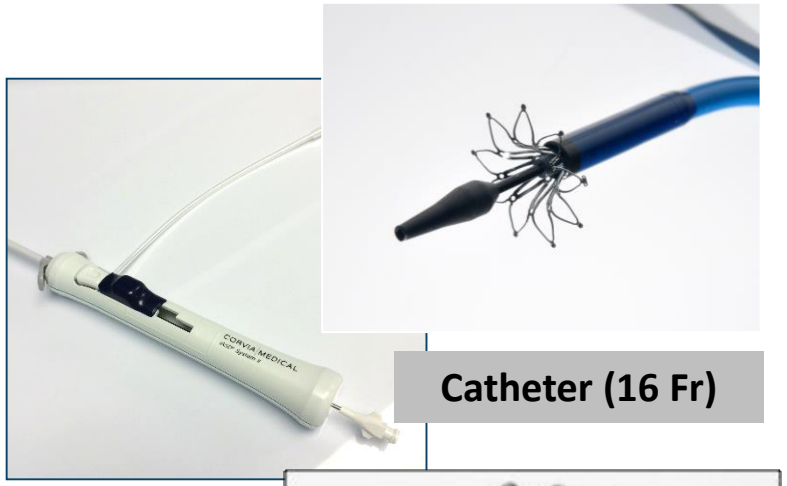
Yen-Nien Lin, MD; Yin-Huei Chen, MD; Huang-Joe Wang, MD; Jui-Sung Hung, PhD; Kuan-Cheng Chang, PhD; Ping-Han Lo, MD

Background: Refractory pulmonary edema is an infrequent but serious complication in patients receiving venoarterial extracorporeal membrane oxygenation (VA-ECMO) for myocardial failure. Left atrial (LA) decompression in this setting is important. Although a few methods have been reported, the experience is mostly limited to children. We aimed to evaluate the feasibility of Inoue balloon catheter in percutaneous trans-septal LA decompression in adult cardiogenic patients.

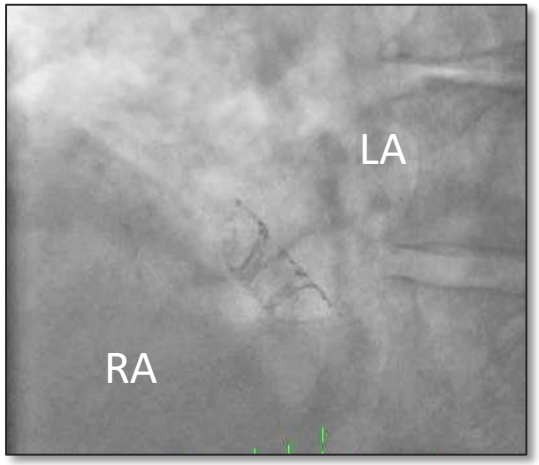
- Mask HFpEF
- Closure precipitates HF
- Relieves Congestiton
- ?Benefit in Left Heart Disease

Heart Failure
Preserved *(& Mid-Range Ejection)* Fraction

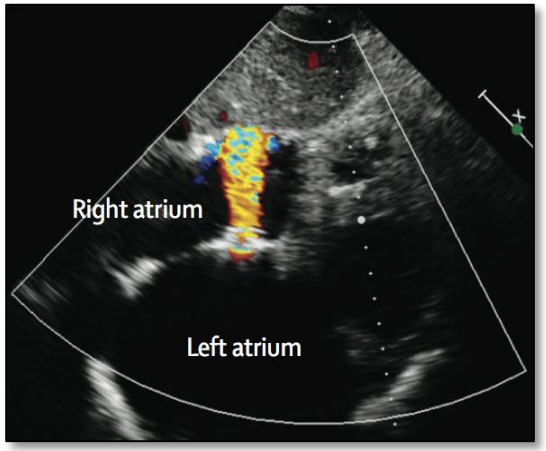
Corvia IASD® Device, Clinical Studies



Catheter (16 Fr)



