Clinical Investigations

# Left Ventricular Decompression During Speed Optimization Ramps in Patients Supported by Continuous-Flow Left Ventricular Assist Devices: Device-Specific Performance Characteristics and Impact on Diagnostic Algorithms

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## ABSTRACT

**Background:** Echocardiographic ramp tests have been widely used to help guide speed adjustments and for identification of potential device malfunctions in patients with axial continuous-flow left ventricular assist devices (LVADs) (Heartmate II LVAD [HMII]). Recently, the use of centrifugal-flow LVADs (Heartware LVAD [HVAD]) has been on the rise. The purpose of this study was to evaluate the utility of ramp tests for assessing ventricular decompression in HVAD patients.

**Methods and Results:** In this prospective study, ramp tests were performed before index hospitalization discharge or at the time of device malfunction. Vital signs, device parameters (including flow), and echocardiographic parameters (including left ventricular end-diastolic dimension [LVEDD], frequency of aortic valve [AV] opening, and valvular insufficiency) were recorded in increments of 100 rpm, from 2,300 rpm to 3,200 rpm. Twenty-six ramp tests were performed, 19 for speed optimization and 7 for device malfunction assessment. The average speed after the speed optimization ramp tests was 2,534.74 ± 156.32 RPM, and the AV closed at a mean speed of 2,751.77 ± 227.16 rpm, with 1 patient's valve remaining open at the maximum speed. The reduction in LVEDD for each speed increase was significantly different when the AV was open or closed, at −0.09 cm/increment and −0.15 cm/increment, respectively ($P = .013$), which is significantly different than previously established HMII LVEDD slopes. There were also significant changes in overall device flow ($P = .001$), upper flow ($P = .031$), and lower flow ($P = .003$) after AV closure. The power slope did not change significantly after the AV closed ($P = .656$). Five of the 19 tests were stopped before completion owing to suction events, but all tests reached ≥3,000 rpm.

**Conclusions:** The parameter slopes for the HMII cannot be directly applied to ramp studies in HVAD patients. Overall, the LVEDD slope is drastically smaller in magnitude than the previously reported HMII findings, and speed adjustments were not based on the degree of left ventricular unloading. Therefore, the slope of the LVEDD-rpm relationship is not likely to be helpful in evaluating HVAD function. (*J Cardiac Fail 2015;21:785−791*)

**Key Words:** Ramp, LVAD, LVEDD slope, unloading.

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Continuous-flow left ventricular assist devices (CF-LVADs) have markedly increased the life expectancy and quality of life for patients with advanced heart failure. Although these devices are easier to implant and more reliable than earlier generations of LVADs, they still lack the ability to dynamically adjust their speed and output based on metabolic demands. Therefore, it is crucial to identify the optimal user-specified fixed speed settings for each patient to maximize physiologic and clinical benefits.

At present, recommendations for device speed adjustment include target measures of mean arterial pressure from 65 to 90 mm Hg, midline interventricular septum position, and intermittent aortic valve (AV) opening while maintaining no more than mild mitral regurgitation (MR) to ensure appropriate unloading of the left ventricle (LV).[1,2]

Previously, we developed the echocardiographic-based Columbia Ramp Test to help guide optimization of device speed for managing the degree of LV unloading and for diagnosis of device malfunction in Heartmate II (HMII; an axial-flow pump) patients. With a normally working HMII device, we reported a linear negative relationship between LVAD speed and left ventricular end-diastolic dimension (LVEDD).[3] However, ramp test results can be affected by preload and afterload conditions, and the amount of support provided by the LVAD depends on the set speed and the pressure-flow characteristics of the device.[4]

