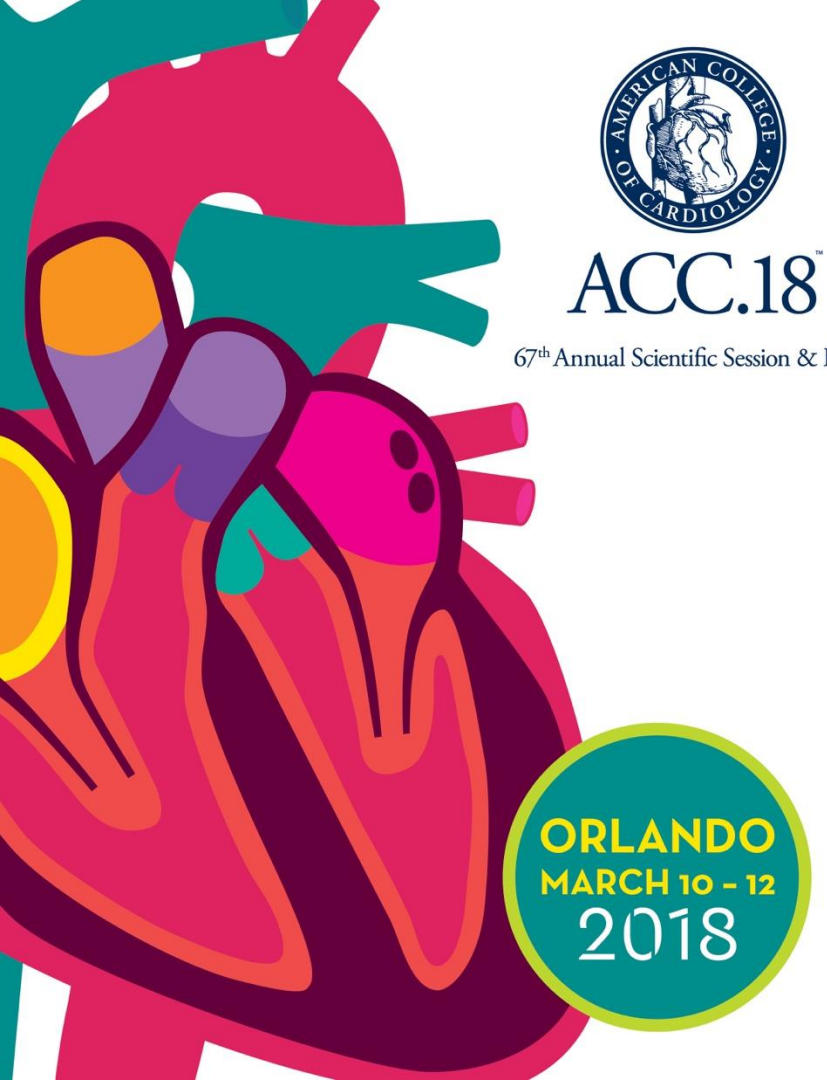


ACC.18

67th Annual Scientific Session & Expo

ORLANDO
MARCH 10 – 12
2018

Interatrial Shunting for Treating Heart Failure: Early and Late Results of the First-in-Human Experience With the V-Wave Interatrial Shunt System

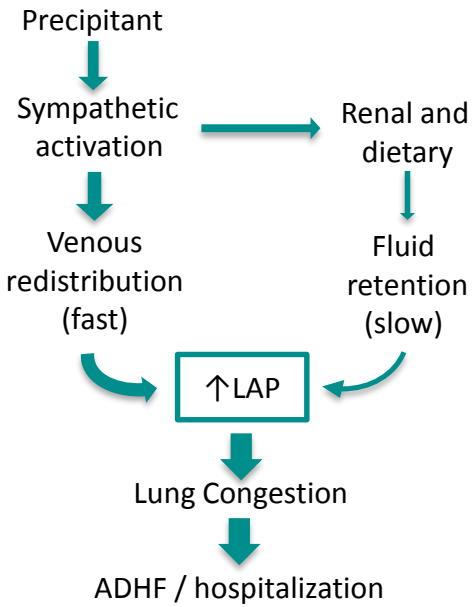
Josep Rodés-Cabau, MD, FACC
Quebec Heart & Lung Institute, Laval University

