Transcatheter Intracardiac Shunt Device Provides Sustained Clinical Benefit at One Year in Heart Failure with Preserved or Mildly Reduced Ejection Fraction: The REDUCE LAP Heart Failure Trial

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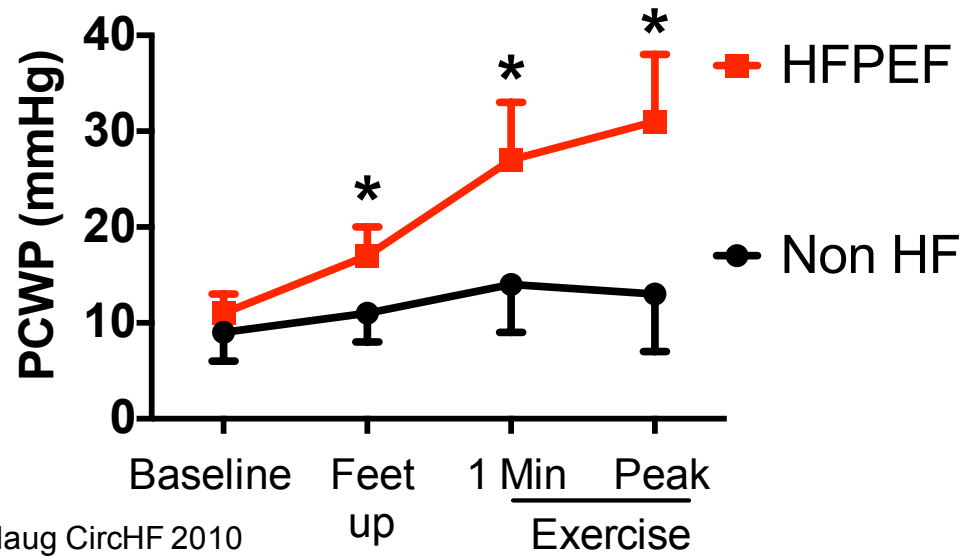
on behalf of the REDUCE LAP HF Investigators

Disclosures

DK is an unpaid member of the Corvia Medical, Inc. Scientific Advisory Group

Introduction

- Heart failure with preserved ejection fraction (HFPEF) has a complex pathophysiology and remains a therapeutic challenge.
- Elevated left atrial pressure, especially during exercise, is a near-universal finding in patients with HFPEF.



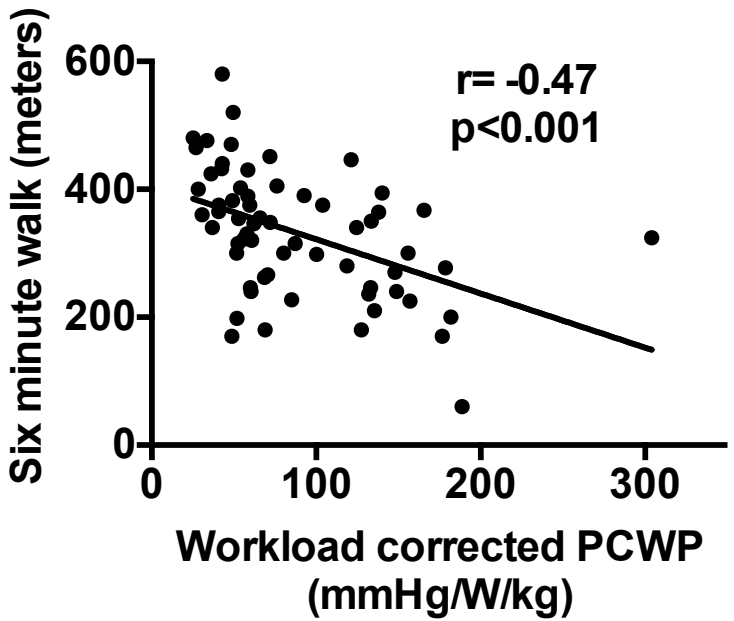
Borlaug CircHF 2010

Increased LV passive stiffness
Reduced active LV relaxation
Reduced LA compliance