Implant
19mm OD
8 mm iASD



- 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)
  - 2Y follow up complete (Kaye, ESC 2018)
- REDUCE LAP-HF I (N=44): RCT mechanistic study
  - FDA IDE 30 Day Complete (Feldman T, Shah SJ. Circulation. 2018;137:364–375)
  - 1Y follow-up complete (Shah SJ, Feldman T, JAMA 2018)
- REDUCE LAP-HF II (N=608): RCT pivotal study
  - FDA approved IDE; recruiting
- HFrEF Feasibility study
  - FDA approved IDE; recruiting
- REDUCE LAP-HF III (N=100): Post-market Registry Germany
  - Recruiting

Heart Failure
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REDUCE LAP HF I

Design

Randomized, sham-controlled trial

1:1 randomization

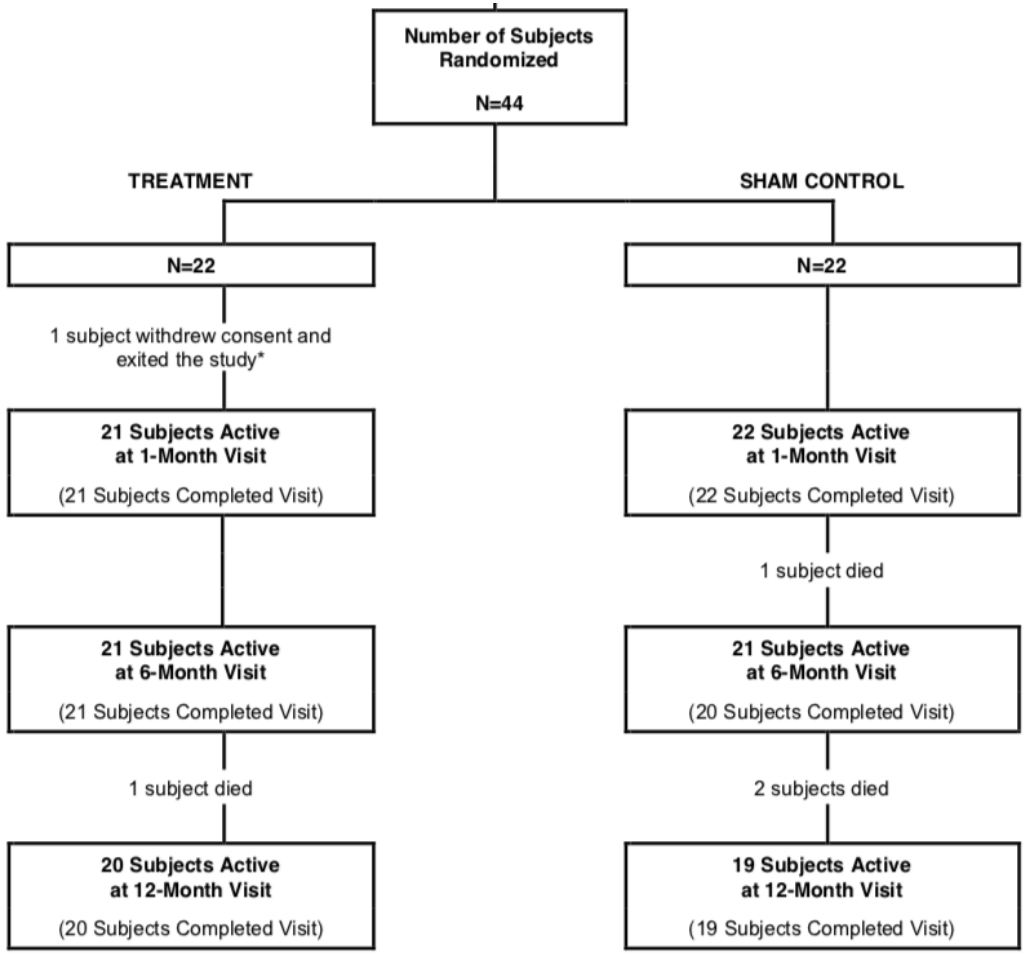
- Sedation, femoral venous access, ICE/TEE
- ± transseptal IASD implantation

