Interatrial Shunting for Heart Failure

THE V-WAVE SHUNT

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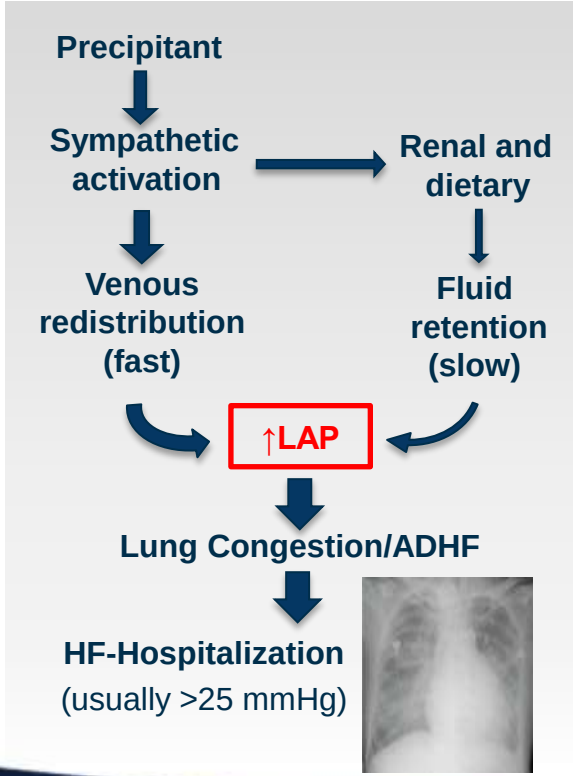
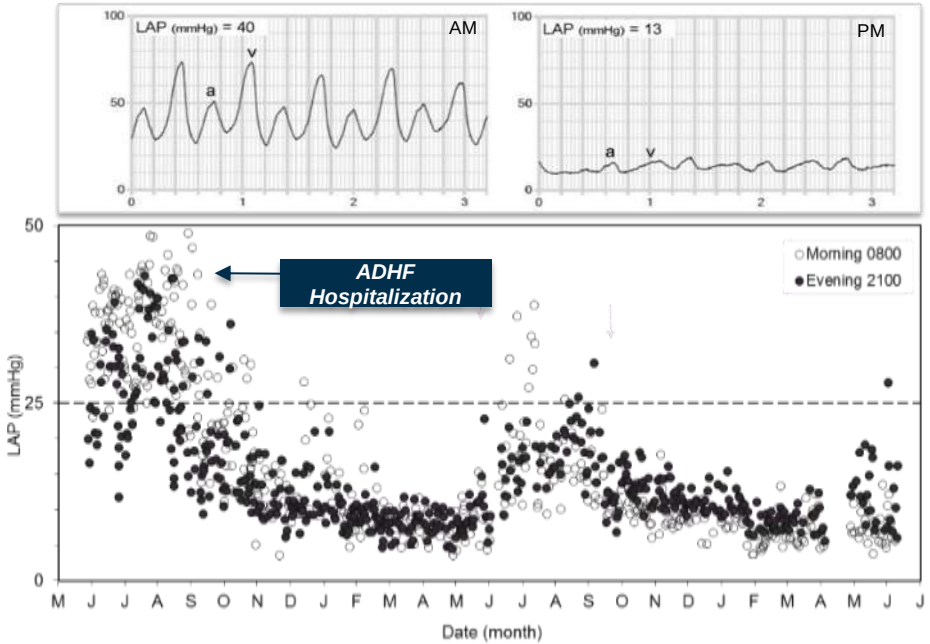
Disclosures