With the use of CF-LVADs on the rise, nonaxial continuous-flow devices have been developed. The Heartware CF-LVAD (HVAD; Framingham, Massachusetts) obtained United States Food and Drug Administration approval in 2012 as a bridge-to-transplantation (BTT) device. In addition to having a smaller profile than the HMII, the HVAD uses a centrifugal pump rather than an axial pump. In addition, the HVAD is placed in the thorax, whereas HMII is placed in a subdiaphragmatic pocket.[5] Because the interaction between patients' hearts and LVADs is complex and device-specific, conclusions made regarding ramp tests in HMII patients may not apply to HVAD patients. This is highlighted by the fact that 1 earlier study reported no consistent impact of HVAD speed on LVEDD.[6] In contrast, theory suggests that the degree of LV unloading should simply depend on the magnitude of LVAD flow. At this time, it is not clear whether this dissonance reflects actual differences in the fundamental unloading characteristics of the HVAD and HMII devices or if 2-dimensional (2D) echocardiography is insufficient for visualizing unloading in centrifugal-flow devices. Furthermore, owing to uncertainty in the equivalence of speeds between HVAD and HMII, it cannot be assumed that the slope of the relationship between rpm and LVEDD (and other parameters of device performance, such as device flow and power) is the same for the two devices. Owing to the importance of appropriate speed selection for the prevention of multiple CF-LVAD complications, it is evident that the ramp test must be adapted to the HVAD.[7,8] We prospectively tested the hypothesis that unloading of the LV based on 2D echocardiography is different in centrifugal- versus axial-flow pumps, which has implications for device management and evaluation for device obstruction.

## Methods

This was a prospective study of ramp tests performed in CF-LVAD patients at Columbia University Medical Center—New York Presbyterian Hospital from June 2011 to March 2014. The Columbia Institutional Review Board approved this study, and all patients signed informed consents. For HVAD patients, a standardized Ramp Test was adapted from the HMII protocol (Fig. 1). A full description of the HMII ramp study protocol was previously provided by Uriel et al.[3] In addition to collecting LVEDD at each rpm, we also collected mean, peak, and trough flows from the HVAD monitor, which will be referred to as flow, upper flow (UF), and lower flow (LF), respectively, throughout this analysis. Also, the range over which HVAD speed was varied was adjusted to the working range of the HVAD (2,300−3,400 rpm). For acute speed optimization, we followed the current recommendations to ensure midline interventricular septum position while maintaining intermittent AV opening.

### HVAD Ramp Test Protocol

Baseline demographics as well as surgical history, current medications, and laboratory parameters, including anticoagulation (international normalized ratio [INR]), platelet count, lactate dehydrogenase (LDH), bilirubin, haptoglobin, and plasma free hemoglobin, where applicable, were collected and reviewed to ensure the safety of performing a ramp test. We used the following guidelines to ensure safety:

1. Appropriate anticoagulation (INR $>1.8$ or partial thromboplastin time $>60$) was confirmed. If adequate anticoagulation was not demonstrated, a routine ramp test for speed adjustment was postponed until therapeutic anticoagulation was reached. In cases of suspected device thrombosis, heparin (60 U/kg) was given intravenously and the ramp test was subsequently performed.
2. Baseline transthoracic echocardiography (TTE) was performed; if it revealed an intraventricular or aortic root thrombus, the ramp study was not performed owing to the possibility of thrombus dislodgement.

Once a patient satisfied the safety criteria to perform the test, device speed was reduced to 2,300 rpm. After 2 minutes, device parameters and TTE images were obtained. TTE images yielded the following parameters: LVEDD and left ventricular end-systolic diameter (LVESD), the frequency of AV opening, the degree of aortic regurgitation (AR), the degree of MR, right ventricular systolic pressure (RVSP) estimated from the peak of the tricuspid regurgitation (TR) jet, Doppler blood pressure, and heart rate (Fig. 1).

TTE parameters were recorded and analyzed according to the following protocol (echo parameters, as described previously for the HMII ramp[3]):

1. LVEDD and LVESD were measured from the parasternal long-axis view.
2. AV opening was assessed with the use of M-mode over the AV in the parasternal long-axis view. At least 10 consecutive

| Speed | LFL | UF | Flow | Power | BP | HR | LVEDD | LVESD | AV Status | Number of beats open / 10 beats | AI | MR | RVSP | Septal Bowing (Y/N) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2300 | | | | | | | | | | | | | | |
| 2400 | | | | | | | | | | | | | | |
| 2500 | | | | | | | | | | | | | | |
| 2600 | | | | | | | | | | | | | | |
| 2700 | | | | | | | | | | | | | | |
| 2800 | | | | | | | | | | | | | | |
| 2900 | | | | | | | | | | | | | | |
| 3000 | | | | | | | | | | | | | | |
| 3100 | | | | | | | | | | | | | | |
| 3200 | | | | | | | | | | | | | | |
| 3300 | | | | | | | | | | | | | | |
| 3400 | | | | | | | | | | | | | | |

**Fig. 1.** HVAD ramp data collection template. LFL, lower flow; UF, upper flow; BP, blood pressure; HR, heart rate; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; AV, aortic valve; AI, aortic insufficiency; MR, mitral regurgitation; RVSP, right ventricular systolic pressure.

cardiac cycles were reviewed, and the frequency of AV opening was recorded as the percentage of cycles with AV opening.