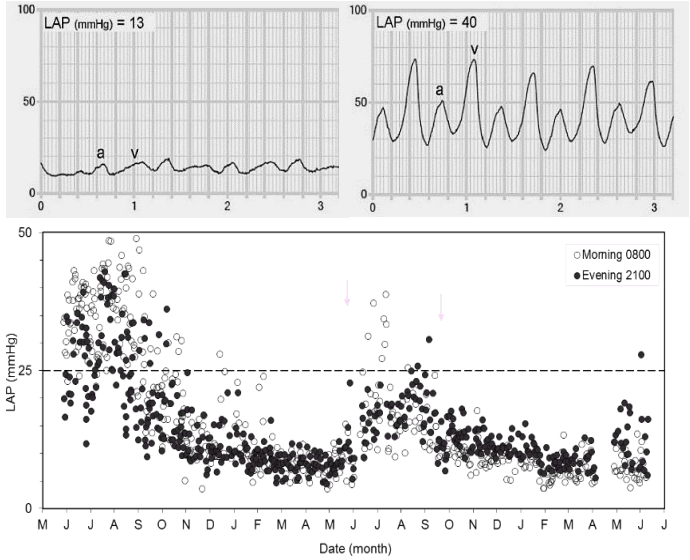
on behalf of V-Wave's FIM/SAP Investigators

Disclosures

- Consultant for and institutional research grants from V-Wave Ltd.

Elevated LAP: The Cause of Lung Congestion in ADHF

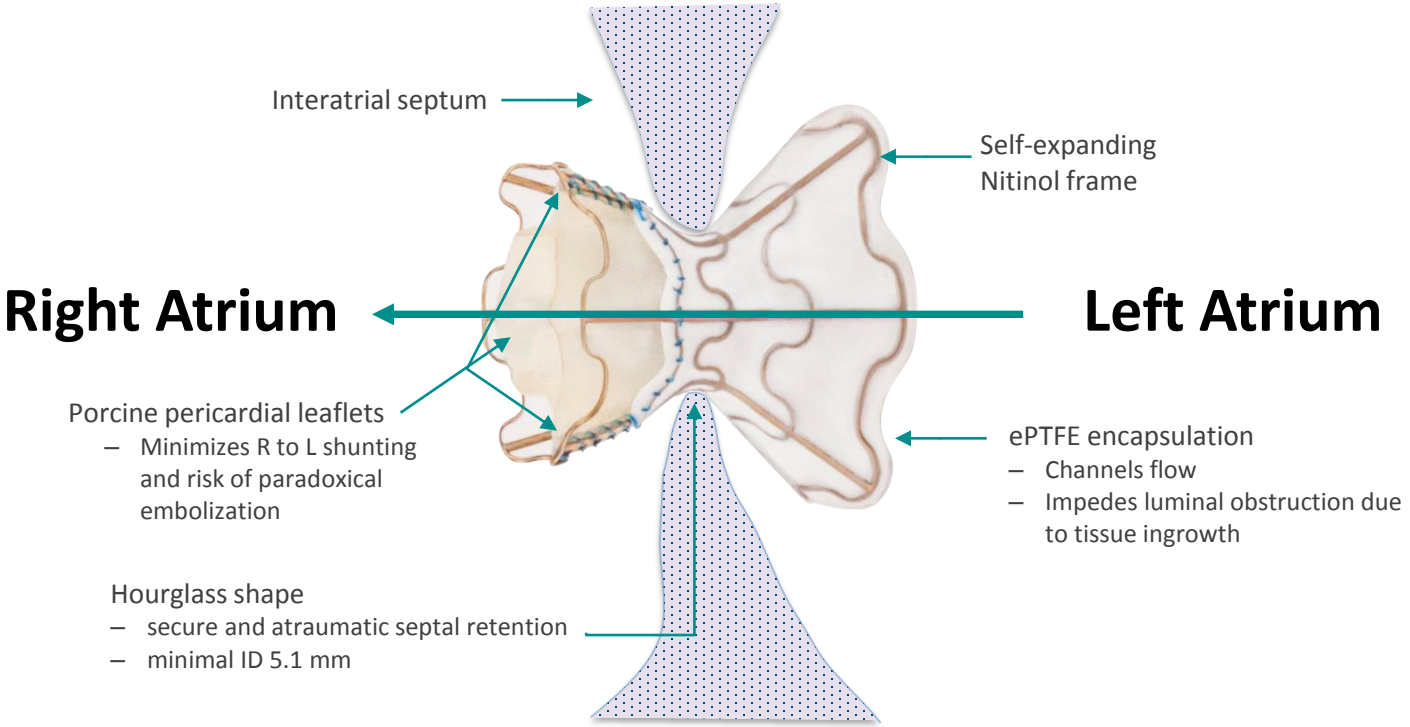




- LAP often highly variable over the course of a day
- Increase of LAP precedes clinical events, averaging >25 mmHg for several days before admission or death

HOMEOSTASIS: Ritzema. Circulation 2010

The V-Wave Shunt



Objective

- First-in-human prospective multicenter open-label experience to assess the feasibility, safety and exploratory efficacy of interatrial shunting with the V-Wave system for patients with heart failure (reduced and preserved left ventricular ejection fraction)

