Inter-atrial Shunt Device

Corvia Medical

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Evanston Hospital

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Transcatheter Cardiovascular Therapeutics

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NorthShore University HealthSystem
Evanston Hospital

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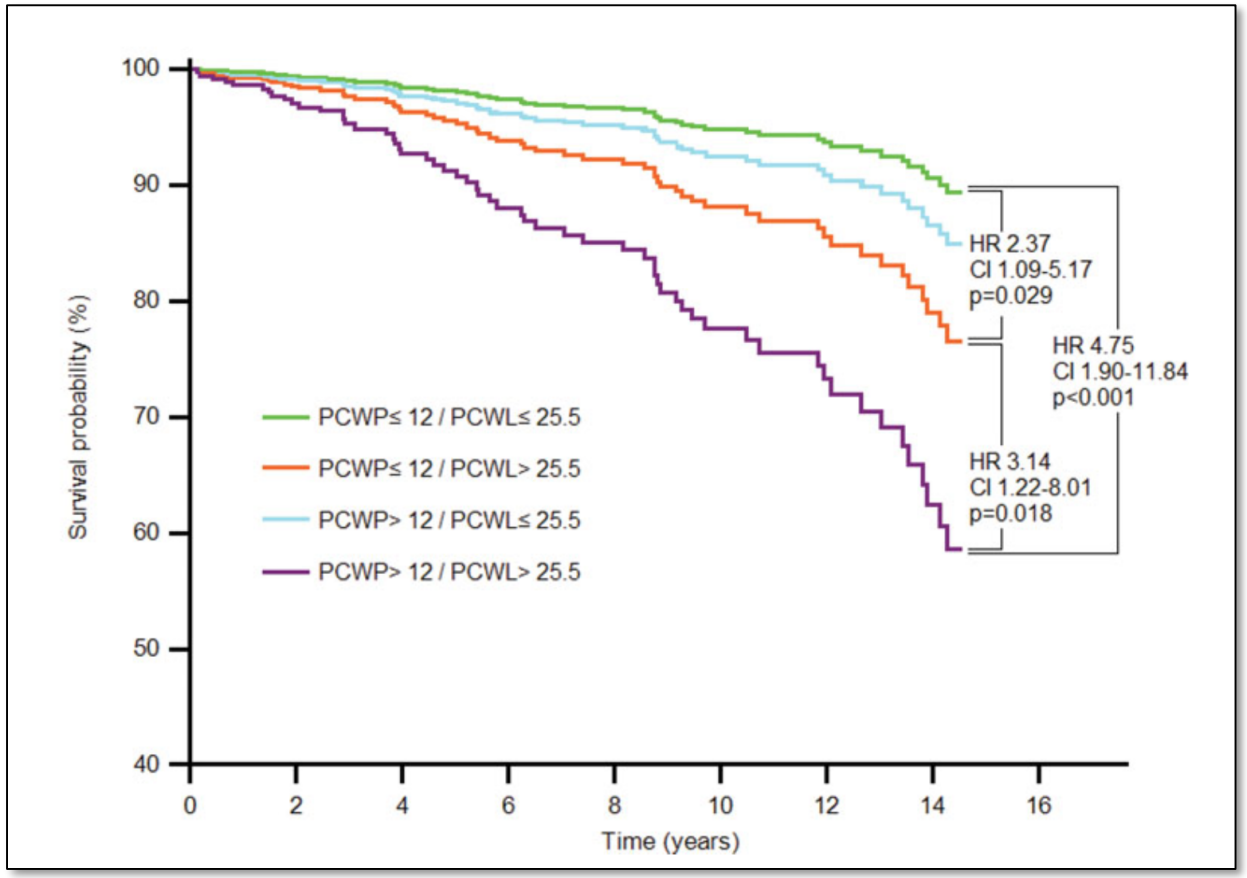
Disclosure Information

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 heart failure with preserved ejection fraction



European Heart Journal (2014) 35, 3103–3112

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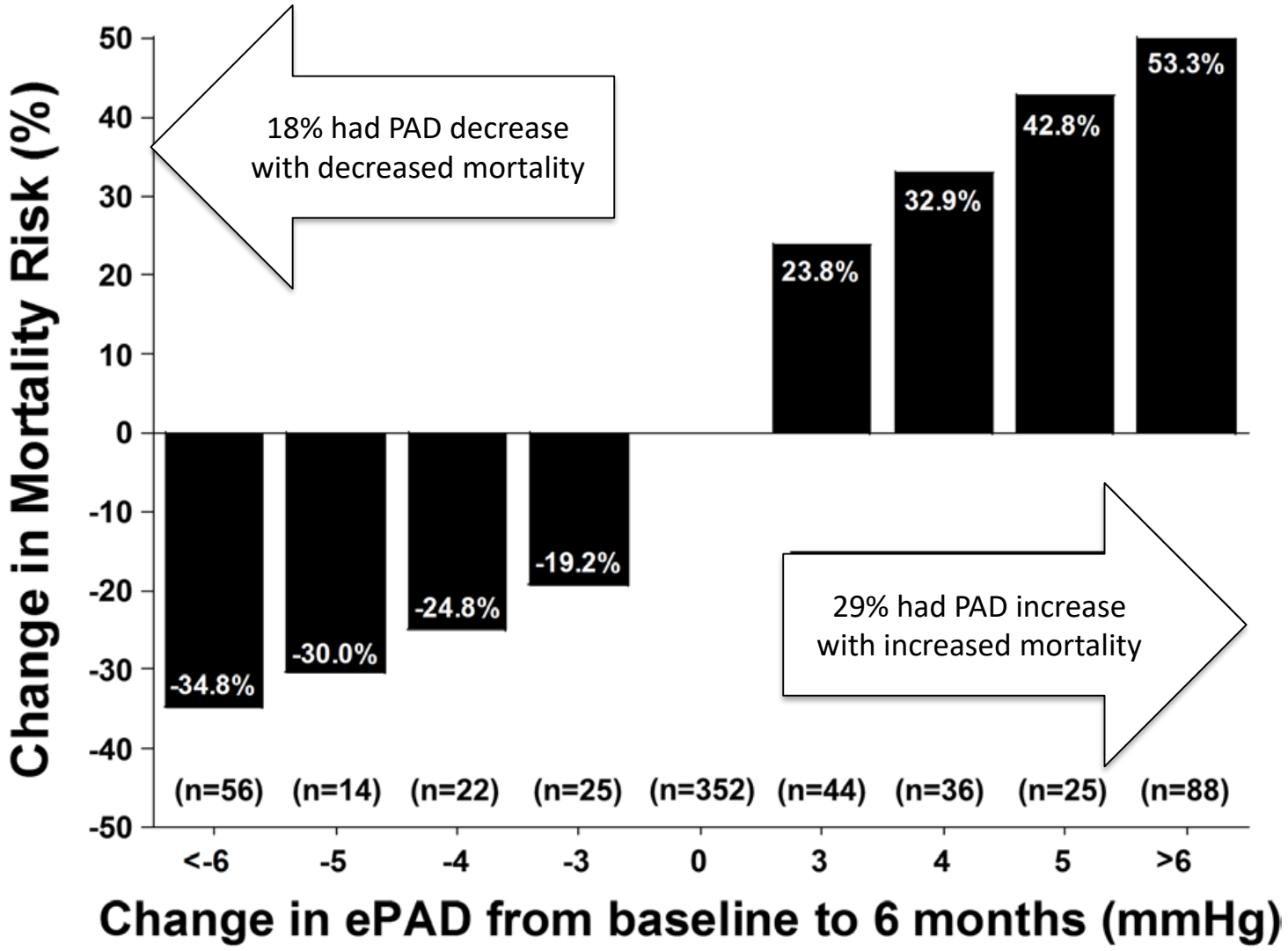
Mortality and modest 6M ePAD changes