- **Consultant to V-Wave**

Elevated LAP is the Proximate Cause of Lung Congestion in ADHF

Insights from implantable hemodynamic monitoring





Single day

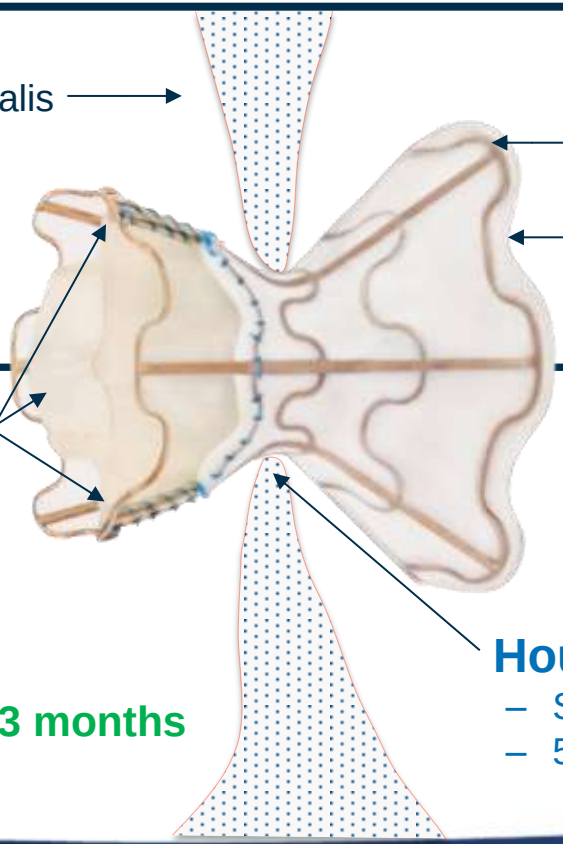
Case study

2 years

LAP is often highly variable over the course of a day. Sustained elevations precede clinical events, averaging >25 mmHg for several days before admission or death.

Ritzema J et al. Circulation 2010;121:1086-95

Legacy V-Wave Valved Interatrial Shunt



14F delivery system

Porcine pericardial leaflets
- To prevent R-to-L shunt and paradoxical emboli

Hourglass shape
- Secure and atraumatic retention
- 5.1 mm orifice, Venturi efficiency

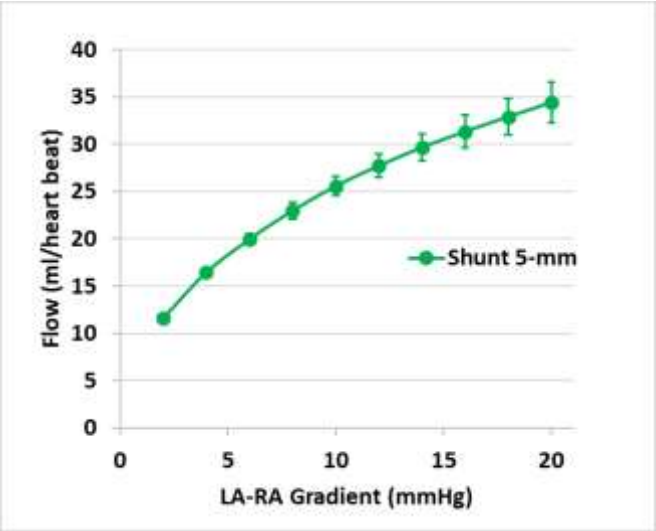
• **Anticoagulation for 3 months**

Shunt Mechanism of Action

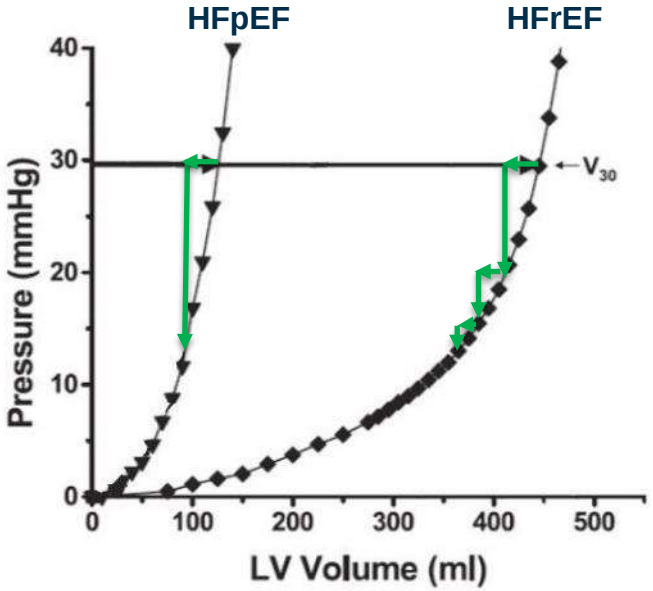
A small shunt lowers LAP in HFpEF & HFrEF by reducing LVEDV.
Shunt "auto-regulates" – shunt flow increases when LAP rises.