Outcomes

- **Primary**
  - *Safety*: device/procedure-related major adverse cardiovascular and neurological events (MACNE), defined as death, stroke, device embolization, pericardial effusion requiring intervention, re-intervention or surgery at 3- and 12-month follow-up
  - *Procedural success*: successful device implantation with no periprocedural death

- **Secondary**
  - *Safety*: all-cause MACNE, all serious adverse events (SAEs) and serious adverse device effects (SADEs)
  - *Exploratory efficacy*: changes in NYHA Class, quality of life, and 6MWT distance at 3- and 12-month follow-up

Main Inclusion/Exclusion Criteria

Inclusion Criteria

- Chronic HF of ischemic or non-ischemic etiology, HFrEF or HFpEF
- NYHA Class III or ambulatory Class IV
- On guideline driven maximally tolerated medical and device therapy
- HF-hospitalization in the prior 12 months or elevated NT-proBNP

Exclusion Criteria

- LVEF<15%
- Isolated right-sided HF
- Moderate-severe RV dysfunction
  - TAPSE < 11mm
- Severe pulmonary hypertension
  - PASP > 70mmHg
- Stroke or thromboembolism past 6 months
- eGFR < 25mL·min^{-1}·1.73m^{-2}

Procedures and Assessments

- Procedures/Follow-Up
  - Transfemoral venous approach, general anesthesia, TEE guidance
  - Anticoagulation for at least 3 months
  - Study follow-up (1, 3, 6, 12m and yearly to 5 y)

- Assessments
  - NYHA Class
  - 6MWT
  - Quality of Life (KCCQ, MHLF)
  - Right heart cath (3, 12m)
  - NT-proBNP
  - TTE
  - TEE (1-3, 12m)

Patient Population

SAP	**S**pecial **A**ccess **P**rogram 22 patients enrolled at 1 center in Canada
FIM	**F**irst-**I**n-**M**an Multicenter Feasibility Study 16 patients enrolled in 5 centers in Israel and Spain
Follow-up	38 patients implanted (30 HFrEF, 8 HFpEF) 28 month median follow-up (Range 18-48 months)

Baseline Demographics

Variable	Patients (n=38)
Demographics	
Age, years	66±9
Male gender	35 (92)
Body mass index, kg/m2	30±6
Medical history	
NYHA class, %	III (97), IV (3)
Ischemic cardiomyopathy)	30 (79)
Myocardial infarction	26 (68)
Atrial fibrillation	20 (53)
Hypertension	32 (84)
Diabetes	26 (68)
Chronic kidney disease	23 (61)
Stroke	4 (11)
Treatment history	
ACE/ARB, : mg enalapril eq.	27 (71): 21±18
β Blocker, : mg carvedilol eq.	38 (100): 30±19
MRA, : mg spironolactone eq.	26 (68): 15±6
Loop Diuretic, : mg furosemide eq.	33 (87): 123±135
CRT-D or ICD	28 (74)
CRT	15 (39)

Variable	Patients (n=38)
Laboratory / Echocardiography	
eGFR, $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$	54 ± 20
NT-proBNP, pg/ml	2640 ± 2301
Ln NT-proBNP, pg/ml	7.5 ± 0.9
LVEF ≥ 0.40	21.1
LVEF, % (HFrEF)	26 ± 7
LVEF, % (HFpEF)	50 ± 9
6-Minute Walk Distance, m	289 ± 112
Hemodynamics	
Systolic BP, mmHg	116 ± 19
Diastolic BP, mmHg	66 ± 9
Heart Rate, bpm	69 ± 9
Pulmonary wedge pressure, mmHg	21 ± 5
Right atrial pressure, mmHg	8 ± 4
Pulmonary artery systolic pressure, mmHg	44 ± 11
Pulmonary artery mean pressure, mmHg	30 ± 7
Pulmonary vascular resistance, Wood Units	2.8 ± 1.6
Cardiac output, L·min-1	4.4 ± 0.9
Cardiac index, L·min-1·m-2	2.2 ± 0.4

Procedural and Safety Outcomes

- Shunt successfully implanted in 38/38 patients.
- Device or procedure related MACNE at 3M and 12M: 2.6%.
- All cause MACNE at 12M: 7.9%.