3. Visual estimation of severity of AR and MR was performed in the parasternal long-axis view with the use of color Doppler. For assessment of AR and MR, the degree of regurgitation was graded from 0 to 6 (0 = none; 1 = trace; 2 = mild; 3 = mild-to-moderate; 4 = moderate; 5 = moderate-to-severe; 6 = severe). Taking into account that AR during CF-LVAD support is generally both systolic and diastolic, AR was deemed to be significant if graded 3 (mild to moderate) or greater.[9]
4. RVSP was estimated from peak TR velocity with the use of the modified Bernoulli equation.

Device speed was then increased by 100 rpm increments at ~2-minute intervals with repeated acquisition of all echocardiographic and device parameters at each speed. This rpm ramp was continued to a maximum of 3,200 rpm. The ramp test was stopped if any suction events occurred, and/or if the LVEDD decreased to <3.0 cm. At the conclusion of the test, the attending cardiologist reviewed the recordings while at the patient's bedside. Device speed was then set to allow at least intermittent AV opening while maintaining Doppler blood pressure >65 mm Hg and avoiding more than mild MR with minimal septal bowing.

Finally, the recordings of the ramp test parameter results at the respective 11 speed points were plotted in Excel software (2010; Microsoft, Redmond, Washington). Linear regression was used to determine the slopes of the relations between rpm and LVEDD, UF, LF, flow, and power. For the slope calculation, each change in 100 rpm was equal to a change in 1 unit. See Appendix 1 for an Excel template for slope calculation and Appendix 2 for its corresponding instructions.

### Statistical Analysis

Data were entered into an Excel database (2007; Microsoft). For clinical purposes, individual patients' slopes were calculated with the use of Excel at the time of the ramp test. The slopes are reported as the change in the ramp parameter for each 100-rpm increase in speed. Thus, speed increment, rather than actual speed, was used as the independent variable (change in parameter/increment). The speed increment was calculated by subtracting 2,300 rpm from each speed level and dividing by 100 (ie, [speed − 2,300]/100), resulting in a maximum of 11 speed increments. The overall slopes were calculated with the use of all data points, regardless of whether the AV was opening or remained shut. In addition, the "AV-open slope" and "AV-closed slope" were calculated with the use of only the data points when the AV was opening and remained closed, respectively. Note that for the HMII patients, the speed increment was calculated by subtracting 8,000 rpm from each speed level, then dividing by 400 rpm (ie, [speed − 8,000]/400).

The overall analysis was performed on the ramps completed for speed optimization (n = 19) with the use of Stata SE (*release 13, 2013*; Statacorp, College Station, Texas). A full analysis was not completed on the ramps completed for device malfunction, because the cohort was prohibitively small (3 for device thrombosis, 4 for device malfunction). Normally distributed continuous variables are reported as mean and standard deviation, and skewed continuous data are reported as median and interquartile range (IQR). Categoric variables are summarized with the use of frequency and percentage. The sample slopes of the ramp parameters were calculated with the use of a linear regression with generalized estimating equations (GEEs) to account for multiple observations for each subject. The use of the exchangeable working correlation matrix was found to minimize the quasi-likelihood information criterion (QIC) value and was used to obtain the optimal regression model.[10] The interaction of speed and AV closure was assessed in the regression models to determine if the slopes while the AV was open and closed were significantly different.

## Results

### Brief HMII Update

To date, 198 ramp tests have been performed on 119 HMII patients. This update to the original Uriel et al HMII ramp study manuscript includes 97 ramp studies for speed optimization in 76 patients.[3] In this updated analysis, we found an LVEDD slope of −0.216 ± 0.035 rpm/increment, which is similar to the slope found in the original study of 28 speed optimization patients (−0.29 ± 0.11 rpm/increment). The model for the estimation of LVEDD revealed a nonsignificant interaction between speed increment and AV closure, and thus the LVEDD slope did not change significantly before and after AV closure ($P$ = .655).