Inclusion

NYHA III-IV, LVEF > 40%,
1-yr HF Hosp or
↑BNP/NT-Pro BNP
ePCW ≥ 25 mm Hg
PCW - RA ≥ 5 mm Hg

Exclusion

Cardiac index < 2.0
Sig valve disease
Sig RV dysfunction
PVR > 4 Wood units



Feldman et al. Circulation 2018; 137:364-375.

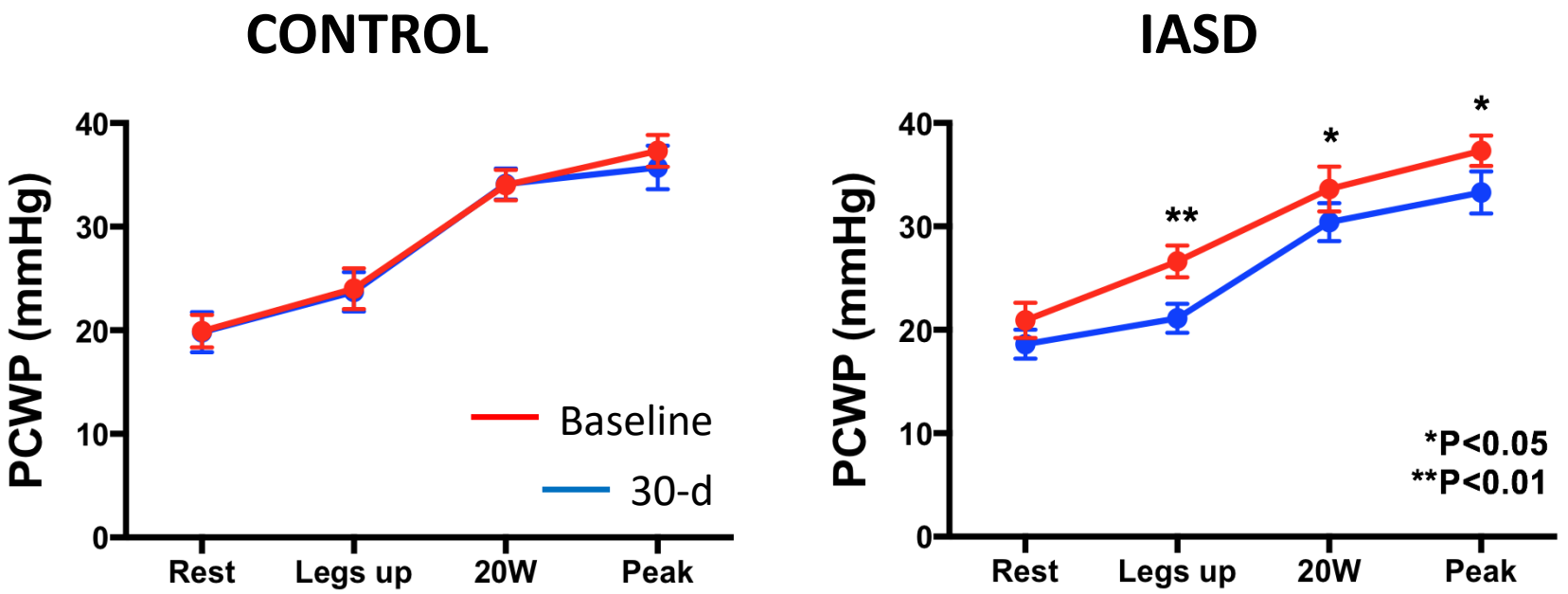
Heart Failure
Preserved & Mid-Range Ejection Fraction