Implications of Elevated LA Pressure in HFPEF

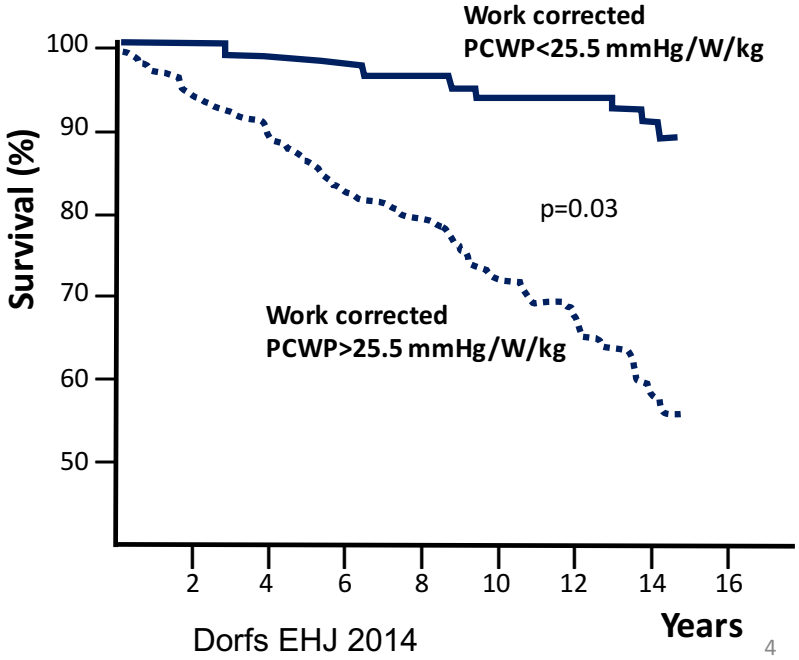
- The magnitude of the exercise - mediated rise in PCWP in HFPEF is related to both symptoms and outcome.