### HVAD Findings

During the study period, 26 ramp tests were performed on 22 HVAD patients. Of the 26 ramp tests, 19 were performed for speed optimization and 7 for device malfunction. In the speed optimization cohort, the median age was 66 years (IQR 52−69), and 11 patients (57.9%) were

male (Table 1). Nineteen ramp tests for speed optimization were performed before discharge at a median of 23 days (IQR 15−30) after HVAD implantation. The INR and LDH values at the beginning of the ramp tests were within normal ranges for CF-LVAD patients, with mean values of 2.59 ± 0.44 and 297.11 ± 97.71 U/L, respectively. Five of the ramp tests were ended before reaching 3,400 rpm owing to suction events, but all tests reached ≥3,000 rpm. There were no adverse events associated with any ramp tests, and none of the tests resulted in sustained ventricular tachyarrhythmias. Blood pressure remained within appropriate limits throughout the ramp test for all patients. The starting mean arterial blood pressures at the conclusion of the ramp test were 3 mm Hg greater, on average, than the starting pressures. See Table 2 for a full description of HVAD ramp test results.

**Speed.** To achieve optimal LVEDD, AV opening, and MR, the device speed was changed from its previously set presumed optimal value in 7 (36.8%) of the 19 tests performed for speed optimization. Of the 7 adjustments, 4 were increased and 3 were decreased, ranging from a decrease in 400 rpm to an increase of 100 rpm. The average absolute change in speed among these 7 patients was 140.00 ± 69.28 rpm. The average speed after the ramp tests was 2,534.74 ± 156.32 rpm. The speed optimization results are summarized in Table 3. The final set speed was not associated with body surface area ($R^2$ = 0.014; $P$ = .627) or sex ($R^2$ = 0.024; $P$ = .525).

**Aortic and Mitral Valve Opening and Regurgitation.** Data from patients who did not undergo any surgical AV manipulation (n = 18) were used for the AV optimization analysis. In these patients, none had a closed AV at the starting speed (2,300 rpm). One patient's AV remained open throughout the ramp, and the other 17 had a mean closure speed of 2,751.77 ± 227.16 rpm (range 2,400−3,000). At their set speeds, 4 patients' AVs remained closed on all beats, 3 had intermittent opening, and 12 opened with each beat. Furthermore, 5 patients had no aortic insufficiency (AI), 10 had trace AI, and 4 had mild AI. Ten patients finished with no MR, 5 had trace MR, 3 had mild MR, and 1 had moderate MR.

**Parameter Slopes.** The estimated models for all parameters (LVEDD, flow, UF, LF, and power) are summarized according to AV status in Table 3. Figure 2 represents a graph of the "average patient," with a change in the slope at the time of AV closure (the average closure speed of 2,750 rpm was used).

The model for the estimation of LVEDD revealed a significant interaction between speed increment and AV closure ($P$ = .013). With a 1-unit increase in speed increment, the LVEDD decreased by 0.09 cm while the AV was open and 0.15 cm while the AV was closed. Of note, both slopes were below the threshold reported for HMII (−0.16 step/increment) where device thrombosis is to be suspected. In the 10 patients with a mitral valve (MV) repair at the time of HVAD implantation, the effect of AV closure on LVEDD slope was more pronounced, increasing from −0.08 to −0.17 ($P$ = .002). In comparison, patients without an MV repair had a slope of −0.10 before AV closure and −0.14 after AV closure ($P$ = .10).

The open-AV and closed-AV slopes were significantly different for the flow ($P$ = .001), UF ($P$ = .031), and LF ($P$ = .003) parameters. The flow increased more rapidly when the AV was open, at 0.244 L min$^{-1}$ increment$^{-1}$, and flattened after AV closure to 0.15 L min$^{-1}$ increment$^{-1}$. The LF followed a similar trend, with the slope decreasing

**Table 1.** Baseline Characteristics of HVAD Speed Optimization Patients

| Characteristic | Speed Optimization (n = 19) |
|---|---|
| Age, y, median (IQR) | 66 (52−69) |
| Male, n (%) | 11 (57.9) |
| BSA, m$^2$, mean ± SD | 1.75 ± 0.19 |
| ICM, n (%) | 10 (52.6) |
| HTN, n (%) | 12 (63.2) |
| BTT, n (%) | 15 (78.9) |
| DM, n (%) | 7 (36.8) |
| Prior sternotomy, n (%) | 5 (26.3) |
| MV repair, n (%) | 10 (52.6) |
| AV closure, n (%) | 1 (5.3) |
| Tricuspid repair, n (%) | 3 (15.8) |
| Pre-implantation LVEDD, mean ± SD | 6.71 ± 1.02 cm |
| Pre-implantation EF, mean ± SD | 16.32 ± 5.96 |
| LVEF at time of Ramp Study, mean ± SD | 15.7 ± 6.7 |
| LVEDD at 2,300 rpm, mean ± SD | 5.38 ± 1.01 |