	Patients (n=38)
PROCEDURAL/IN-HOSPITAL	
Successful device implantation	38 (100)
Shunt patency at procedural TEE	38 (100)
Device embolization/dislocation	0
Need for a 2nd device	0
Procedural time, min	72 ± 24
Hospitalization days (median, IQR)	1, 1-2
Device/procedure-related MACNE	
Cardiac tamponade	1 (2.6%)

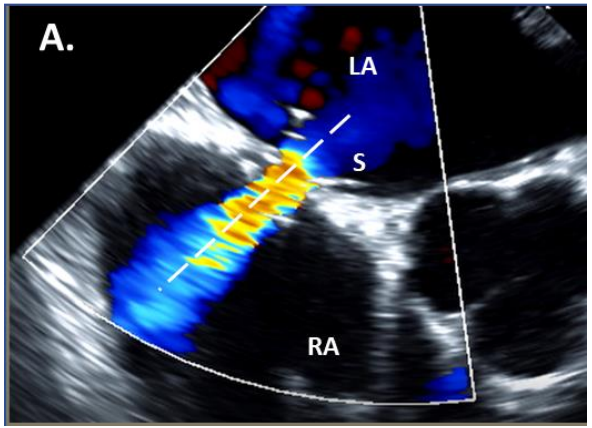
SAFETY OUTCOMES (full 12-month follow-up)	
Cumulative device/procedure-related MACNEs	
Death	0
Stroke	0
Cardiac tamponade	1 (2.6)
Device embolization	0
Device infection	0
Reintervention or surgery	0
Overall device/procedure-related MACNE	1 (2.6)
Cumulative all-cause MACNEs	
Death	2 (5.2)
Stroke	0
Systemic embolism	0
Ventricular tachycardia	1 (2.6)
Myocardial infarction	0

Functional, Echo and Hemodynamic Parameters

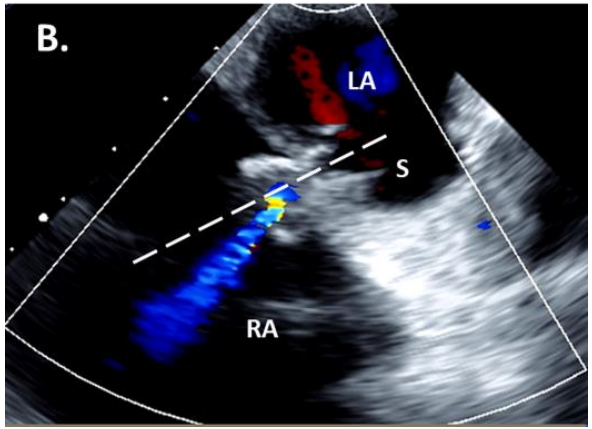
Variable	Baseline (n=38)	3 Months (n=36)	12 months (n=36)	*p-value
Functional Status/Quality-of-Life				
NYHA III-IV	38 (100)	8 (22)	14 (39)	<0.001
NYHA I-II	0 (0)	28 (78)	22 (61)	
KCCQ/MLHFQ (improve ≥5 points)	-	27 (74)	26 (73)	<0.001
6-MWT (m)	290±112	340±94	324±105	0.012
Laboratory parameters				
Ln NT-pro BNP (pg/mL)	7.5 ± 0.9	7.4 ± 1.0	7.5 ± 0.9	0.83
eGFR (ml·min^{-1}·1.73 m^{-2})	54± 20	55 ± 23	53 ± 22	0.92
Echocardiographic variables				
LVEF (HFrEF, %)	26 ± 7	27 ± 9	28 ± 8	0.54
LVEF (HFpEF, %)	50 ± 9	52 ± 10	54 ± 9	0.74
MR Grade	3.9 ± 1.5	3.5 ± 1.2	3.5 ± 1.3	0.51
LAVI (ml/m^2)	42 ± 13	42 ± 13	41 ± 15	0.84
TAPSE (mm)	16 ± 4	17 ± 4	16 ± 4	0.94
Qp/Qs	0.99 ± 0.11	1.17 ± 0.12	1.10 ± 0.13	0.005
Hemodynamics				
PCWP (mmHg)	21 ± 5	20 ± 7	19 ± 7	0.49
RAP (mmHg)	8 ± 4	9 ± 5	9 ± 4	0.51
PAP, mean (mmHg)	30 ± 7	29 ± 8	30 ± 10	0.97
CI (L/min/m^2)	2.2 ± 0.4	2.4 ± 0.4	2.3 ± 0.5	0.27
PVR (Wood Units)	2.8 ± 1.6	2.6 ± 1.1	2.8 ± 1.9	0.73

Shunt Valve Function at 1-3 and 12 Months (TEE)

