

# Interatrial shunt with the second-generation V-Wave system for patients with advanced chronic heart failure



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## Introduction

Left atrial decompression by creating an interatrial shunt has been associated with significant improvements in functional status and quality of life in patients with heart failure (HF) with reduced and preserved left ventricular ejection fraction (HFrEF, HFpEF)<sup>1</sup>.

The initial experience with the V-Wave shunt (V-Wave Ltd, Caesarea, Israel) showed its safety and preliminary efficacy for treating patients with HFrEF and HFpEF<sup>2,3</sup>. However, shunt narrowing/occlusion was observed in up to 50% of the patients at 12-month follow-up, secondary to early valve degeneration<sup>3</sup>. Following this initial experience, modifications were implemented in order to improve late device patency and continued efficacy, with valve removal being the most relevant feature of the newer (second) generation of the V-Wave shunt (**Figure 1**). The present study reports the first-in-human experience with the second generation of the V-Wave shunt in patients with advanced chronic HF.

## Methods

A total of 10 patients underwent an interatrial shunting procedure with the second-generation V-Wave shunt between September and November 2017 at the Quebec Heart & Lung Institute. Patients had a history of chronic HF and New York Heart Association (NYHA) Class  $\geq$ III despite optimal tolerated drug and device therapies as defined by American College of Cardiology (ACC)/ American Heart Association (AHA) guidelines.

## PROCEDURES

**Supplementary Figure 1** illustrates the main steps of V-Wave implantation. Following the procedure, patients received dual antiplatelet therapy (aspirin plus clopidogrel) for three months, and aspirin indefinitely. Those patients receiving anticoagulation therapy pre-procedure continued with the same anticoagulation regime post procedure.

## FOLLOW-UP

Patients were followed in an HF clinic at 1, 3, 6 and 12 months. Transthoracic echocardiography (TTE) was performed at each clinical visit; if the shunt was not properly visualised, transoesophageal echocardiography (TEE) was performed. Assessments of functional status, quality of life and laboratory tests were also performed during each follow-up visit.

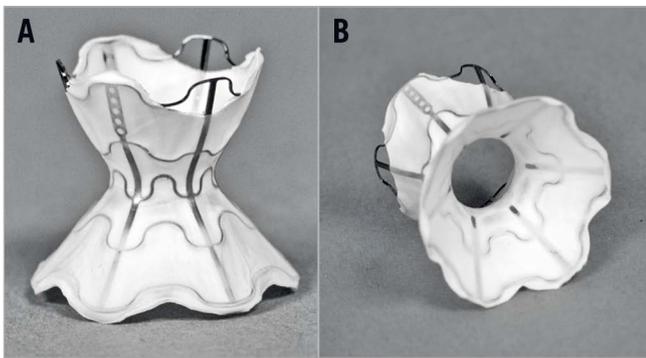
## OUTCOMES

Clinical outcomes included major adverse cardiovascular and neurological events (MACNE), and HF hospitalisation.

## STATISTICAL ANALYSIS

Categorical variables are reported as number (percent) and continuous variables as mean $\pm$ SD. Changes in continuous variables were analysed using the paired t-test or Wilcoxon signed-rank test, as appropriate. Categorical variables were compared with the

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**Figure 1.** Second-generation (valveless) V-Wave device. A) Hourglass-shaped device made of nitinol with expanded polytetrafluoroethylene encapsulation. B) View of the device valveless lumen.

Fisher's exact test. Statistical significance was set at a two-tailed probability level of 0.05. Data were analysed with SAS statistical software, version 9.3 (SAS Institute Inc., Cary, NC, USA).

## Results

Baseline characteristics of the study population are shown in **Supplementary Table 1**.

### PROCEDURAL AND CLINICAL OUTCOMES

The device was successfully implanted in all patients with no immediate procedural complications. Procedural success was obtained in nine patients (90%); one patient died in the hours following the procedure due to an electrical storm unresponsive to medical therapy and mechanical ventilation. TTE was performed showing the good position of the device and the absence of pericardial effusion. This patient had an advanced ischaemic heart failure with a left ventricular ejection fraction (LVEF) of 20% and a high wedge pressure (48 mmHg) at the time of the procedure. The other nine patients were discharged the day after the procedure without complications.