SYMPTOMS



REDUCE LAP-HF Unpublished data

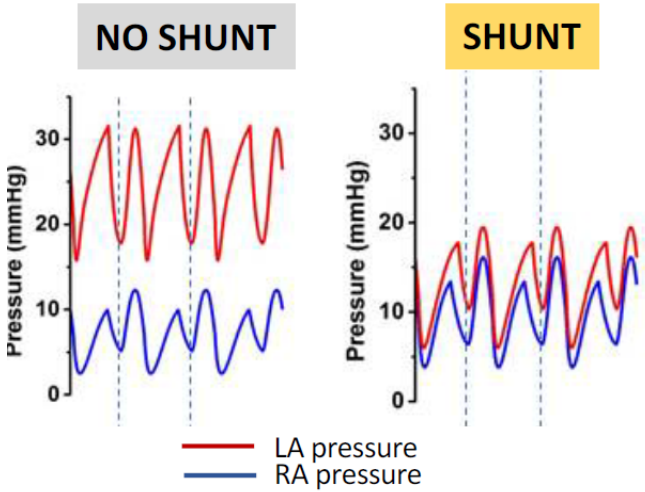
SURVIVAL

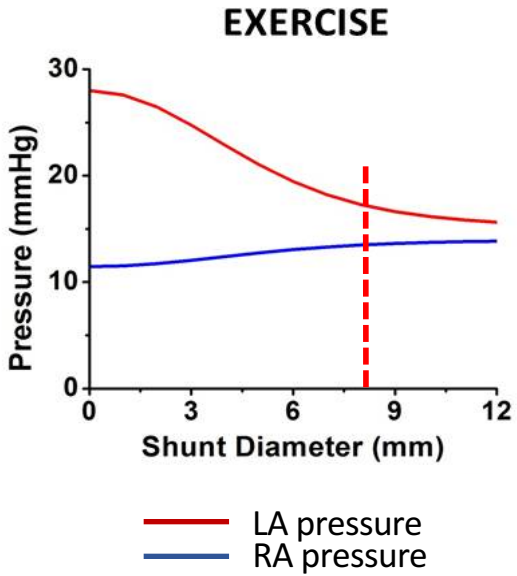


Dorfs EHJ 2014

Left Atrial Decompression: IASD Rationale

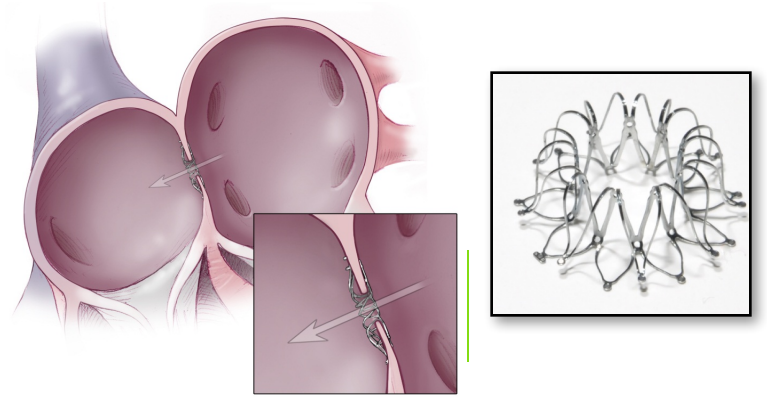
- Computer simulation demonstrated that an 8mm interatrial shunt device (IASD®) would provide acute LA decompression during exercise

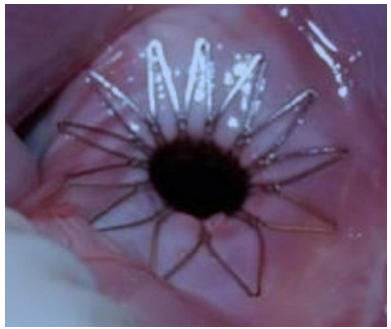


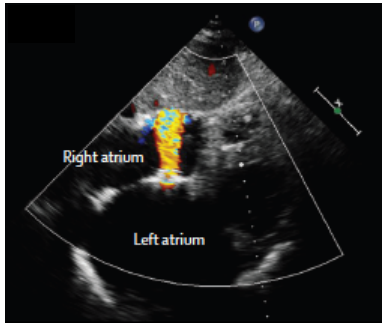


Kaye et al JCardFail 2014

InterAtrial Shunt Device - Mode of Action







Transcatheter interatrial shunt device

Elevated LV filling pressures (Elevated LAP)

Pulmonary Venous hypertension

Pulmonary Congestion & Dyspnea (rest/exercise)

REDUCE LAP-HF Trial

Inclusion Criteria (n=64):

Open label

LVEF ≥ 40%,

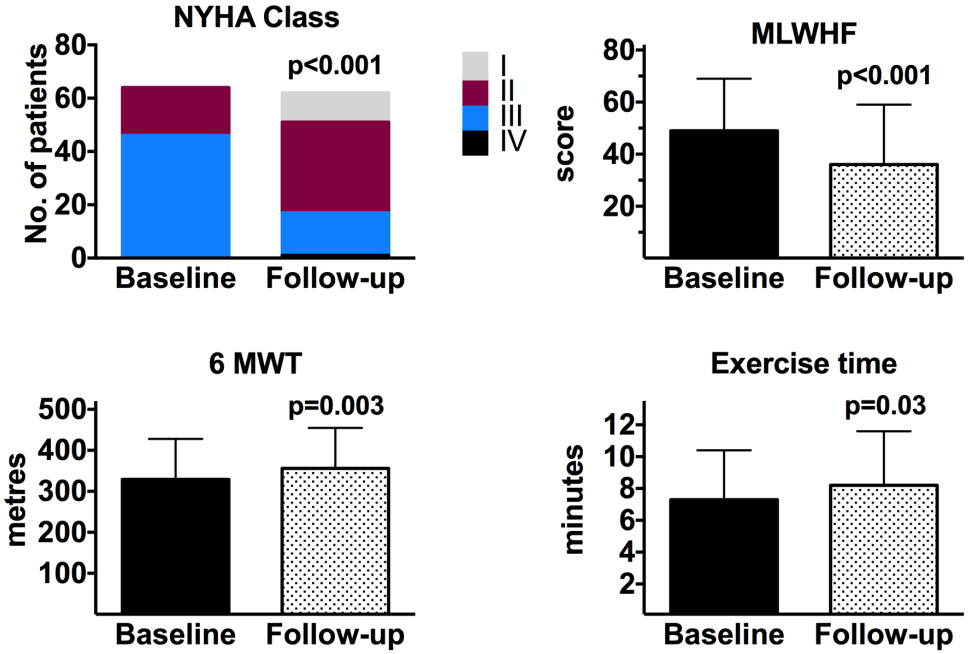
NYHA class II-IV

Elevated PCWP

≥ 15 mmHg (rest) or

≥ 25 (supine bicycle exercise)