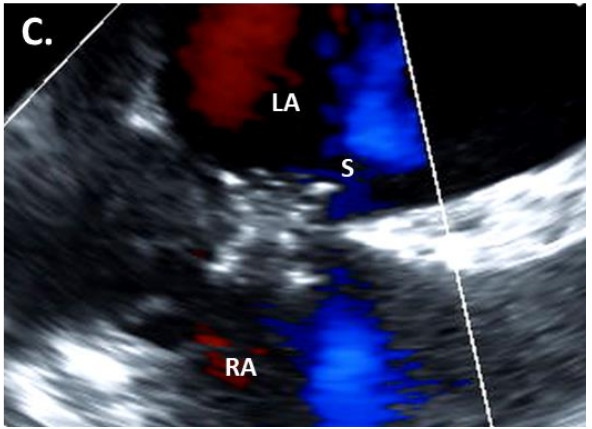
- Shunt patency at 1-3 months: 36/36 (100%)
- 12-month shunt occlusion: 5/36 (14%)
- 12-month shunt stenosis (TEE Color Doppler *vena contracta* in valve region narrowed/skewed): 13/36 (36%)
- No thrombus, no shunt migration, no erosion of adjacent structures



A. Widely Patent Shunt



B. Stenotic Shunt; narrowed/skewed



C. Occluded Shunt

	Patent	Stenotic	p
Vena Contracta	3.3±0.6 mm	1.5±1.5 mm	*0.001*
Qp:Qs	1.17±0.12 mm	1.05±0.12 mm	*0.023*

Pathological Examination (Stenotic Shunt)

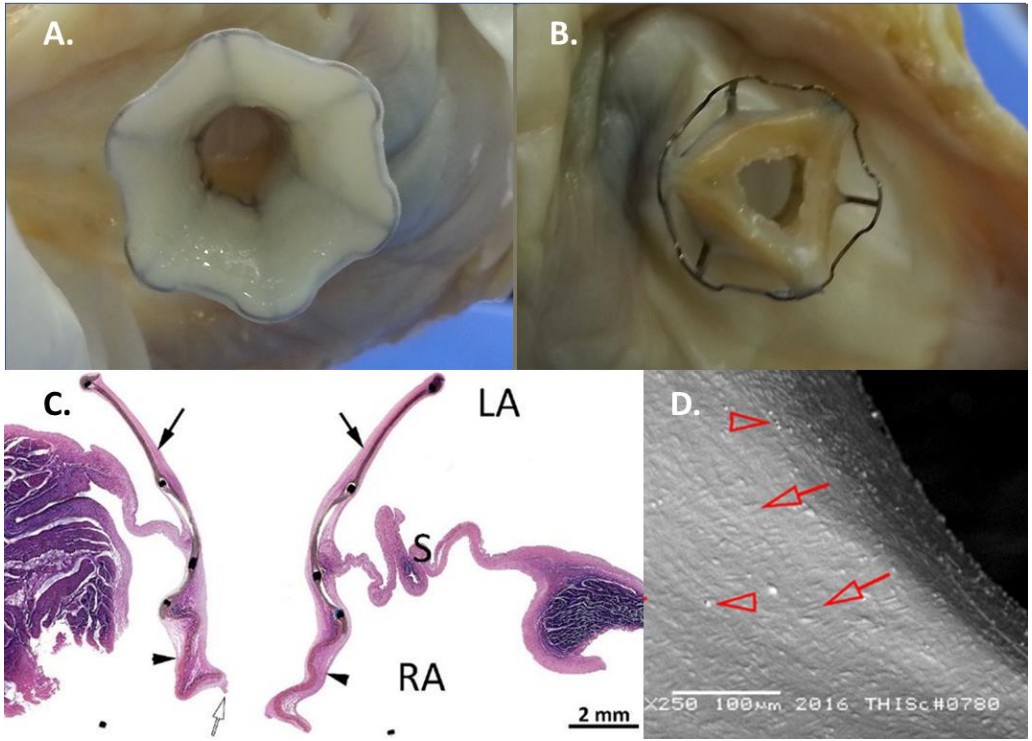
2.5 year explant specimen from transplanted patient