Clinical outcomes are summarised in **Supplementary Table 2**. A total of 6 patients (5: HF<sub>r</sub>EF, 1: HF<sub>p</sub>EF) were alive and completed the one-year follow-up. **Table 1** shows patients' symptoms, quality of life, exercise capacity and echocardiographic parameters at one-year follow-up (compared to baseline).

### FOLLOW-UP ECHOCARDIOGRAPHY

The V-Wave shunt was adequately visualised by TTE in all cases but one (a TEE was performed in this case), and the patency of the shunt with left-to-right shunting was confirmed in all patients with no signs of shunt narrowing (**Figure 2**). The echocardiography data at one-year follow-up are summarised in **Table 1**.

## Discussion

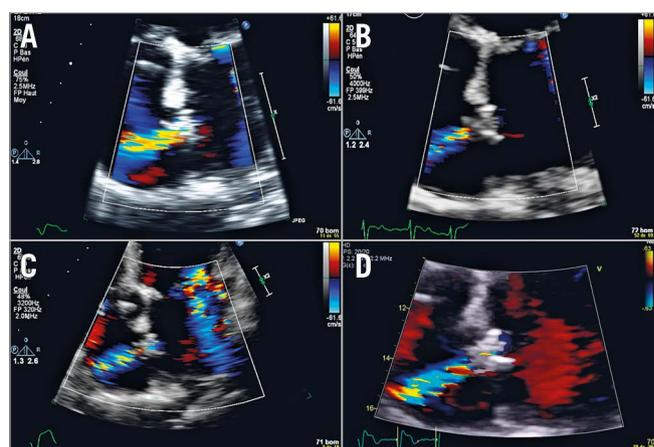
The main limitation of the first generation of the V-Wave device was related to the rate (up to 50%) of stenosis/occlusion at one-year

**Table 1.** Functional, laboratory and echocardiographic parameters at baseline and at one-year follow-up.

Variable	Baseline (n=6)	1 year (n=6)	p-value
<b>Functional status and quality of life</b>			
NYHA Class (III-IV)	6 (100)	1 (16.7)	0.013
Duke activity status index	11.0±2.9	26.3±17.4	0.085
KCCQ	51.1±9.7	83.0±15.4	0.006
6-min walk test (m)	274±65	338±104	0.169
<b>Laboratory</b>			
NT-proBNP (pg/ml)	1,313±873	1,223±1,420	0.775
<b>Echocardiographic variables</b>			
LVEF (%)	34±12	38±9	0.233
LV end-diastolic diameter (cm)	5.7±0.8	5.8±0.8	0.376
Moderate to severe MR	1 (16.7)	1 (16.7)	1.000
LAVI (ml/m <sup>2</sup> )	47.0±15.7	45.0±23.2	0.687
TAPSE (mm)	16.7±4.1	18.5±6.1	0.376
RVEDD basal (mm)	32.8±8.0	38.5±10.7	0.152
RVEDD mid cavity (mm)	26.8±8.2	33.8±10.5	0.094
RV volume (ml)	51.8±34.2	50.7±35.4	0.851
Qp:Qs	–	1.16±0.17	–

Values are expressed as n (%) or mean±SD. KCCQ: Kansas City Cardiomyopathy Questionnaire; LAVI: left atrial volume index; LVEF: left ventricle ejection fraction; MR: mitral regurgitation; NYHA: New York Heart Association; Qp:Qs: ratio of pulmonary to systemic blood flow; RVEDD: right ventricle end-diastolic diameter; TAPSE: tricuspid annular plane systolic excursion

follow-up secondary to intra-shunt valve degeneration<sup>3</sup>. In an animal model including 11 sheep, the valveless V-Wave shunt remained patent with no late loss in lumen diameter at five- to six-month follow-up (data provided by V-Wave Inc., unpublished) (**Supplementary**



**Figure 2.** Serial echocardiography examinations (at 1, 3, 6 and 12 months) showing the shunt patency up to one-year follow-up. A) 1-month follow-up. B) 3-month follow-up. C) 6-month follow-up. D) 12-month follow-up.