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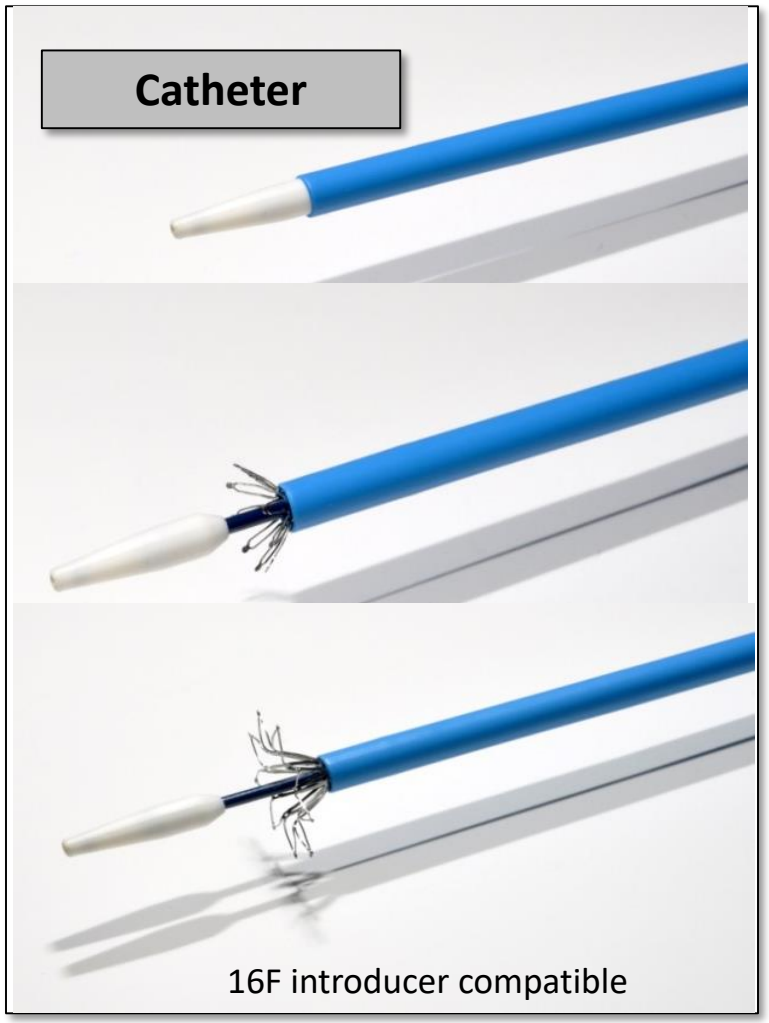
n=790