Shunt Flow

5.1-mm shunt at HR 65 bpm



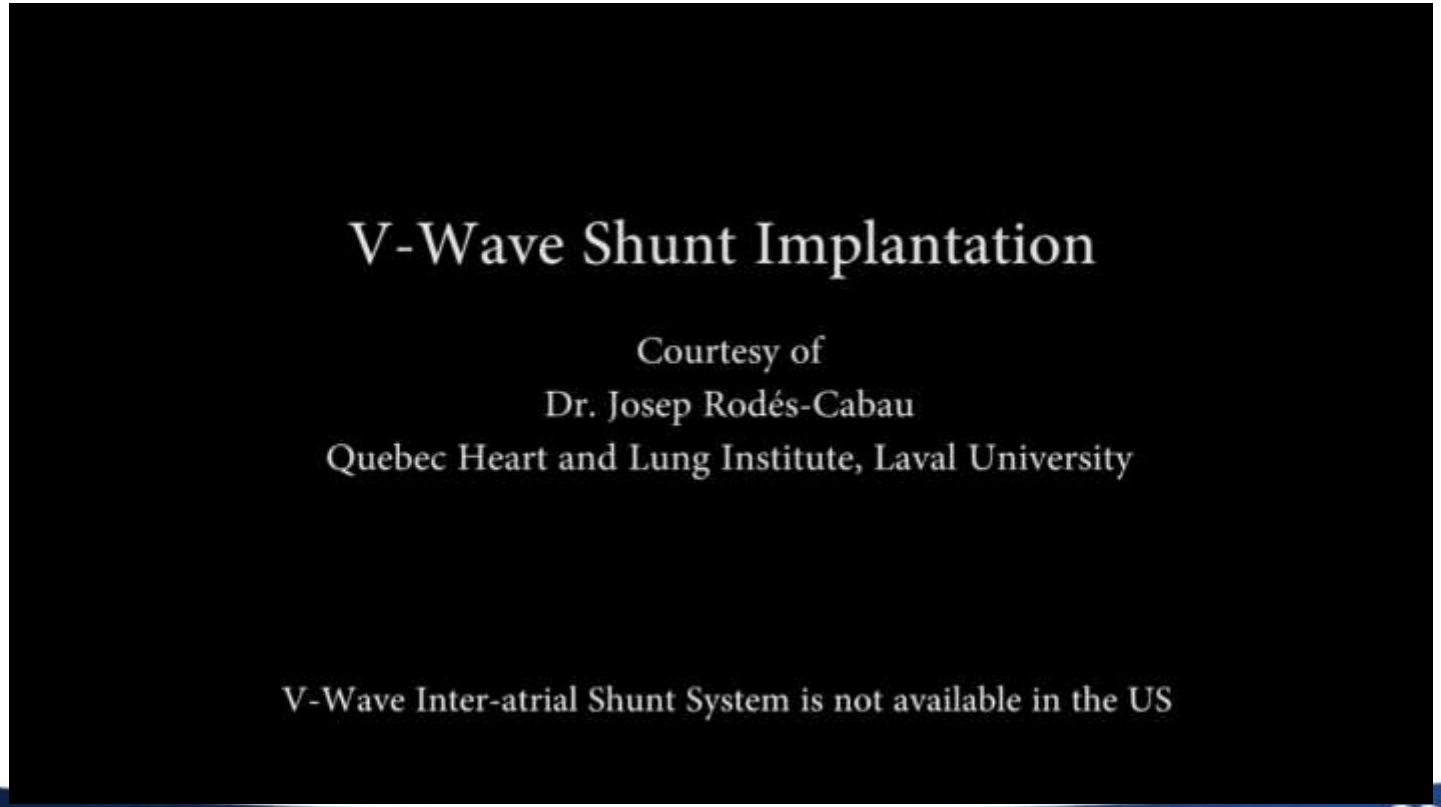
LV Diastolic Filling Curves



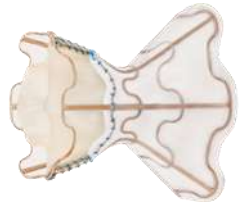
Burkhoff D et al. Am J Physiol Heart Circ Physiol 2005;89:H501-12

V-Wave Shunt Procedure

Transseptal approach with TEE/ICE guidance



V-Wave Human Feasibility Studies



Eligibility Criteria

Major Inclusion Criteria

- Chronic HF, ischemic or non-ischemic etiology
- HFrEF and HFpEF
- NYHA class III or ambulatory class IV
- On GDMT and device therapies
- HF-hospitalization or elevated BNP/NT-proBNP

Major Exclusion Criteria

- Isolated right-sided HF
- Moderate-severe RV dysfunction
- Severe pulmonary hypertension

38 Patients Implanted

Special Access Program (compassionate use)
- 22 patients enrolled at 1 center in Canada
  - 16 HFrEF, 6 HFpEF

First-In-Human Multicenter Feasibility Study
- 16 patients enrolled at 5 centers in Israel and Spain
  - 14 HFrEF, 2 HFpEF

Total 38 pts (30 HFrEF, 8 HFpEF)
All completed 12-month follow-up

Baseline Patient Characteristics (Compared to CHAMPION)