A. LA view. Orifice widely patent.

B. RA view. Pannus thickening with stenosis of bioprosthetic leaflets.

C. Axial Section (H&E). Fibrocellular neoendocardium (pannus) infiltration of leaflets.

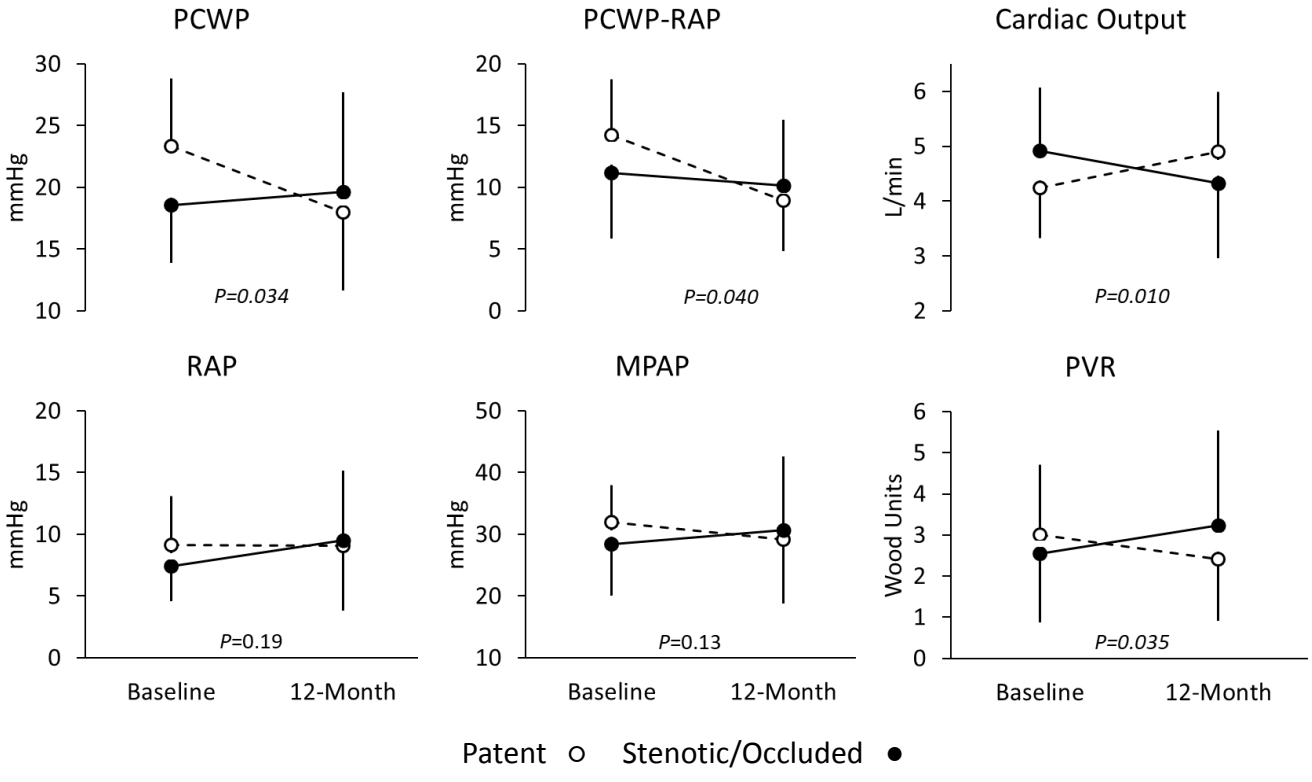
D. SEM. Full endothelialization of lumen (CD31+)



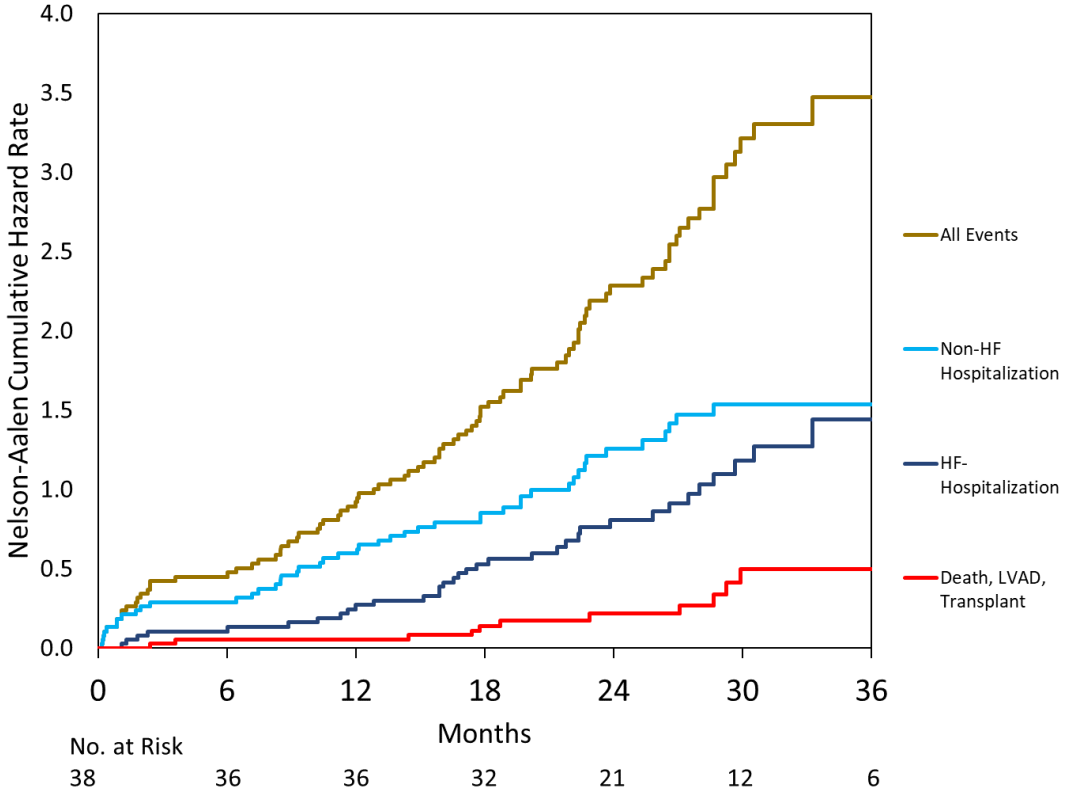
Hemodynamic Changes Grouped by Shunt Patency at 1-Year Follow-Up