HVAD, Heartware left ventricular assist device; IQR, interquartile range; BSA, body surface area; ICM, ischemic cardiomyopathy; HTN, hypertension; BTT, bridge to transplantation; DM, diabetes mellitus; MV, mitral valve; AV, aortic valve; LVEDD, left ventricular end-diastolic diameter; EF, ejection fraction; LVEF, left ventricular ejection fraction.

**Table 2.** HVAD Speed Optimization Ramp Test Results

| Parameter | Speed Optimization Ramps (n = 19) |
|---|---|
| Days to ramp, median (IQR) | 23 (15−30) |
| INR, mean ± SD | 2.5 9 ± 0.44 |
| LDH, U/L, mean ± SD | 297.11 ± 97.71 |
| Current speed, rpm, mean ± SD | 2,548.42 ± 99.63 |
| AV closure speed, rpm, mean ± SD | 2,751.77 ± 227.16 |
| Speed adjusted, n (%) | |
| Increased | 4 (21.1) |
| Decreased | 3 (15.7) |
| AI at set speed, n (%) | |
| None | 5 (26.3) |
| Trace | 10 (52.6) |
| Mild | 4 (21.1) |
| AV status at set speed | |
| Open | 12 (63.2) |
| Intermittent | 3 (15.8) |
| Closed | 4 (21.1) |
| MR at set speed | |
| None | 10 (52.6) |
| Trace | 5 (26.3) |
| Mild | 3 (15.8) |
| Moderate | 1 (5.3) |

INR, international normalized ratio; LDH, lactate dehydrogenase; AI, aortic insufficiency; MR, mitral regurgitation; other abbreviations as in Table 2.

**Table 3.** Estimated Model for HVAD Parameters According to AV Status

| Parameter | Estimated Model | | Interaction Term | |
|---|---|---|---|---|
| | AV Open | AV Closed | Δ Slope | *P* Value |
| LVEDD | y = −0.09x + 5.43 | y = −0.15x + 5.51 | −0.06 ± 0.025 | .013 |
| Flow | y = 0.24x + 4.08 | y = 0.15x + 4.75 | −0.09 ± 0.27 | .001 |
| Upper Flow | y = 0.03x + 7.33 | y = −0.10x + 7.45 | −0.13 ± 0.60 | .031 |
| Lower Flow | y = 0.37x + 2.03 | y = 0.28x + 2.41 | −0.09 ± 0.03 | .003 |
| Power | y = 0.41x + 2.44 | y = −0.40 + 2.43 | −0.007 ± 0.016 | .656 |

General estimating equation analysis results of all patients' (n = 19) speed optimization ramp tests. The slope for the AV-closed model is computed by adding the β coefficient for the speed (ie, the slope while the AV is open) and the β coefficient for the interaction between the speed and AV closure. The Δ slope is reported as the β coefficient and its corresponding standard error. Abbreviations as in Table 1.

from 0.37 L min$^{-1}$ increment$^{-1}$ to 0.28 L min$^{-1}$ increment$^{-1}$ after AV closure. For each 1-unit increase in speed increment, the UF increased by 0.03 while the AV was open and decreased by 0.10 L/min while the AV was closed.

There was no significant interaction between speed increment and AV closure for HVAD power ($P$ = .656). The slopes before and after AV closure were very similar, at 0.41 and 0.40 L min$^{-1}$ increment$^{-1}$, respectively.

**Blood Pressure During the Ramp Test.** The blood pressure remained within appropriate limits throughout the ramp test for all patients (82 mm Hg [IQR 78−91] before ramp study and 84 mm Hg [IQR 80−94] at end of ramp study). Before AV closure, the blood pressure increased by 1.61 mm Hg per speed increment, compared with 0.55 mm Hg per speed increment after AV closure. Despite the clinically relevant reduction in blood pressure slope after AV closure, the interaction between AV status and blood pressure was found to be nonsignificant ($P$ = .158).