		V-Wave (SAP + FIM) (n=38)	CHAMPION (n=550)
Clinical parameters	Age, years	66 ± 9	62 ± 13†
	Male gender, %	92	73†
	Body mass index, kg/m^2	30 ± 6	31 ± 7
	NYHA class, %	III (97), IV (3)	III (100)
	Ischemic Cardiomyopathy, %	76	60†
	DM / HTN / AFIB, %	68 / 84 / 53	49†/ 78/ 46
	ACEi-ARB / BB / MRA / DIUR, %	78 / 100 / 75 / 94	76 / 89 / 43 / 92
	ICD / CRT, %	74 / 39	68 / 35
	eGFR , mL•min^{-1}•1.73 m^{-2}	53 ± 20	61 ± 23†
Echocardiographic / Hemodynamic	Frequency EF ≥ 0.40, %	21.1	21.6
	LVEF HFrEF / HFpEF	26 ± 7 / 50 ± 9	23 ± 7 / 51 ± 1
	PCWP, mmHg	21 ± 6	18 ± 8†
	RAP, mmHg	8 ± 4	-
	PAP systolic, mmHg	44 ± 11	45 ± 15
	PVR, Wood Units	2.8 ± 1.6	2.8 ± 1.9
	Cardiac Index, L•min-1•m^{-2}	2.2 ± 0.4	2.3 ± 0.7
	6-Minute walk, m	290 ± 112	
	NT-proBNP, pg/ml	2640 ± 2301	

† P<0.05

Abraham W et al. CHAMPION trial. Lancet 2016;387:453-61

Outcome Measures

Procedural success = 38/38 (100%)

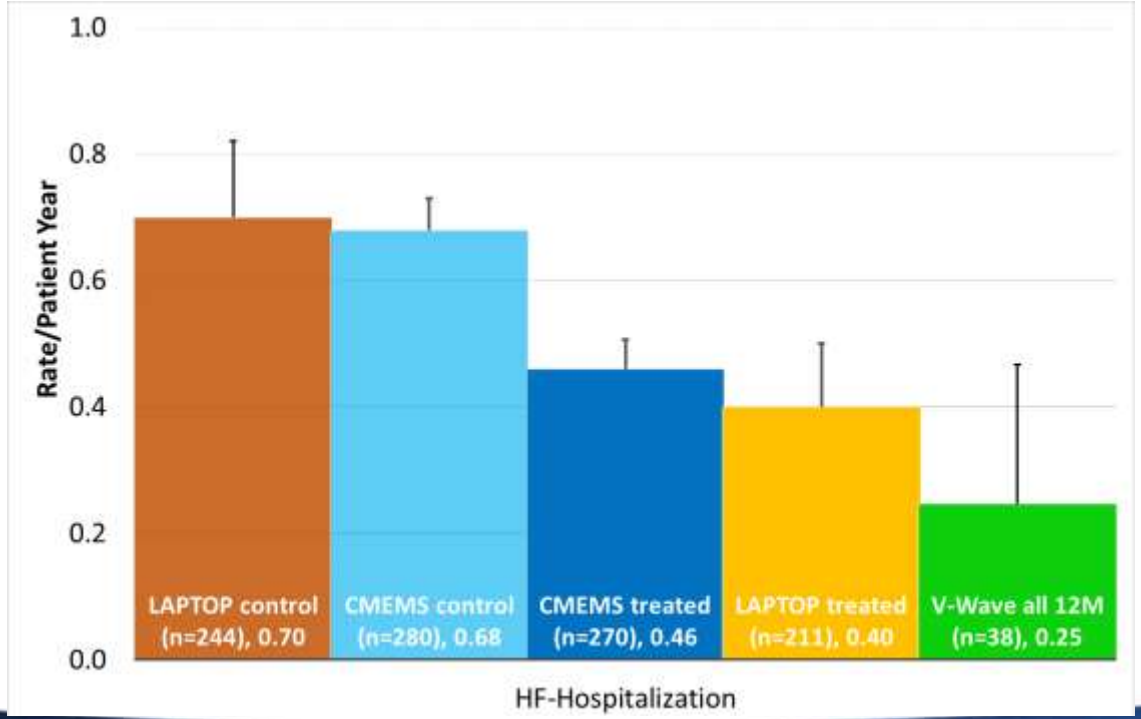
- No device malpositioning, dislodgement, embolization, replacements
- Procedure time = 72 ± 24 min (*includes: TEE, RHC, transseptal, shunt placement, all study measurements)*
- Median LOS: 2 days (IQR: 1-3)

Safety (12-month FU)

- Device- or procedure-related major adverse cardiac and neurological events (MACNE) in 1 pt (2.6%)
  - 1 cardiac tamponade (pericardiocentesis)
  - 0 deaths, strokes, MIs, or device embolizations
- All-cause MACNE in 3 pts (7.9%)
  - 2 deaths (CV, non-device-related)
  - 1 procedural tamponade
  - 0 strokes or MIs