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

Corvia Medical Investigational Device

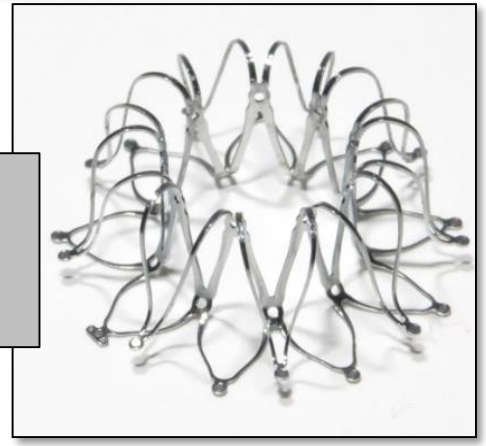
Handle

Catheter

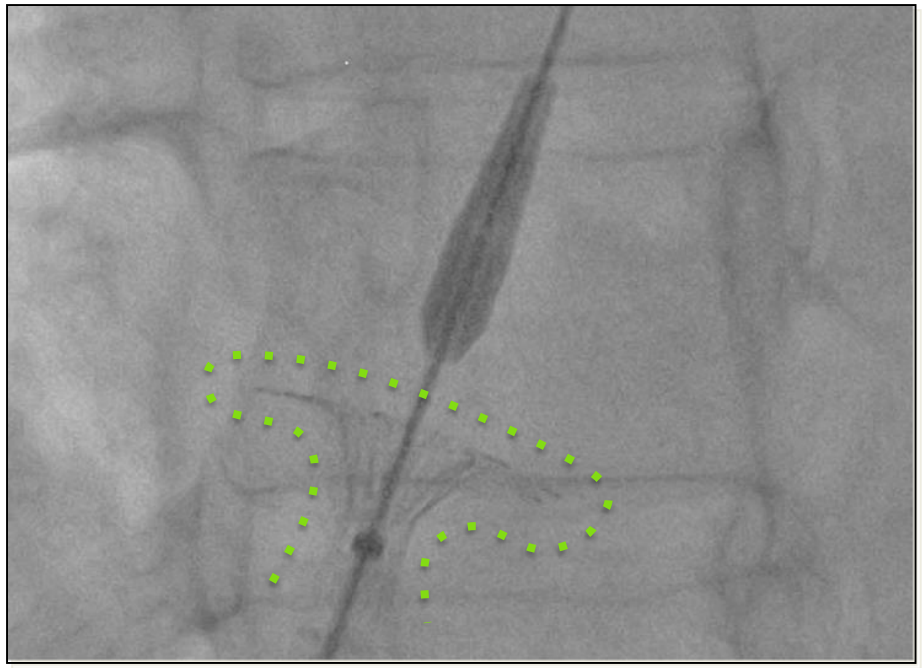


16F introducer compatible

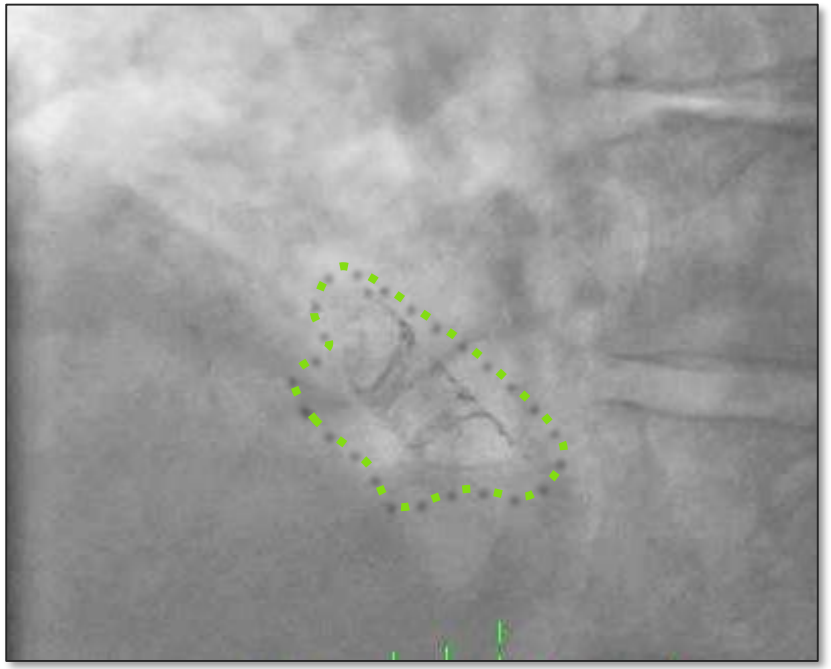
Implant
19mm OD
8 mm ASD



Fluoroscopic Images



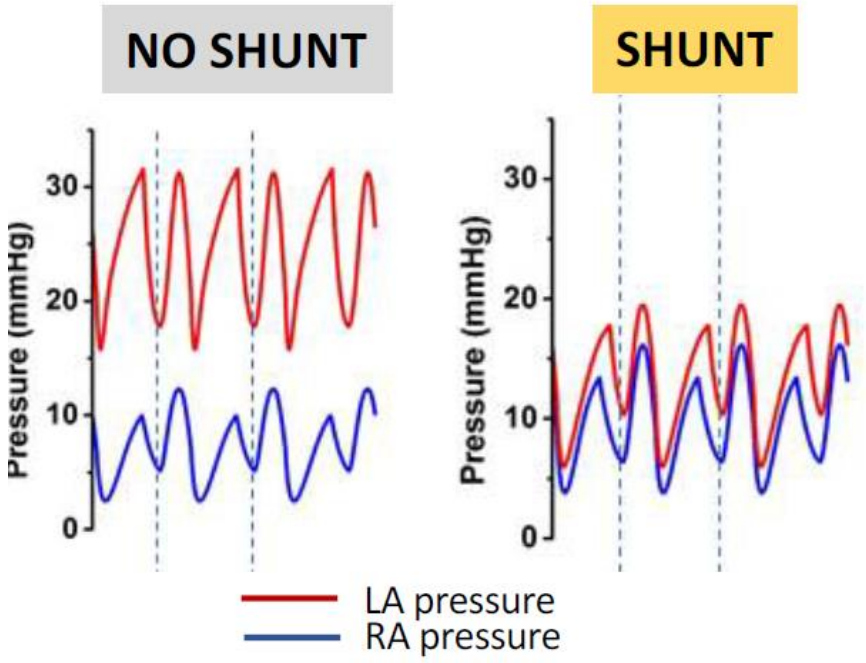
LA legs deployed

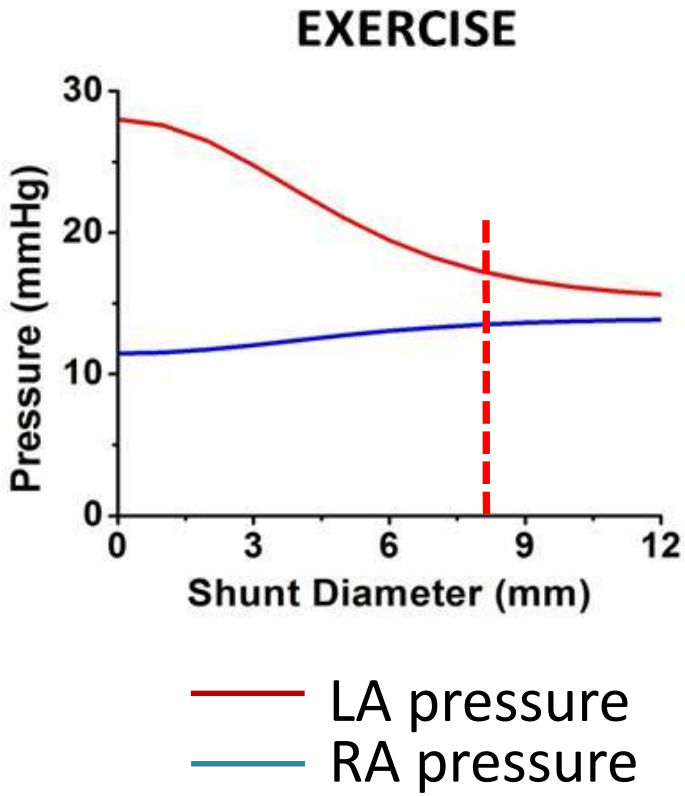


Post deployment

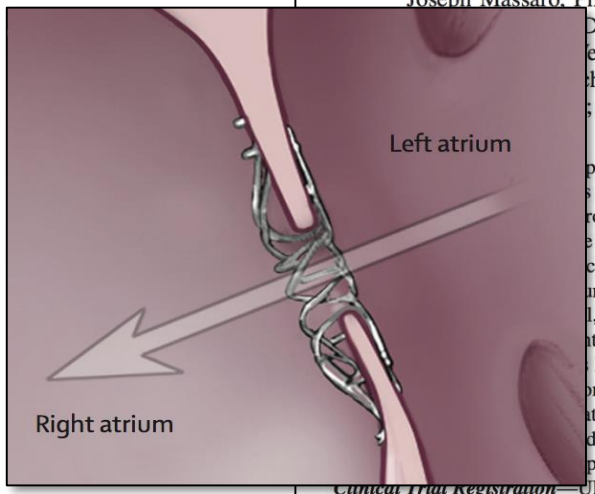
Left Atrial Decompression:

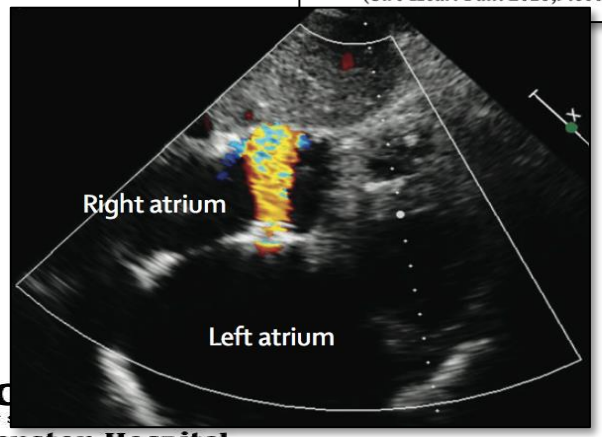
Computer simulation: 8mm interatrial shunt device (IASD) provides acute LA decompression at rest & during exercise





Kaye et al J Cardiac Fail 2014;20:212e221





Advances in Clinical Trials

Transcatheter Interatrial Shunt Device for the Treatment of Heart Failure

Rationale and Design of the Randomized Trial to REDUCE Elevated Left Atrial Pressure in Heart Failure (REDUCE LAP-HF I)

Ted Feldman, MD; Jan Komtebedde, DVM; Daniel Burkhoff, MD, PhD;
Joseph Massaro, PhD; Mathew S. Maurer, MD; Martin B. Leon, MD; David Kaye, MD;
D; John G.F. Cleland, MD; Dalane Kitzman, MD; Spencer H. Kubo, MD;
eldhuisen, MD; Franz Kleber, MD; Jean-Noël Trochu, MD, PhD;
hio, MD, PhD; Finn Gustafsson, MD, PhD; Gerd Hasenfuß, MD;
; Gerasimos Filippatos, MD; Laura Mauri, MD, MSc; Sanjiv J. Shah, MD

preserved ejection fraction (HFpEF), a major public health problem with high morbidity
difficult to manage because of a lack of effective treatment options. Although HFpEF is a
rome, elevated left atrial pressure—either at rest or with exertion—is a common factor among
of the primary reasons for dyspnea and exercise intolerance in these patients. On the basis
congenital interatrial shunts in mitral stenosis, it has been hypothesized that the creation of
nt to decompress the left atrium (without compromising left ventricular filling or forward
l, nonpharmacological strategy for alleviating symptoms in patients with HFpEF. A novel
t device has been developed and evaluated in patients with HFpEF in single-arm, nonblinded
have demonstrated the safety and potential efficacy of the device. However, a randomized,
n of the device is required to further evaluate its safety and efficacy in patients with HFpEF.
tionale for a therapeutic transcatheter interatrial shunt device in HFpEF, and we describe the
d Left Atrial Pressure in Heart Failure (REDUCE LAP-HF I), the first randomized controlled
y to reduce left atrial pressure in HFpEF.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT02600234.
(*Circ Heart Fail*. 2016;9:e003025. DOI: 10.1161/CIRCHEARTFAILURE.116.003025.)

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

A transcatheter intracardiac shunt device for heart failure with preserved ejection fraction (REDUCE LAP-HF): a multicentre, open-label, single-arm, phase 1 trial

*Gerd Hasenfuß, Chris Hayward, Dan Burkhoff, Frank E Silvestry, Scott McKenzie, Finn Gustafsson, Filip Malek, Jan Van der Heyden, Irene Lang, Mark C Petrie, John G F Cleland, Martin Leon, David M Kaye, on behalf of the REDUCE LAP-HF study investigators**

Summary

Background Heart failure with preserved ejection fraction (HFPEF) is a common, globally recognised, form of heart failure for which no treatment has yet been shown to improve symptoms or prognosis. The pathophysiology of HFPEF is complex but characterised by increased left atrial pressure, especially during exertion, which might be a key therapeutic target. The rationale for the present study was that a mechanical approach to reducing left atrial pressure might be effective in HFPEF.

Methods The REDUCe Elevated Left Atrial Pressure in Patients with Heart Failure (REDUCE LAP-HF) study was an open-label, single-arm, phase 1 study designed to assess the performance and safety of a transcatheter interatrial shunt device (IASD, Corvia Medical, Tewkesbury, MA, USA) in patients older than 40 years of age with symptoms of HFPEF despite pharmacological therapy, left ventricular ejection fraction higher than 40%, and a raised pulmonary capillary wedge pressure at rest (>15 mm Hg) or during exercise (>25 mm Hg). The study was done at 21 centres (all departments of cardiology in the UK, Netherlands, Belgium, France, Germany, Austria, Denmark, Australia, and New Zealand). The co-primary endpoints were the safety and performance of the IASD at 6 months, together with measures of clinical efficacy, including functional capacity and clinical status, analysed per protocol. This study is registered with ClinicalTrials.gov, number NCT01913613.

Findings Between Feb 8, 2014, and June 10, 2015, 68 eligible patients were entered into the study. IASD placement was successful in 64 patients and seemed to be safe and well tolerated; no patient had a peri-procedural or major adverse cardiac or cerebrovascular event or need for cardiac surgical intervention for device-related complications during 6 months of follow-up. At 6 months, 31 (52%) of 60 patients had a reduction in pulmonary capillary wedge pressure at rest, 34 (58%) of 59 had a lower pulmonary capillary wedge pressure during exertion, and 23 (39%) of 59 fulfilled both these criteria. Mean exercise pulmonary capillary wedge pressure was lower at 6 months than at baseline, both at 20 watts workload (mean 32 mm Hg [SD 8] at baseline *vs* 29 mm Hg [9] at 6 months, p=0·0124) and at peak exercise (34 mm Hg [8] *vs* 32 [8], p=0·0255), despite increased mean exercise duration (baseline *vs* 6 months: 7·3 min [SD 3·1] *vs* 8·2 min [3·4], p=0·03). Sustained device patency at 6 months was confirmed by left-to-right shunting (pulmonary/systemic flow ratio: 1·06 [SD 0·32] at baseline *vs* 1·27 [0·20] at 6 months, p=0·0004).