## Discussion

In this study, we describe a standardized clinical Ramp Test protocol for HVAD speed optimization for routine clinical use before hospital discharge and presented updated data for HMII patients. Our principal findings are as follows[1]: The parameter slopes found in HVAD patients are drastically different from HMII patients' slopes, and therefore it is extremely important that clinicians do not use the HMII slopes to diagnose device malfunction in HVAD patients.

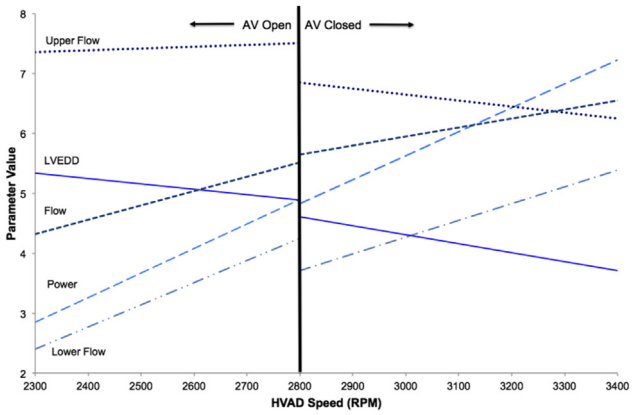


**Fig. 2.** Change in ramp test parameter at the average AV closure speed. AV closure is denoted by the black vertical line at HVAD speed 2800 rpm. The regression lines to the left depict the average parameter slopes before AV closure, and those to the right depict the average parameter slopes after AV closure.

It is clear that the HVAD LVEDD slope has a smaller magnitude than that of HMII, regardless of AV closure status. It is important to note that the average HVAD slope was below the −0.16 rpm/increment threshold established by Uriel et al for the diagnosis of device malfunction, and HVAD patients should not be exchanged solely due to a "flattened" ramp study. This finding reinforces the importance of understanding each pump's unique bioengineering when making decisions about patient management. Physiological principles derived from one LVAD should not be directly applied to other LVADs without confirmatory testing.[2] The parameter slopes are significantly affected by AV status changes in HVAD but not HMII patients, which suggests different unloading properties. Namely, in the centrigufal HVAD pump the LV is unloaded in 2 distinct phases. First, while the AV is open (usually at lower speeds), there is minimal change in LVEDD with an increase in device RPM. Second, when the AV closes as the device speed is increased, there is more LV unloading and the aortic valve remains closed, the magnitude of the LVEDD slope increases by 66%, and there is a more robust reduction in the LVEDD. In contrast, there is no significant difference in LVEDD slopes before and after AV closure in HMII patients.

Echocardiography has assumed a central role in understanding the complex patient-device interface. We previously reported a negative linear relationship between LVAD speed and LVEDD changes in patients supported by the HMII axial-flow continuous-flow pump.[3] This linear relationship assumed that the volumetric change we see during the ramp test, as reflected by changes in the LVEDD, could help in adjusting the device speed to ensure LV decompression with at least intermittent AV opening. The use of this test has become routine and is useful in the diagnosis and troubleshooting of device malfunction.[11,12]

Our finding of the reduced LVEDD slope in the HVAD compared with the HMII is consistent with the

bioengineering principles of centrifugal-flow pumps as described previously by Moazami et al.[13] These pumps operate on a flat pressure-flow curve, such that large changes in flow are accompanied by minimal changes in pressure across the pump. If one assumes that LVEDD is a surrogate for pressure, our study is an in vivo demonstration of the biomechanics of centrifugal-flow pumps. However, this assumption may not be valid, because LVEDD is a 2D measurement of a 3-dimensional ventricle. Another potential explanation for our finding is that owing to its intrapericardial position, the HVAD may have a regional effect on volume unloading, such that the base of the heart, where LVEDD is measured, is relatively spared. Therefore, the lack of change in LVEDD may not necessarily reflect a lack of change in LV pressure or volume.