V-Wave HF-Hospitalization Rates

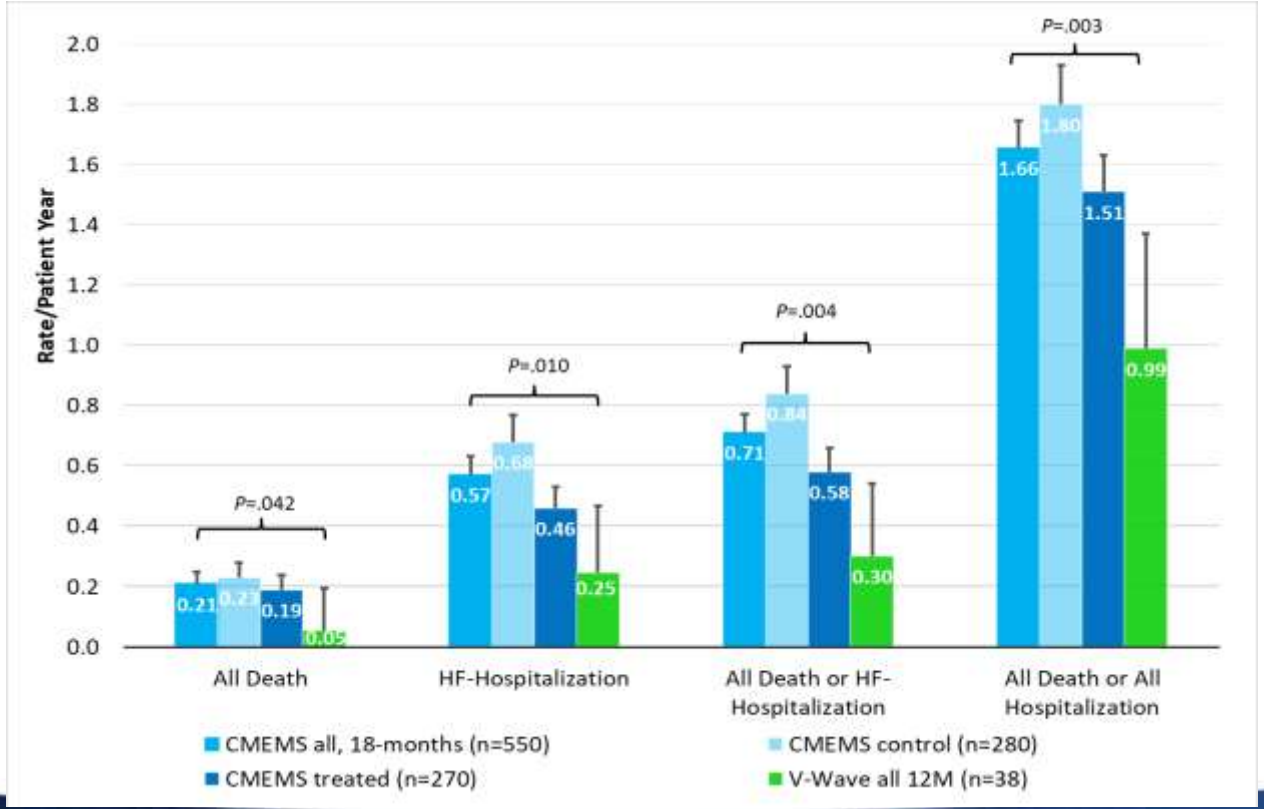
Comparison with outcomes from implantable hemodynamic monitoring trials with similar HF populations



Abraham W et al. CHAMPION trial. Lancet 2016;387:453-61
Abraham W et al. LAPTOP-HF trial. HFSA 2015

HF-Hospitalization, Mortality and All-Cause Hospitalization

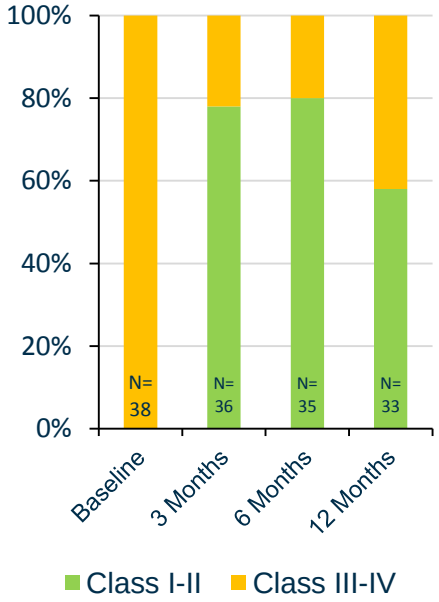
Comparison to CHAMPION control and treatment arm populations