Interpretation Implantation of an interatrial shunt device is feasible, seems to be safe, reduces left atrial pressure during exercise, and could be a new strategy for the management of HFPEF. The effectiveness of IASD compared with existing treatment for patients with HFPEF requires validation in a randomised controlled trial.

Hasenfuß G: Lancet 2016; 387: 1298–304

Intracardiac 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%)

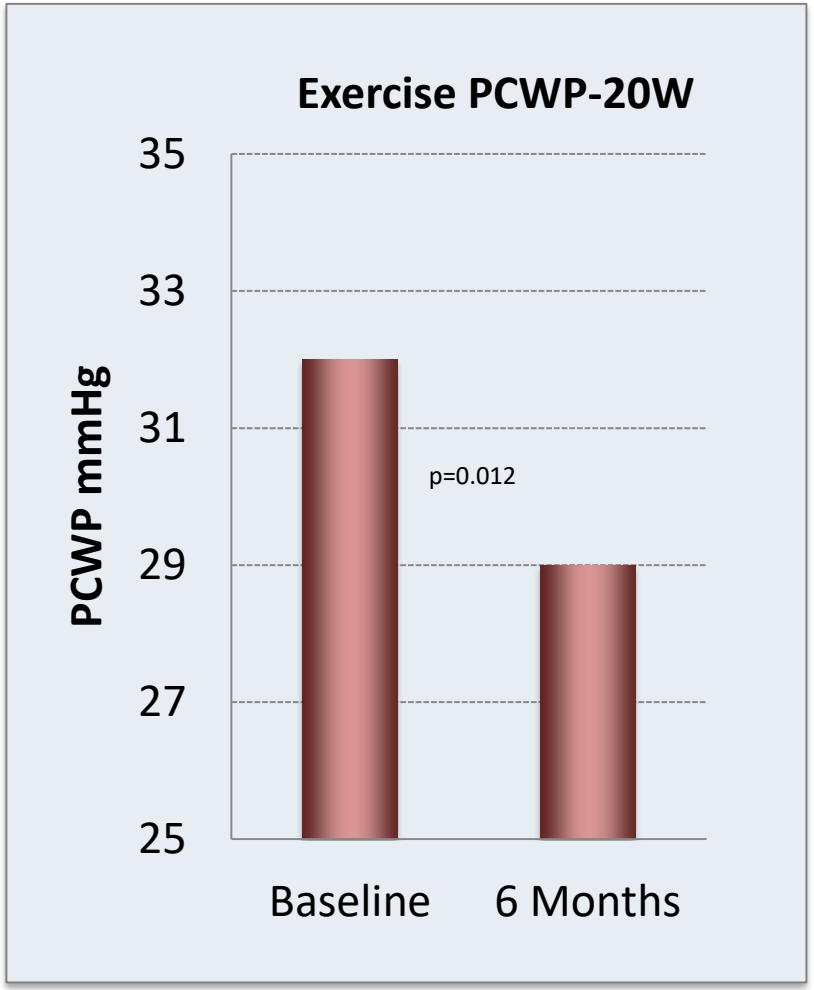
Echocardiography	
Left ventricular end diastolic volume index, mL/m²	68 (13)
Left ventricular ejection fraction, %	47 (7)
Left ventricular mass index, g/m²	119 (36)
Left arterial diastolic volume index, mL/m²	34 (17)
Right ventricle diastolic volume index, mL/m²	22 (9)
Right artery volume index, mL/m²	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)