6 month outcomes



& reduced exercise PCWP

Hasenfuß G et al: Lancet 2016; 387: 1298–304

One year REDUCE LAP-HF OUTCOMES

TheAlfred

Objective & Methods

- To assess **device safety** (major adverse cardiac, cerebrovascular and systemic embolic events -MACCE), and **device performance** one year post implant.
  - device performance: shunting (echocardiography)
- To evaluate **persistence of clinical benefit**:
  - clinical efficacy: NYHA class, quality of life (MLWHFQ), 6MW distance
  - cardiac structure and function (echocardiography)
  - rest and exercise hemodynamics (optional sub-study, n=18)
    - oximetry to assess Qp:Qs (n=13)
- Study monitored by independent CEC and DSMB

Baseline Characteristics (n=64)

Age (Y)	69±8
Gender (% Female/Male)	66 / 34
LVEF (%)	47 ± 7
NYHA Class (n, II/III/IV)	18/46/0
Minnesota Living with HF Score	49 ± 20
BMI kg/m^2	33 ± 6
Permanent AF (%)	36
NT-Pro BNP (median, IQR pg./ml)	377 (222-925)
Hypertension (%)	81
Diabetes (%)	33
Coronary artery disease (%)	36
Diuretics at baseline (%)	91
Resting CVP (mm Hg)	9 ± 4
Resting PCWP (mm Hg)	17 ± 5

TheAlfred

Safety (MACCE) and Device Performance

MACCE event	Six months %	One year %
Death	0	4.7 (3/64)
Stroke	0	1.5 (1/64)* (pt died)
MI	0	0
Systemic embolic event	0	0
Implant removal	0	0

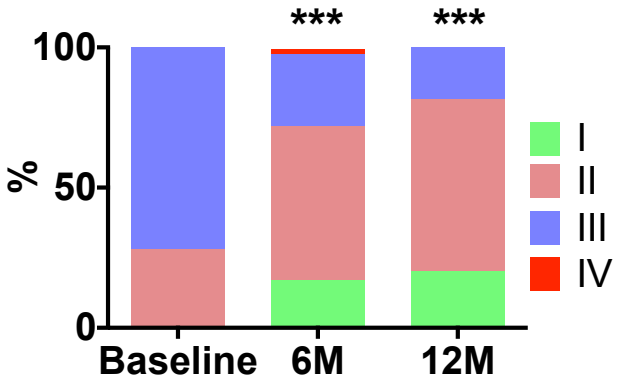
Effectiveness	Six months %	One year %
L→ R Shunt flow (Echo)	100 (49/49)	100 (48/48)
R→ L Shunt flow (Echo)	0	0
Qp:Qs	1.27 ± 0.24	1.28 ± 0.25

Device patency confirmed in 54 subjects (by echo or oximetry)

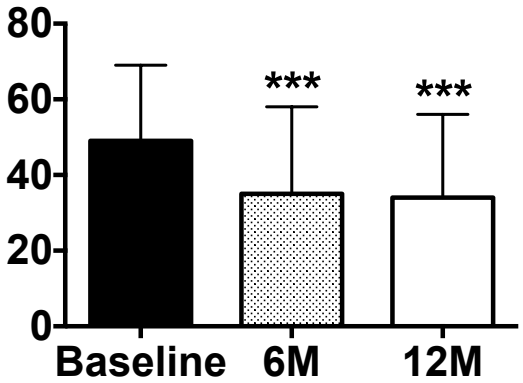
Sustained Clinical Efficacy

Patients with data at all 3 time points.