REDUCE LAP-HF I (n=44)

Randomized, controlled trial (1:1)

NYHA III-IV, LVEF > 40%, HF Hosp or ↑BNP

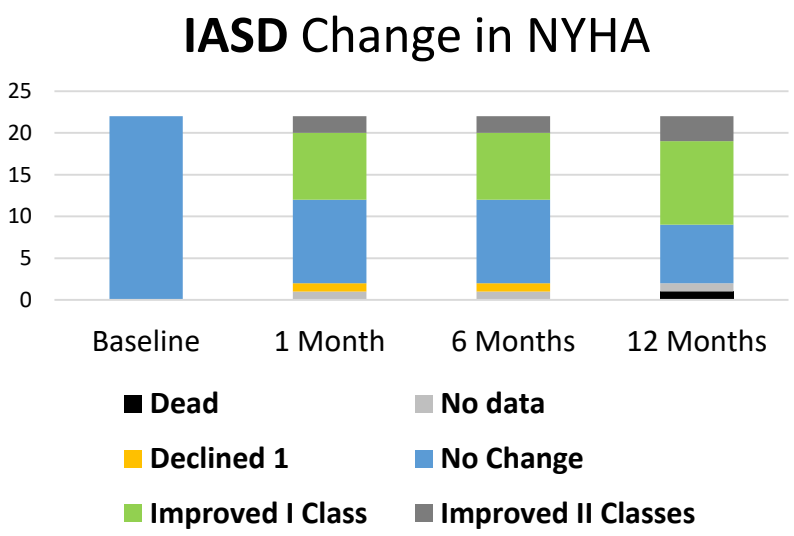
PCW ≥ 25 mm Hg (Exercise); PCW - RA ≥ 5 mm Hg

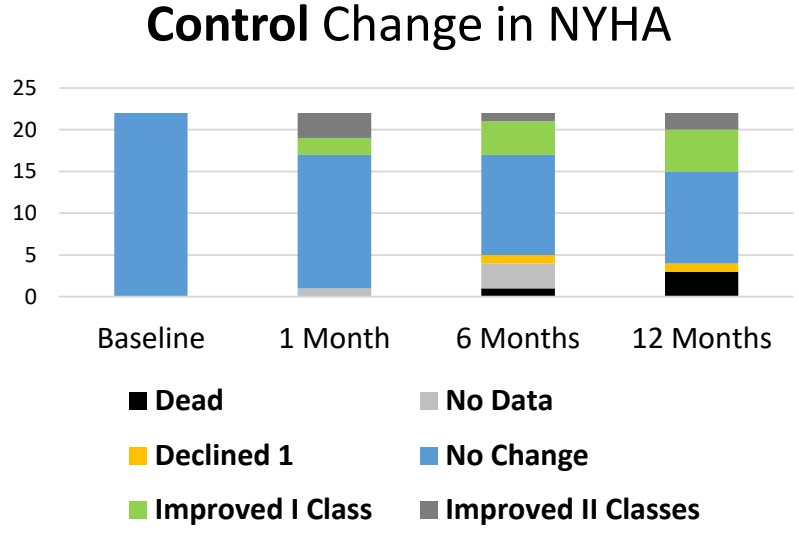


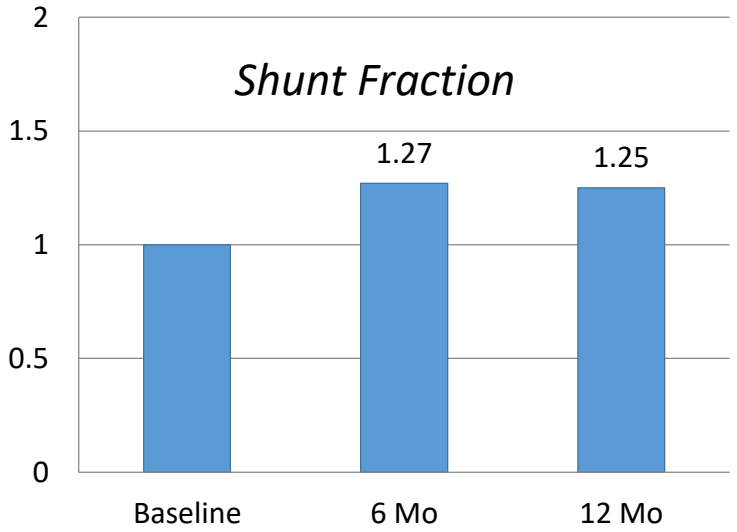
Feldman et al. Circulation 2018; 137:364-375.