**Figure 2).** The results of our study showed the patency and absence of shunt stenosis in all cases, strongly suggesting the superiority of the second-generation device with respect to late shunt patency. These results are also in accordance with those obtained with other valveless shunt devices<sup>4</sup>. In addition to echocardiography, other imaging modalities such as computed tomography or magnetic resonance imaging (MRI) could be useful for evaluating shunt patency.

The patients selected for this initial experience with the second-generation V-Wave shunt were older and presented a more advanced cardiac failure condition (higher pro-BNP, pulmonary wedge and right atrial pressure values; lower exercise capacity) compared to those included in the studies with the first-generation device<sup>3</sup>. Despite a worse initial condition, significant improvements in functional status and quality of life along with a tendency towards improved exercise capacity were observed at one-year follow-up, supporting the beneficial effects of this therapy in HF patients. The efficacy of the second-generation V-Wave device is currently being evaluated in a large randomised trial (RELIEVE-HF; ClinicalTrials.gov NCT03499236).

### Limitations

The main limitations of this study were its small sample size, non-randomised design, absence of haemodynamic data at follow-up, and potential observer bias limiting the ability to reach definitive conclusions about device efficacy.

### Conclusion

In conclusion, the confirmation of shunt patency without narrowing up to one-year follow-up in all cases suggests that the changes implemented in the device (mainly valve removal) may have overcome the late patency issues observed in the initial experience with the first-generation device.

### Impact on daily practice

The confirmation of shunt patency without narrowing up to one-year follow-up in all cases following the implantation of the second-generation (valveless) V-Wave shunt suggests that the changes implemented (mainly valve removal) have overcome the most important limitation of the first-generation device.

### Acknowledgements

J. Rodés-Cabau and L. Guimaraes had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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### Conflict of interest statement

J. Rodés-Cabau is consultant for and has received institutional research grants from V-Wave Inc. N. Eigler and W.T. Abraham are employees of V-Wave Inc. The other authors have no conflicts of interest to declare.

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### Supplementary data

**Supplementary Figure 1.** V-Wave implantation technique.

**Supplementary Figure 2.** Pictures from non-diseased juvenile ovine model (n=4) at six-month follow-up showing no lumen loss on both sides (left and right atrial) of the shunt.