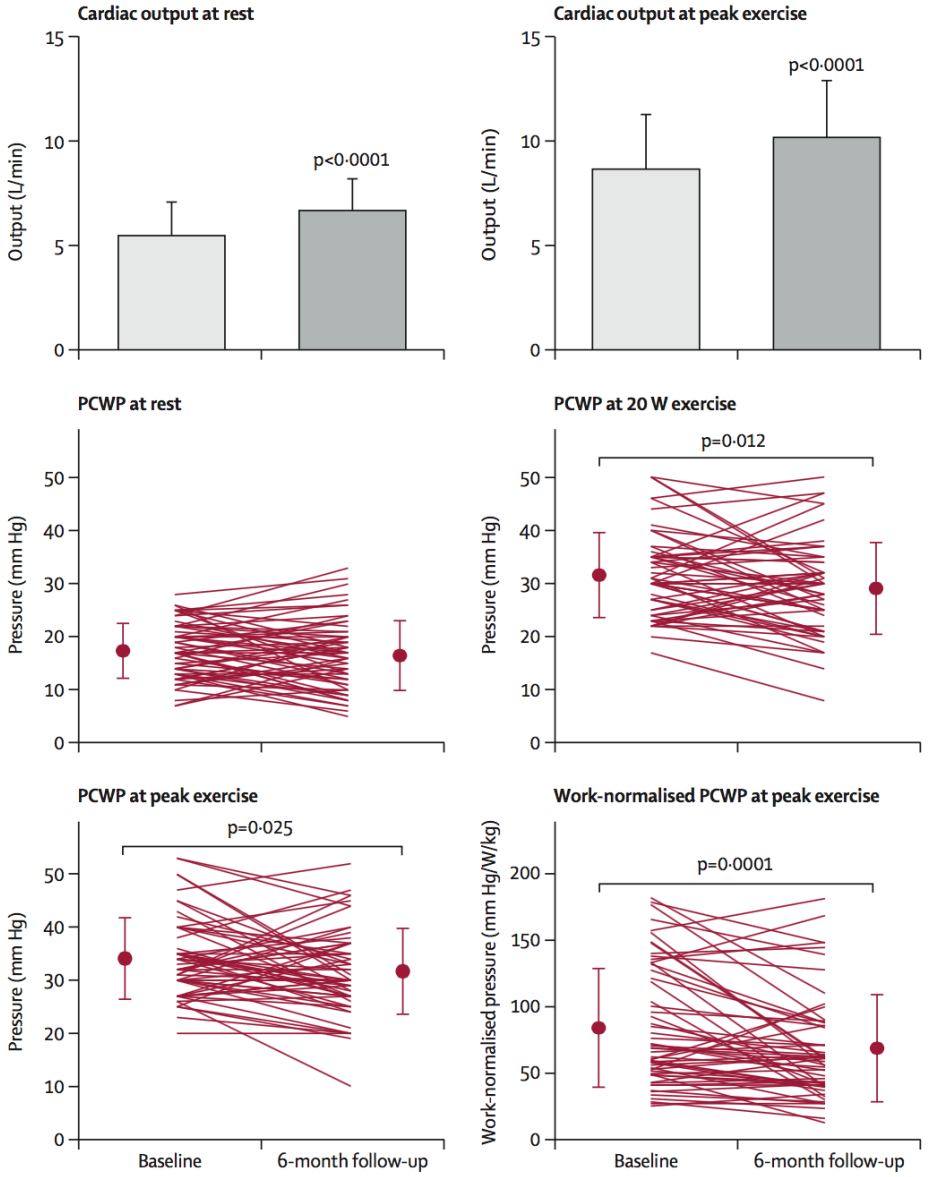
n=64

Hasenfuß G: Lancet 2016; 387: 1298–304

Intracardiac shunt device for HFpEF

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





n=64

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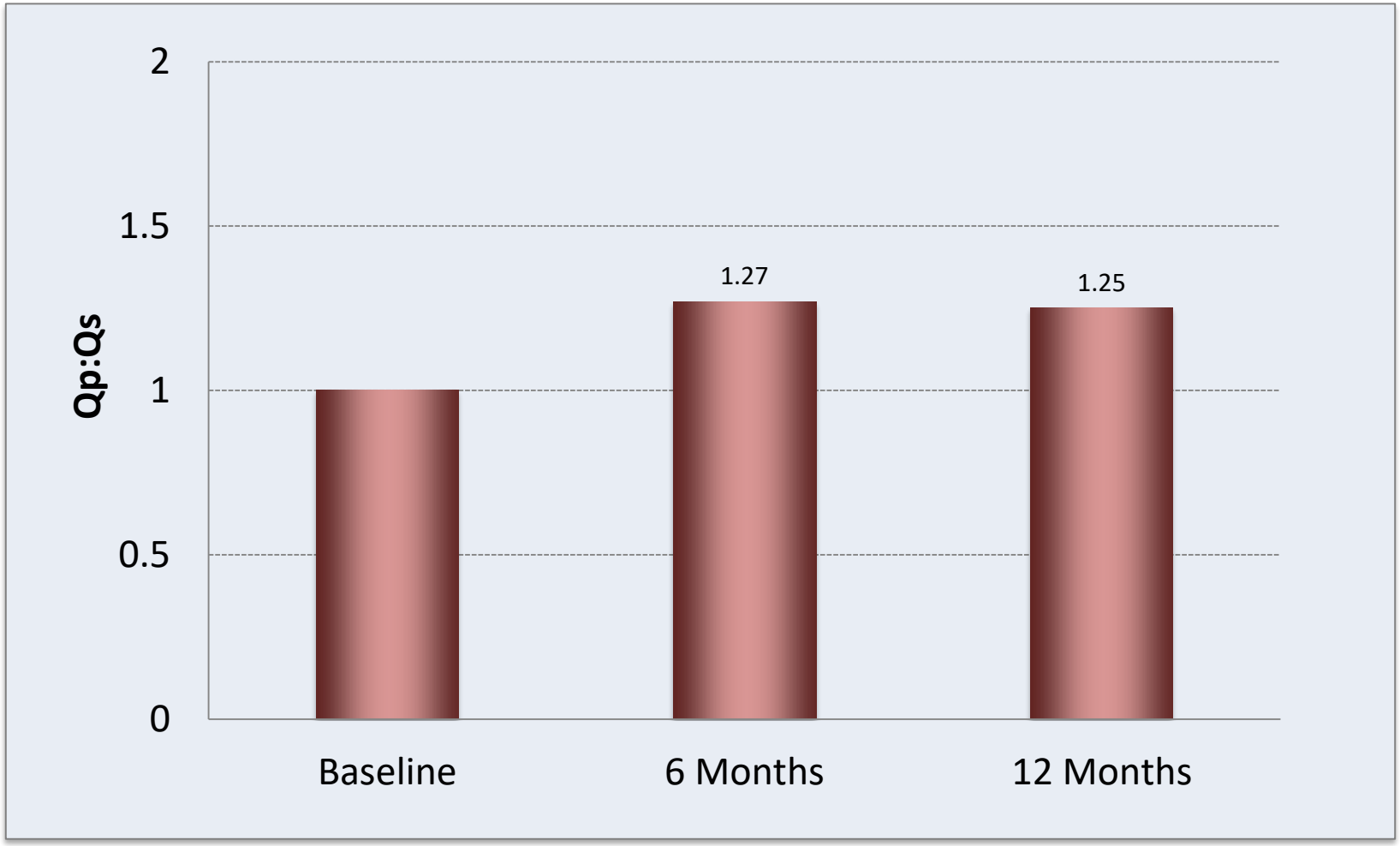
1-Year Outcomes After InterAtrial Shunt Device for HFpEF