Heart Failure
Preserved & Mid-Range Ejection Fraction

REDUCE LAP-HF I One Year Results







At 12 months, even with a small sample size there was a trend toward greater improvement in NYHA class compared to control

Shunt patency has been 100%, and the QpQs has been stable over the observed study period

Shah et al. JAMA Cardiol. 2019; 3:968-977.

Heart Failure
Preserved & Mid-Range Ejection Fraction

REDUCE LAP-HF I One Year Results

	IASD	Control	P-Value
Change in NYHA class (12M – baseline)	-1 (-1,0) [n=20]	0 (-1,0) [n=19]	0.083
Change in 6MWT distance (12M – baseline)	16 (-57,30) [n=20]	13.6 (-10,72) [n=19]	0.308
Change in QOL (12M – baseline)			
KCCQ	[n=20]	[n=19]	
Overall Summary score	+10.5 (0.7,18.8)	+8.1 (-5.7,20.6)	0.570
Clinical Summary score	+10.4 (-6.5,26.0)	+3.1 (-4.2,18.8)	0.827

Heart Failure

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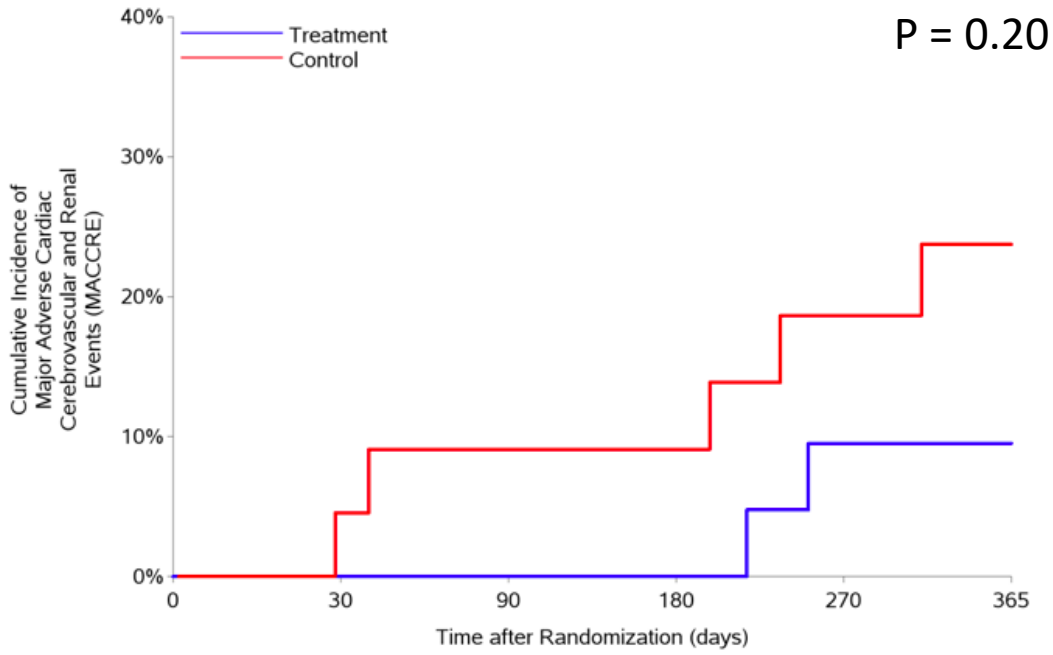
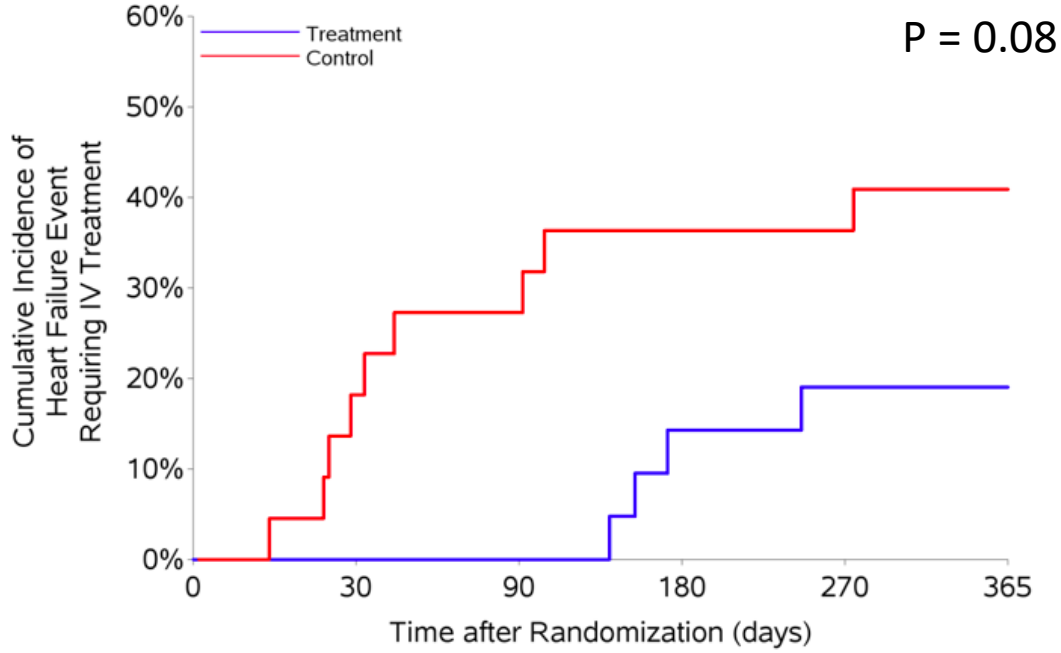
REDUCE LAP-HF I One Year Results



P = 0.20

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



P = 0.08

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

MACCRE: Major adverse cardiac, cerebrovascular and renal events