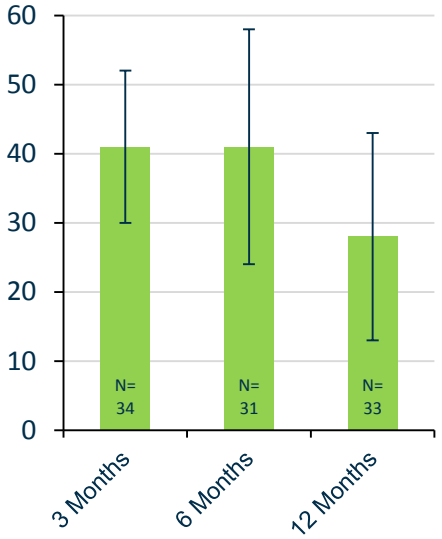
Abraham W et al. CHAMPION trial. Lancet 2016;387:453-61

Improvement in Functional Endpoints

NYHA Class*



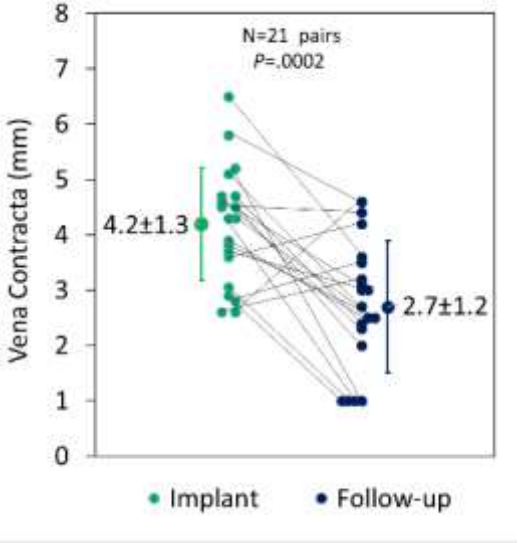
6MWT Change (m)*

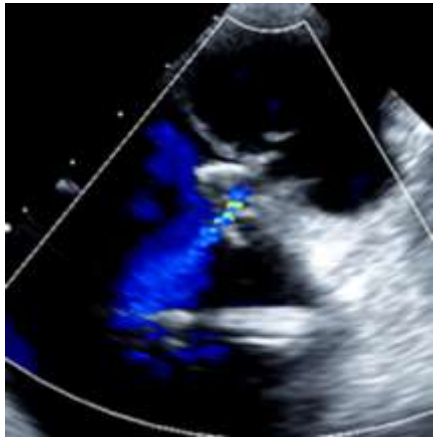


*p<0.04 (baseline vs. follow-up)

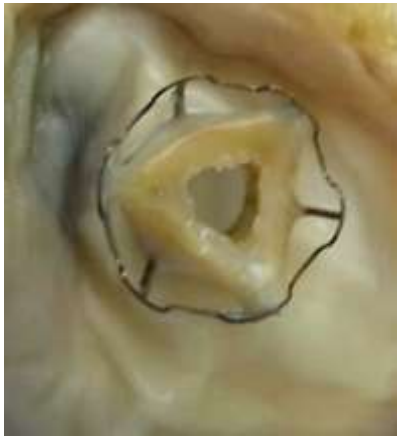
Legacy V-Wave Shunt: Valve Function at 1 Year

- Absence of L-R shunt flow was observed in 5/36 (14%) surviving patients
- Color Doppler vena contracta jet in the valve region was narrowed or skewed off-axis in 13/36 (36%) pts
- Qp:Qs 1.17 ± 0.12 at implant fell to 1.10 ± 0.13 at 1 year (*P*=0.04)
- Bioprosthetic leaflets developed neointimal proliferation (pannus) with thickening, commissural fusion, fixation and stenosis - not associated with acute deterioration or thromboembolic events