NYHA Class

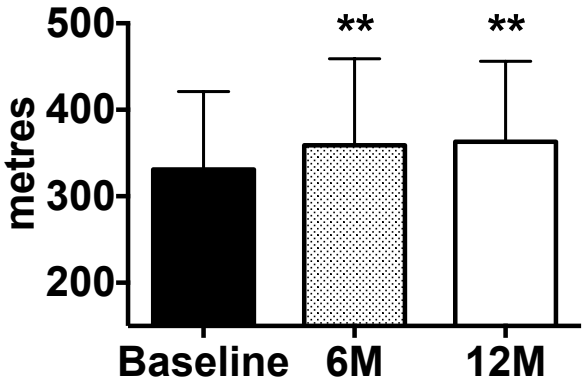


MLWHF Score



Mean Δ at 1 year: 15 points

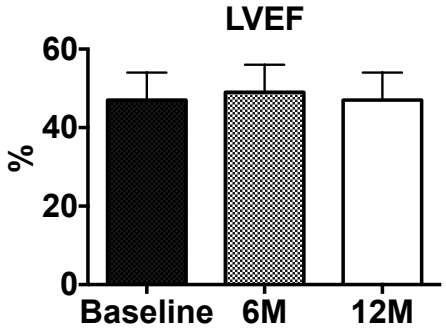
6MWD

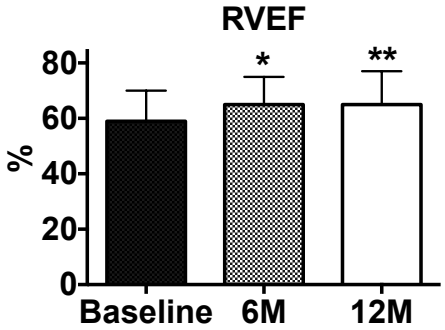


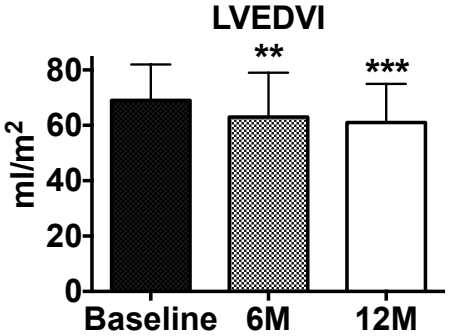
Mean Δ at 1 year: 33m

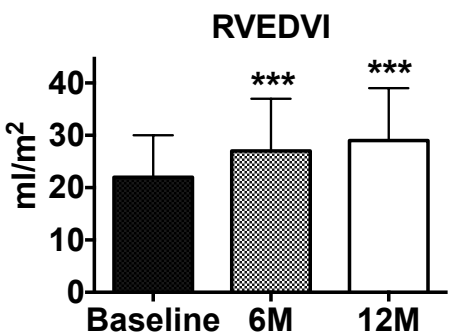
RM-ANOVA with Bonferroni post hoc:
**p<0.01, ***p<0.001

Echocardiographic Results









*p<0.05, **p<0.01, ***p<0.001

No change in atrial volumes

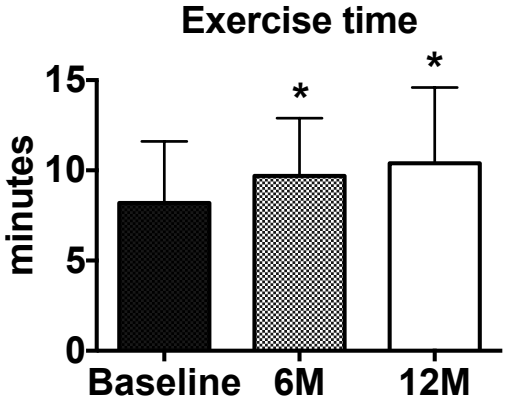
Invasive Hemodynamic Results (rest)

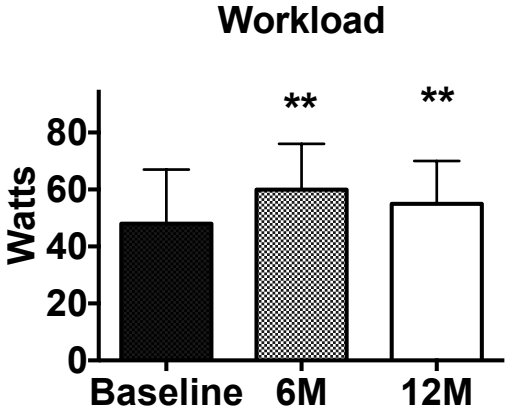
	Baseline	Six months	One year
RA pressure	8 ± 3	11 ± 6	10 ± 4
PA_{mean} pressure	25 ± 8	23 ± 7	26 ± 8
Wedge pressure	19 ± 6	16 ± 8	17 ± 6
Cardiac output	5.2 ± 1.3	6.3 ± 1.4**	6.7 ± 1.8**