At baseline, patients with patent shunts were:

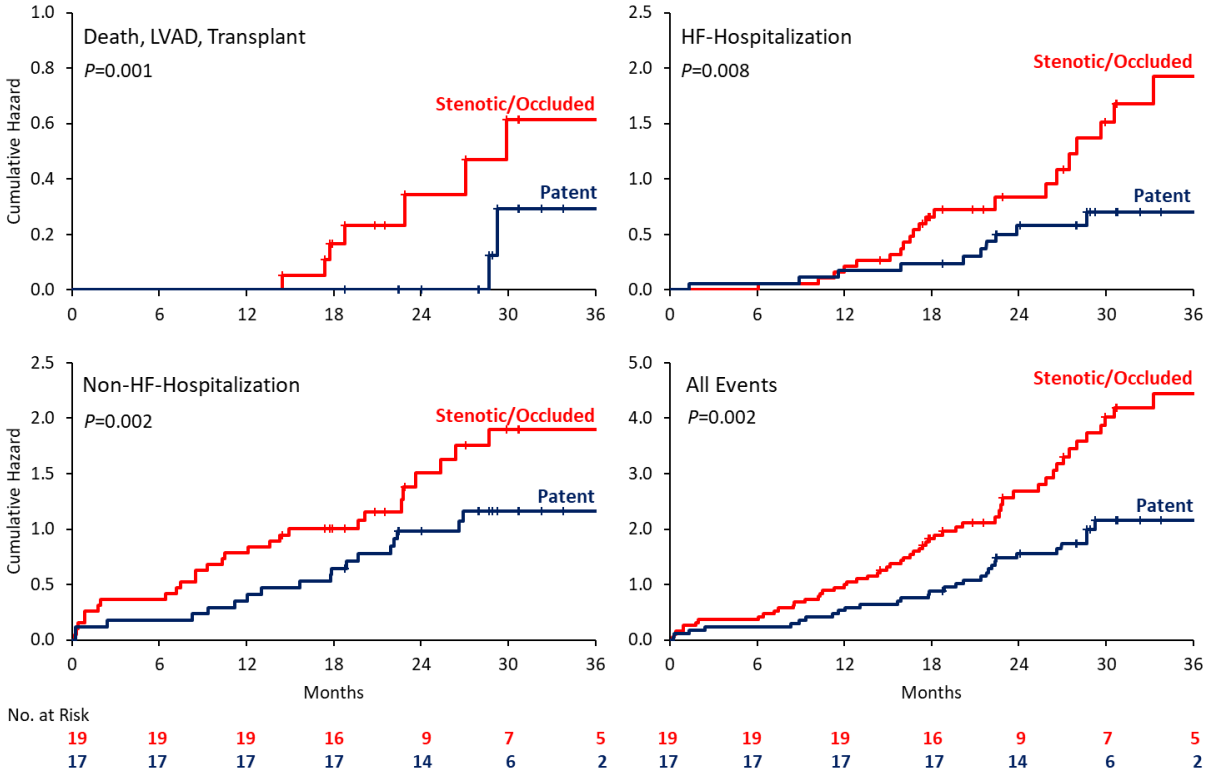
- Older
- ↑ AF
- ↓ eGFR
- ↓ 6MWT
- ↑ PCWP, ↓ CO