Qp:Qs



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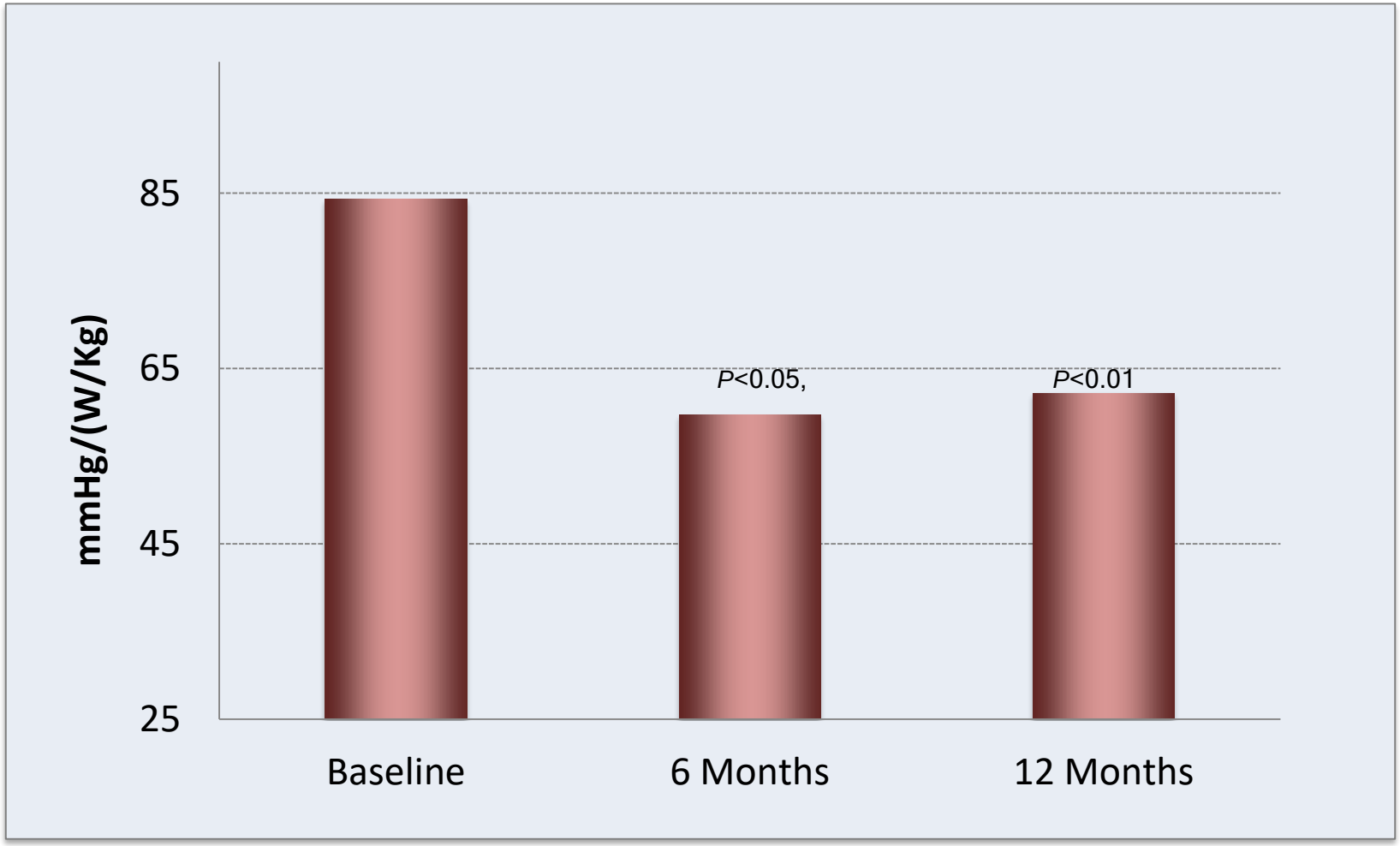
REDUCE LAP-HF *Kaye Circ Heart Fail. 2016 Dec;9(12). pii: e003662*

1-Year Outcomes After InterAtrial Shunt Device for HFpEF

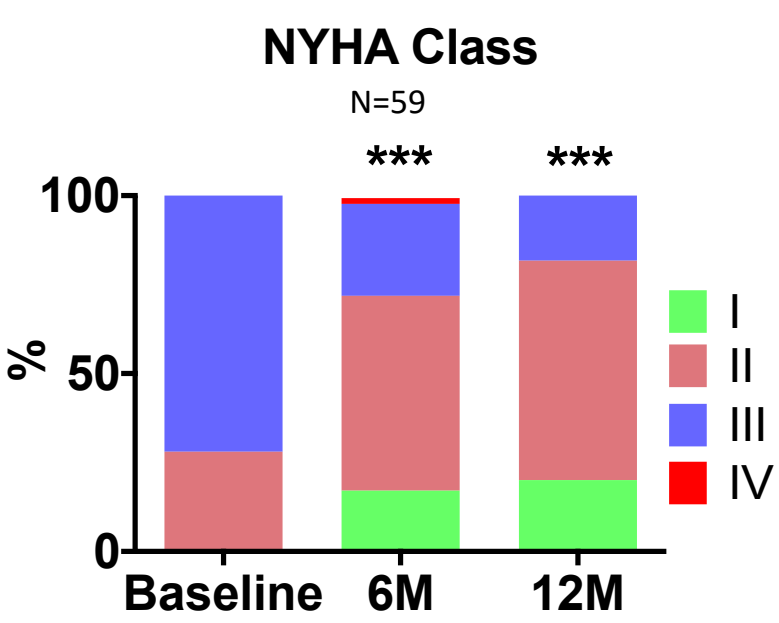
Workload indexed peak exertion wedge pressure