**Supplementary Table 1.** Baseline characteristics of the study population.

**Supplementary Table 2.** Individual baseline characteristics and outcomes of the study population (n=10).

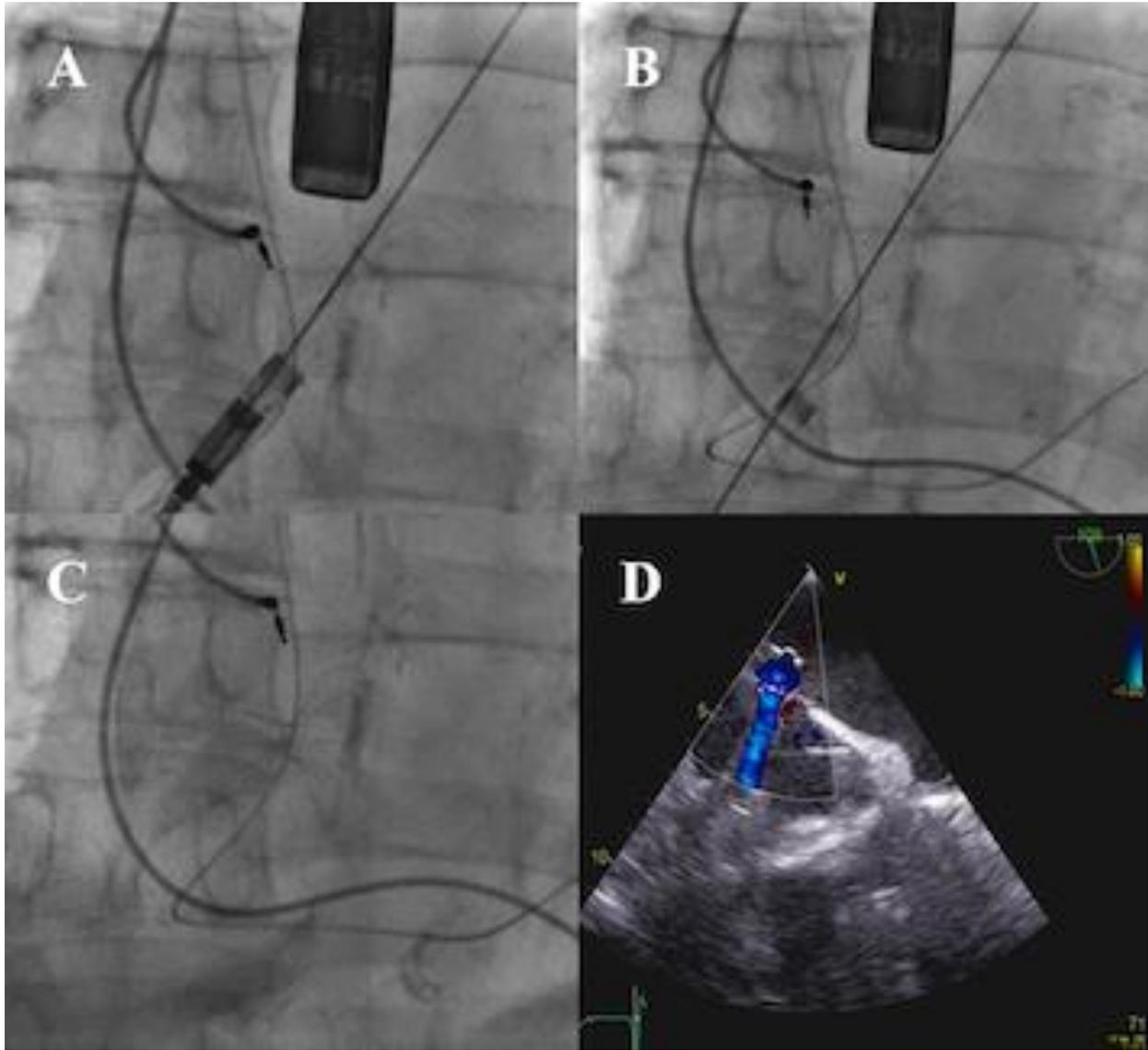
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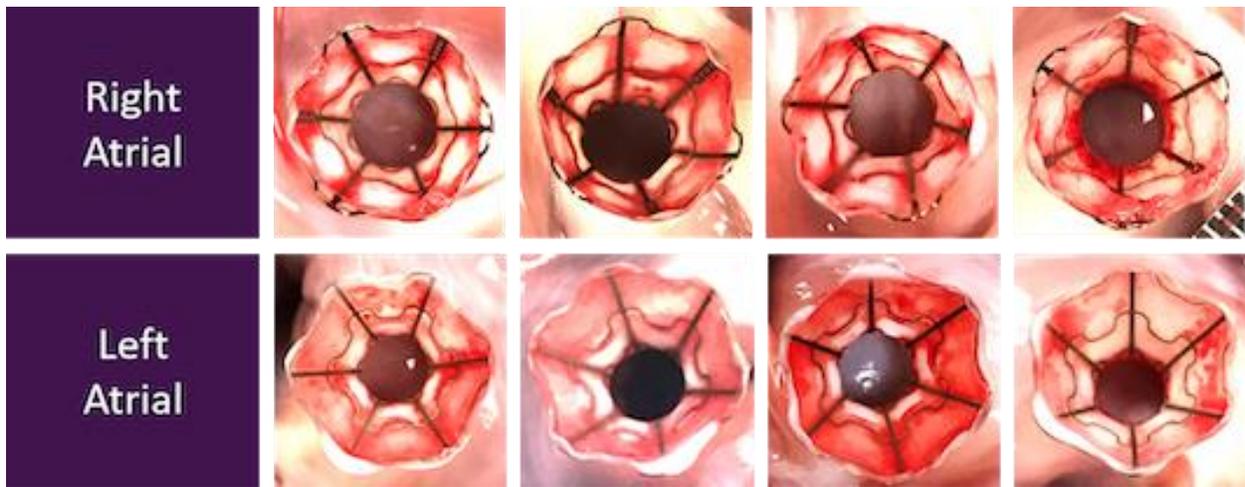


## Supplementary data



### Supplementary Figure 1. V-Wave implantation technique.

- A. V-Wave device with the left side deployed.
- B. V-Wave device with both sides deployed (right and left). A guidewire remains across the device until the very end of the procedure.
- C. V-Wave completely deployed.
- D. Transoesophageal echocardiogram showing left-to-right shunt through V-Wave device.