Shah et al. JAMA Cardiol. 2019; 3:968-977.

Heart Failure

Preserved & Mid-Range Ejection Fraction

Aggregate Efficacy Profile

325 Patient Years of follow-up	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	
3Y % NYHA I/II vs. baseline	NA	65% vs. 27%	TBD	
1Y Freedom from IV HFH	82%	80%[1]	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%[2]	100%[2]	100%	100%

Heart Failure

Preserved & Mid-Range Ejection Fraction

Aggregate Safety Profile

325 Patient Years of follow-up	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%	96%
2 Year Survival	91%	92%	91%	91%
3 Year Survival	82%	89%	TBD	
4 Year Survival	73%	84%	TBD	
1 Year Freedom from CVA	100%	98.5%	100%	99%
2 Year Freedom from CVA	100%	98.5%	100%	99%
3 Year Freedom from CVA	100%	98.5%	TBD	
4 Year Freedom from CVA	100%	NA	TBD	
IASD thrombosis/removal	0%	0%	0%	0%

Conclusions

- Interatrial shunt therapies can reduce activity-related elevations in left atrial pressure (eRHC)
- Mid-term safety and efficacy profiles are favorable
- Patient-selection is important (eRHC)
- Shunt diameter is important, may relate to patency and efficacy

Thank You

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