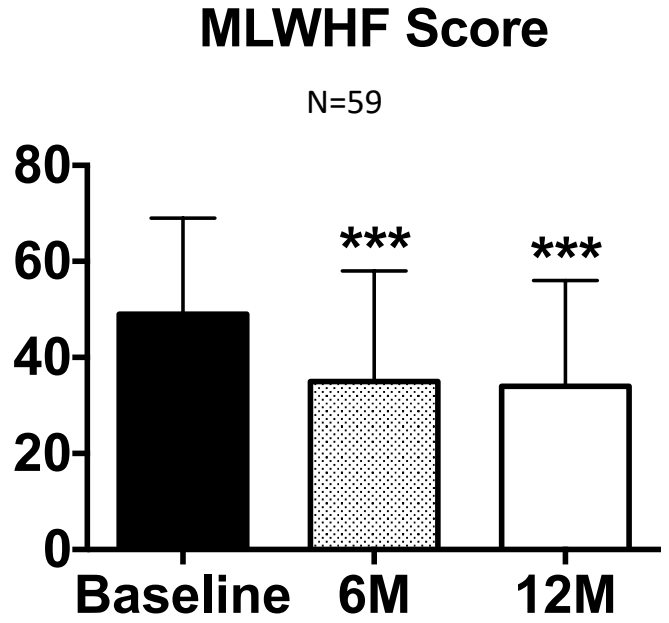


REDUCE LAP-HF *Kaye Circ Heart Fail. 2016 Dec;9(12). pii: e003662*

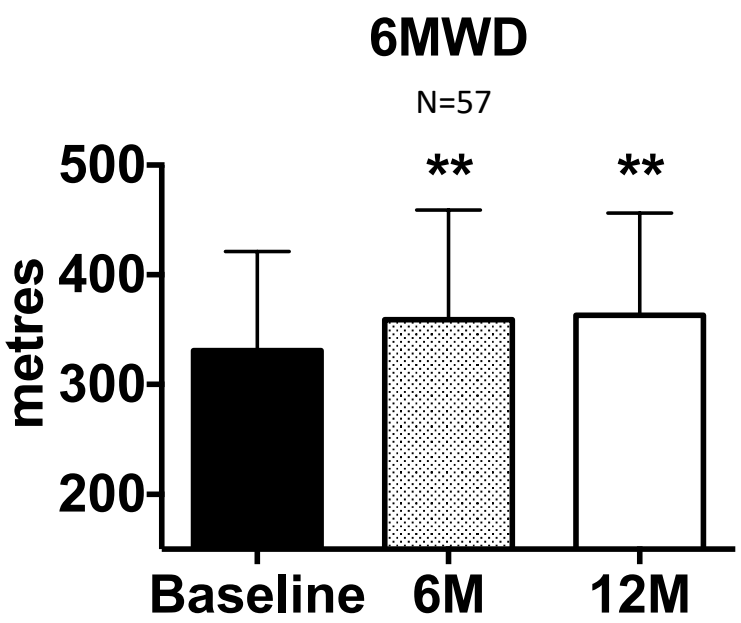
Sustained Clinical Efficacy

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





Mean Δ at 1 year: 15 points



Mean Δ at 1 year: 33m

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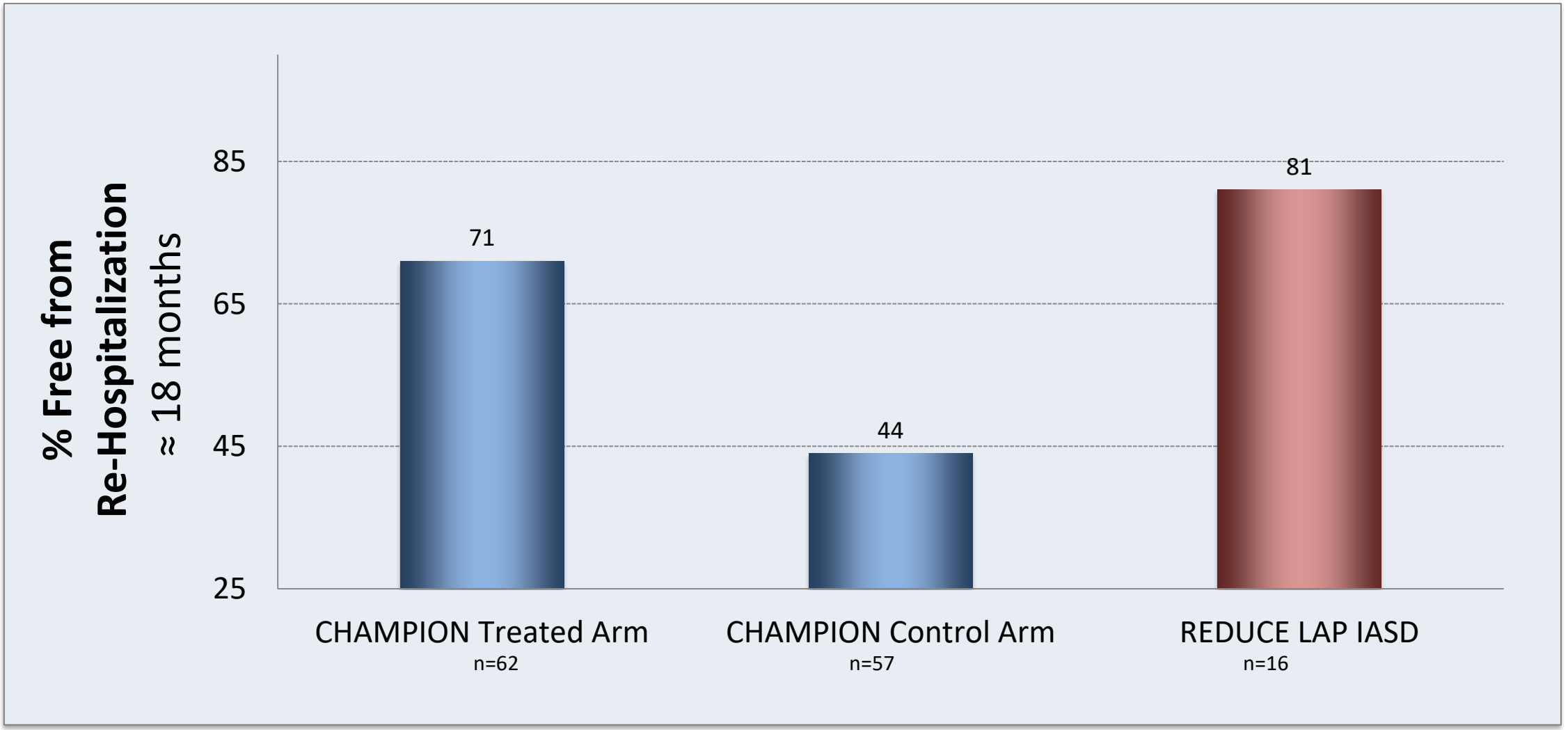
RM-Friedman's test:
**p<0.01, ***p<0.001

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

Freedom from HF Re-Hospitalization

Comparison to CARDIOMEMS Preserved EF Cohort



Cardiomems data: FDA panel pack

Circ Heart Fail. 2016 Dec;9(12)

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Transcatheter InterAtrial Shunt Device for the Treatment of Heart Failure:
Rationale and Design of the Randomized Trial to REDUCE Elevated Left Atrial Pressure in Heart Failure (REDUCE LAP-HF I)

- HF patients with an **LV ejection fraction >40%** and elevated left sided filling pressures who remain symptomatic despite optimal guideline directed medical therapy
- multicenter, prospective, randomized, controlled, single blinded trial
- **40 subjects** at 20 investigational sites in the U.S. and 5 sites OUS
- Non-implant control group and **1:1 randomization**
- qualification with supine bicycle **exercise testing during right heart catheterization**
  - elevated PCWP and gradient between PCWP and RA pressure
- all patients will be sedated and both arms will undergo femoral venous access
  - blinding will include sedation, earphones with music, and blindfolding, or the use of opaque screens to prevent viewing imaging screens
  - each site will assign blinded and un-blinded staff to facilitate unbiased patient assessments through 12 months of follow- up
- control patients who still meet inclusion criteria allowed to crossover to treatment at ≥12 months after the baseline procedure
- **30 day results presented as LBCT at AHA**

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Circ Heart Fail. 2016 Jul;9(7). pii: e003025. doi: 10.1161/CIRCHEARTFAILURE.116.003025.

Corvia Medical Clinical Study Pipeline

- Pilot study (n=11): non-randomized, single-arm
  - Completed (Søndergaard L, et al. Eur J Heart Fail 2014); extended follow-up ongoing
- CE Mark Study (n=64): non-randomized, single-arm
  - Completed (Hasenfuß Lancet 2016; Kaye Circ. HF 2016); 2Y follow-up complete Q3 2017
- REDUCE LAP-HF I (n=44): RCT mechanistic study
  - FDA approved IDE; (enrollment complete); 1Y follow-up complete Dec 2017
- **REDUCE LAP-HF II (n=380): 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