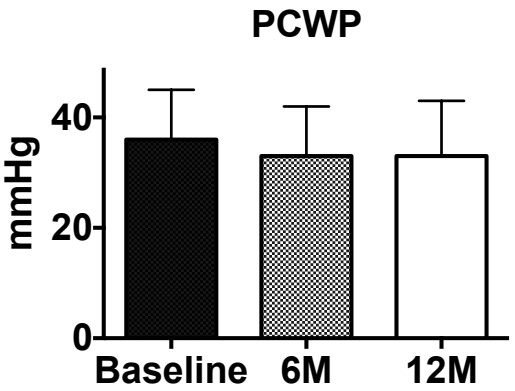
Patients with data at all 3 time points.

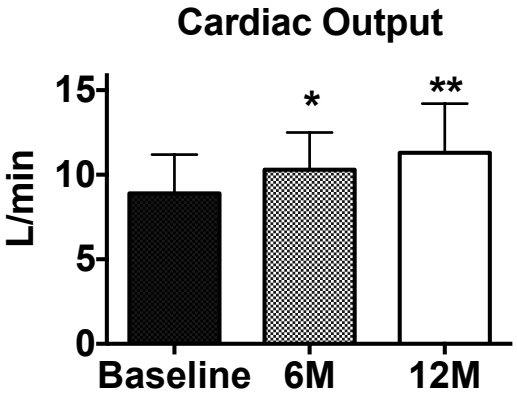
** $p<0.01$ vs baseline

Exercise Hemodynamic Results-1



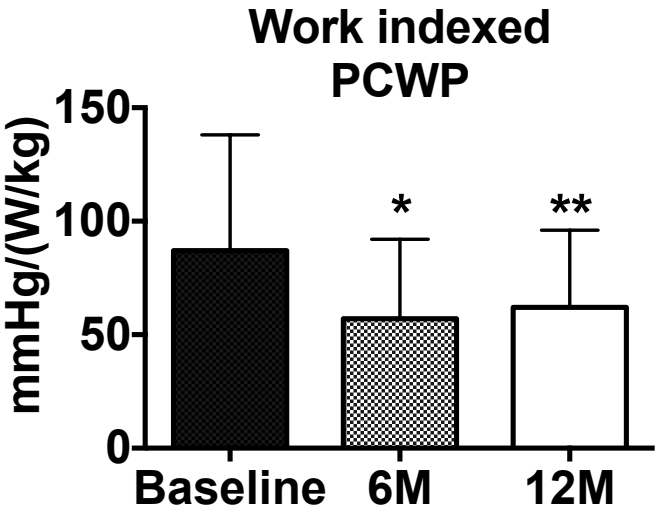






* p<0.05, ** p<0.01 vs baseline

Exercise Hemodynamic Results-2



IASD therapy provides increased work capacity for a given LA pressure

* p<0.05, ** p<0.01 vs baseline

Summary and Conclusions

- Implantation of an interatrial shunt device appears to be safe with an acceptable MACCE rate through one year of follow-up.

- Interatrial shunt device patency was maintained through one year

- The clinical and hemodynamic benefit observed 6 months after implant was sustained through one year, with no evidence of adverse sequelae
  - Meaningful improvements in NHYA class, exercise capacity and QOL
  - Clinically meaningful reduction in normalized PCWP

- Randomised trials are required and ongoing to determine the value of this novel strategy for the management of HFPEF.

Back-up

Clinical Efficacy

Parameter*	Baseline	Six months	One year
NYHA class (60)	2.7 ± 0.5	2.1 ± 0.7 $p < 0.001$	2.0 ± 0.6 $p < 0.001$
MLWHF score (59)	49.1 ± 20.1	35.1 ± 23 $p < 0.001$	34 ± 33 $p < 0.001$
6MWT (m) (55)	331 ± 90	359 ± 100 $p < 0.01$	364 ± 92 $p < 0.01$

* Patients with data at all 3 time points.
RM-ANOVA with Bonferroni post hoc