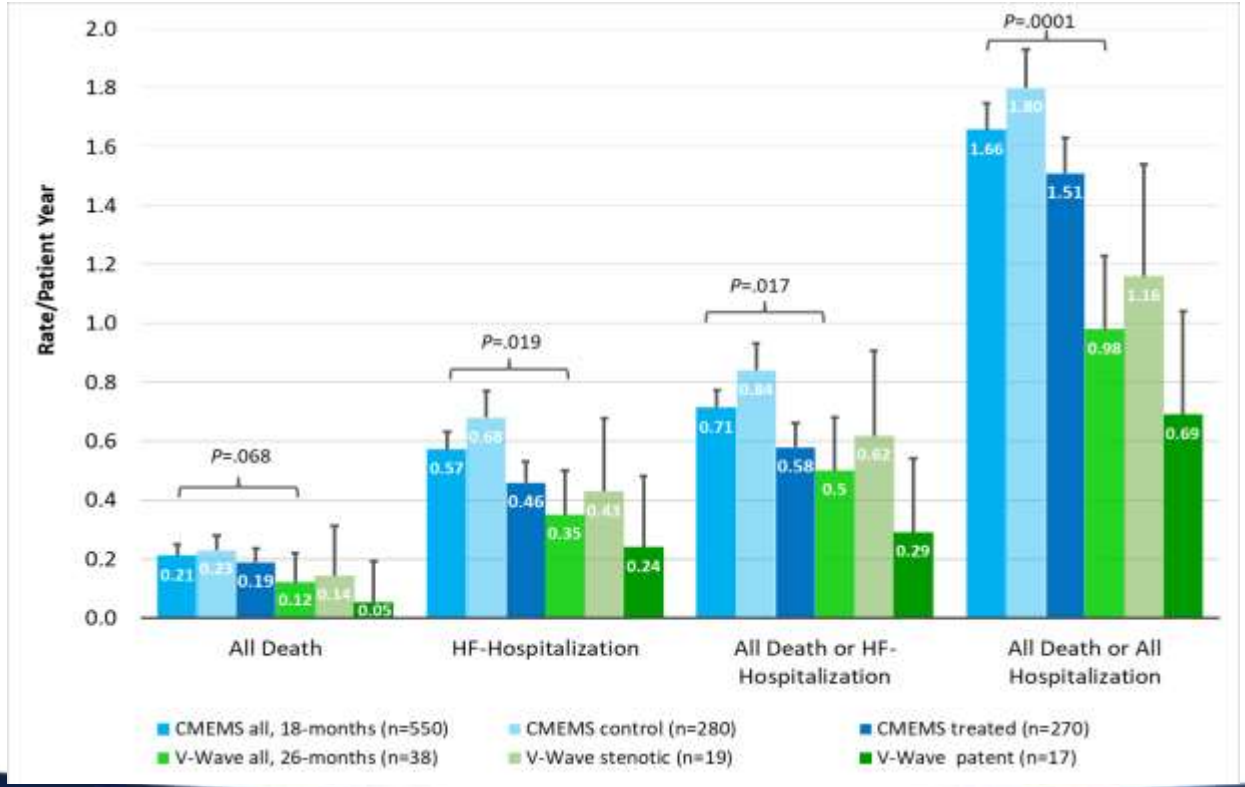


TEE L-R jet narrowed and skewed through valve



2.5 yr explant specimen from transplanted pt. Neck orifice widely patent. Pannus thickening and stenosis of bioprosthetic leaflets.

Widely Patent Shunts were Associated with Reduced Mortality and Hospitalizations (mean 26-month FU)

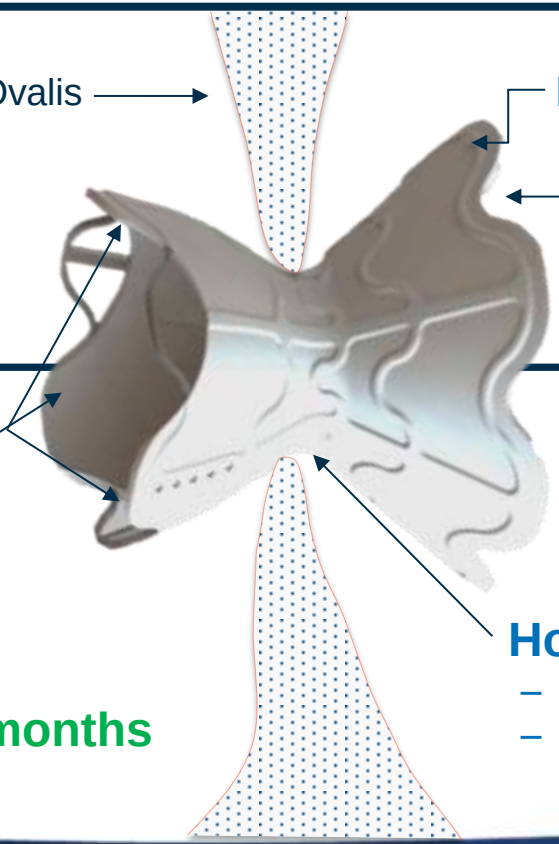


Patients with patent shunts were higher risk at baseline:

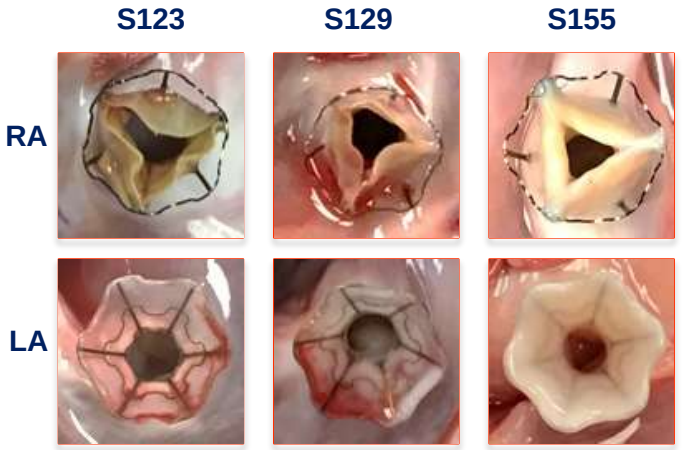
- *Older*
- *Worse comorbidity profile*
- *Reduced exercise capacity*
- *Lower LVEF*
- *Worse hemodynamics*

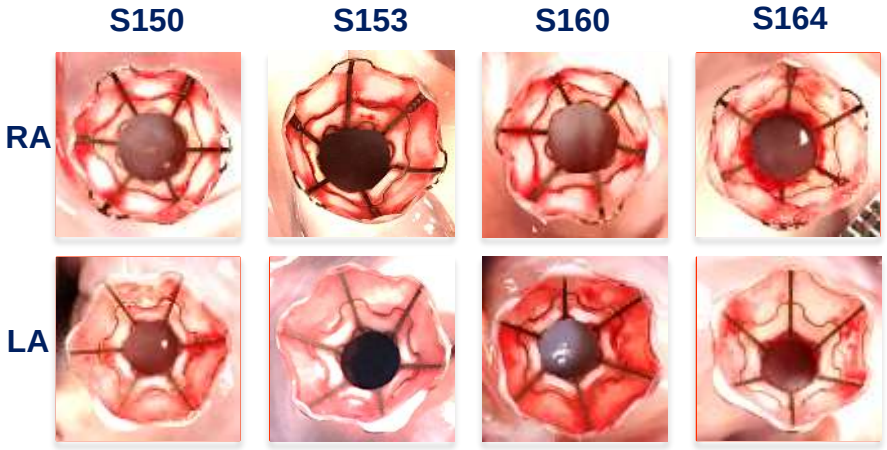
Abraham W et al. CHAMPION trial. Lancet 2016;387:453-61

Generation 2: V-Wave Interatrial Shunt



Gen 2 Shunts were Superior to Legacy Valved Shunts in Pre-clinical Ovine Models with Normal Physiology (2-3 mmHg L-R gradient)





Valved Shunts at 3 months

Pannus infiltration of bioprosthetic leaflets with shunt narrowing/obstruction by 3 months in 11/12 shunts.

Gen 2 Shunts at 6 months

30/30 (100%) Gen 2 shunts had no late lumen loss at up to 6 months. Anticoagulation and DAPT regimens tested. No device thrombus and no downstream thromboemboli were seen.

RELIEVE-HF Pivotal RCT

Design

- Sham-controlled, blinded (patient and HF team), adaptive design
- ~400 randomized + ~120 roll-in patients at 60 sites (40 US + 20 OUS)

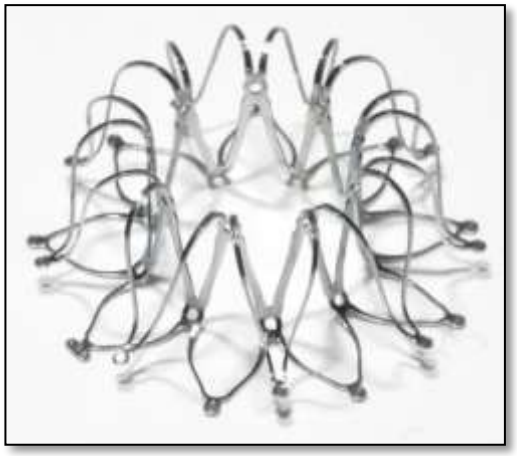
Population

- NYHA class III or ambulatory class IV on GDMT (eligibility committee review)
- HFrEF or HFpEF – no specific LVEF criteria
- Hospitalization for worsening HF within 1 year or elevated BNP/NT-proBNP

Outcome Measures

- Primary Effectiveness: Hierarchical comparison of mortality, transplant, LVAD, HF hospitalization, and 6MWD using Finkelstein-Schoenfeld / Win Ratio
- Primary Safety: Device-related MACNE at 30 days (performance criteria)
- Health economic metrics

Inter-atrial Shunts for Heart Failure
Pivotal RCTs



V-Wave

RELIEVE-HF
in HFrEF and HFpEF
N=400

PIs: GW Stone, S. Anker, J. Lindenfeld, J. Rodes-Cabau,

Corvia

REDUCE LAP-HF II
in HFpEF
N=380

PIs: S. Shah and T. Feldman