**Supplementary Figure 2.** Pictures from a non-diseased juvenile ovine model (n=4) at six-month follow-up showing no lumen loss on both sides (left and right atrial) of the shunt.

**Supplementary Table 1. Baseline characteristics of the study population.**

<b>Variable</b>	<b>Patients (n=10)</b>
<b>Demographics</b>	
Age, years	68±9
Male sex	8 (80)
BMI, kg/m <sup>2</sup>	30.8±9.9
Hypertension	7 (70)
Diabetes	5 (50)
Atrial fibrillation	6 (60)
Coronary artery disease	8 (80)
<b>Treatment history</b>	
ACE/ARB	4 (40)
Sacubitril/valsartan	5 (50)
Beta-blocker	10 (100)
MRA	2 (20)
Loop diuretics: mg furosemide eq.	10 (100): 129±113
CRT-D or ICD	5 (50)
CRT	3 (30)
<b>Laboratory tests</b>	
NT-proBNP (pg/ml)	2,887±3,518
Haemoglobin (g/L)	116.1±12.2
eGFR <60 ml/min/1.73 m <sup>2</sup>	8 (80)
<b>Echocardiographic data</b>	
LVEF ≥0.40	2 (20)
LV end-diastolic diameter (cm)	5.6±0.8
LVEF, % (HFrEF)	27±8
LVEF, % (HFpEF)	58±11
TAPSE (mm)	16.1±3.8
Moderate to severe MR	4 (40)
<b>Functional status and quality of life</b>	
NYHA Class III	10 (100)
VO <sub>2</sub> max	10.7±3.7
Duke activity status index	10.6±2.6
Kansas City Cardiomyopathy Questionnaire	50.8±9.8
6 min walk test (m)	255±68
<b>Haemodynamics</b>	
Pulmonary capillary wedge pressure (mmHg)	24±11
Right atrial pressure (mmHg)	16±7
Mean pulmonary artery pressure (mmHg)	35±16
Cardiac index (L/min per m <sup>2</sup> )	2.53±0.52

Values are n (%) or mean±SD.

ACE/ARB: angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; BMI: body mass index; CRT: cardiac resynchronisation therapy; eGFR: estimated glomerular filtration rate; ICD: implantable cardioverter defibrillator; LVEF: left ventricular ejection fraction; MR: mitral regurgitation; MRA: mineralocorticoid receptor antagonist; NT-proBNP: N-terminal pro-brain natriuretic peptide; NYHA: New York Heart Association; TAPSE: tricuspid annular plane systolic excursion

**Supplementary Table 2. Individual baseline characteristics and outcomes of the study population (n=10).**

Patient	1	2	3	4	5	6	7	8	9	10
<b>Demographics</b>										
Age	80	77	78	58	58	65	72	64	72	58
Sex	M	M	M	F	M	M	M	F	M	M
BMI, kg/m <sup>2</sup>	19.6	31.8	34.8	45.9	43.1	18.2	22.5	35.1	20.9	35.5
<b>Haemodynamics</b>										
PCWP (mmHg)	12	23	29	19	20	12	17	27	48	29
RAP (mmHg)	6	19	21	12	18	10	10	15	29	18
Mean PAP (mmHg)	12	51	42	26	34	17	28	29	56	40
CI (L/min per m <sup>2</sup> )	-	-	-	2.8	2.6	2.6	1.7	2.3	2.3	3.4
<b>Severe adverse events</b>										
Cause of death			Pneumonia		Pneumonia		Terminal HF		VF	
Number of hospitalisations	-	-	1	-	4	-	1	-	-	-
Number of HF hospitalisations			0		1		1			
Time to procedure–first hospitalisation (months)			4.7		3.9		3.0			
Follow-up (months)	12	12	5.5	12	6.9	12	10	12	0	12

BMI: body mass index; CI: cardiac index; F: female; M: male; PAP: pulmonary artery pressure; PCWP: pulmonary capillary wedge pressure; RAP: right atrial pressure