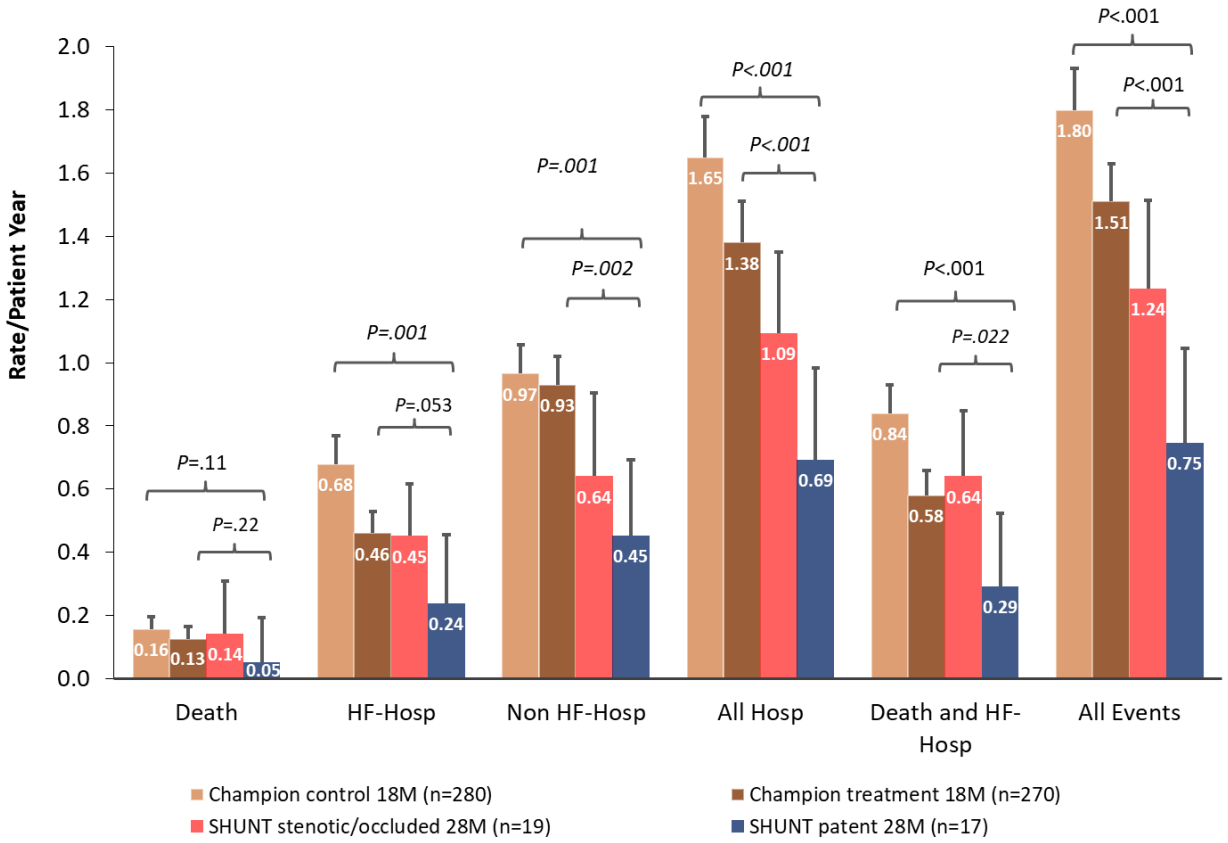
Cumulative Clinical Events (all patients)



Long-term Clinical Outcomes Grouped by Shunt Patency



Comparison with CMEMs Champion Study



Studies had similar:

- eligibility criteria
- baseline characteristics including hemodynamics
- use of medical and device therapies including dosing

Conclusions

- Interatrial shunting with the V-Wave system for treating patients with HFrEF and HFpEF was feasible, safe, and associated with promising efficacy data in terms of functional improvement and reduction of cardiovascular events
- There was a high frequency of shunt stenosis/occlusion at 1-year, likely secondary to pannus infiltration of the bioprosthetic leaflets, which associated with poorer hemodynamic and longer-term clinical outcomes
- Shunt patency was associated with sustained low morbidity and mortality
- Implementing modifications to improve device patency over time while maintaining hemodynamic and functional benefits is worthwhile prior to launching a randomized trial to confirm these findings

Participating Centers / Investigators

- Quebec Heart and Lung Institute, Laval University, Quebec City, Canada
  - Josep Rodés-Cabau, Sebastien Bergeron, Mathieu Bernier
- Hospital Clinico Universitario de Valladolid, Valladolid, Spain
  - Ignacio Amat-Santos
- Rabin Medical Center, Petah Tikva, Israel
  - Tuvia Ben Gal
- Hospital Clinico San Carlos, Madrid, Spain
  - Luis Nombela-Franco
- Hospital Universitari Vall d'Hebron, Barcelona, Spain
  - Bruno Garcia del Blanco
- Rambam Medical Center, Haifa, Israel
  - Arthur Kerner