The quantification of the relationship between LVEDD and device speed requires consideration of the status of AV opening. Because the HVAD did not change the LVEDD significantly while the AV was still open, the LV pressure must be, at least intermittently, higher than the pressure in the ascending aorta. In contrast, when the ascending aortic pressure becomes higher than the LV end-diastolic pressure, and the AV closes, the LVEDD can begin to decrease markedly. This finding may reflect the HVAD's sensitivity to changes in its loading conditions. When the AV is closed, preload is diminished and there is less arterial pulsatility, both of which may serve to enhance pump function. Alternatively, the change in LVEDD slope may be due to a change in ventricular shape following AV closure, such that the effects of volume unloading are more readily transmitted to the base of the heart. The interaction with MV repair suggests that ventricular geometry affects the unloading properties of the HVAD. By decreasing the size of the mitral annulus, the MV repair amplifies the effects of ventricular decompression at the base of the heart. One may hypothesize that HVAD patients should undergo concomitant mitral valve repair at the time of implantation to maximize the efficiency of LV decompression by the LVAD.

Although there was only 1 patient in this study with more than mild valvular disease, it is important to remember that both AI and MR may alter the results of a ramp study.[14] In particular, aortic insufficiency imparts an additional volume load on the LV that may prevent adequate decompression during increases in LVAD speed. Although MR often decreases with higher speeds, it may persist in the setting of structural valve disease. Because of the alterations in LV physiology with LVAD support, it is possible that we are underestimating the impact of even mild valvular lesions in the context of a continuous-flow pump. An investigation of the hemodynamic impact of valvular disease on LV unloading is warranted.

The reason for the difference in behavior noted during HVAD and HMII ramp tests is not clear from the present study. One potential explanation for the differences may be the intrathoracic location of the HVAD, rather than the intra-abdominal location of the HMII. The HVAD may push the ventricular apex toward the base of the heart whereas the HMII may pull the apex away from the base, resulting in very different ventricular geometries. Accordingly, changes in volume achieved during ramps may manifest very differently when viewed only by 2D echocardiographic measurement of the dimension of the base of the heart.

In the present study, we did not correlate the 2D echocardiographic changes with hemodynamics, so we were not able to directly address the effect of changing speeds on the more important hemodynamic parameters. One may question if LVEDD is the right parameter to follow during the ramp test performed in HVAD patients. Currently, the established understanding of CF-LVADs is that LV volume decreases when device speed is increased. However, this may not be captured by changes in the LVEDD alone. Although the present results of the HVAD ramp with the use of 2D echocardiography would seem to support the hypothesis that the HVAD decompresses the LV less than the HMII does, the ADVANCE and continued access protocol (CAP) studies report 90% or greater 1-year survival and significant improvements in the quality of life.[15] Because it is unlikely that the observed clinical improvements would be accomplished without significant improvements in central hemodynamics, it is evident that new techniques should be developed to accurately assess the LV decompression achieved by the HVAD. If this is the case, the HVAD decompresses the LV in a different way than the HMII, and 2D LVEDD changes may not provide an accurate assessment of LV unloading. From the above, we may speculate that the clinical relevance for 2D echocardiographic ramp test in patients supported with HVAD is limited. In our cohort, the LVEDD changes were not significant enough to guide speed adjustment, and the adjustments in speed were based mostly on AV opening. As a result, only 39% of the patients' speeds were adjusted at the conclusion of the HVAD ramp tests, in contrast to 61% of patients in the HMII cohort.[3]

Over the past year, we have witnessed an increase in the reported rate of device thrombosis. In the HMII population, Starling et al reported a concerning estimated rate of 11.3% at 1 year in the current era, and an Interagency Registry for Mechanically Assisted Circulatory Support analysis by Kirklin et al reported a decrease in the 6th-month freedom from device thrombosis from 99% to 94%.[16,17] In HVAD patients, Najjar et al reported an 8.1% rate at 1 year.[18] Najjar et al also reported a specific HVAD log file fingerprint that can aid in the diagnosis of device thrombosis that requires further testing, which facilitated early intervention and successful medical treatment in $>50\%$ of cases. The authors demonstrated that without a change in device speed, patients with device thrombosis will have a rapid increase in the power followed by a significant increase in the flow, which can be seen on the log file. In a previous report, we demonstrated the benefit of ramp test as a tool for diagnosis of obstruction to flow, and the ramp test was adapted to confirm device thrombosis.[19] However, using either HMII method, the majority of the HVAD patients in this cohort would have been diagnosed with a device

thrombosis. The present findings diminish the utility of using an echocardiographic-guided ramp test for diagnosing device thrombosis in HVAD patients and challenge the rationale of 2D echocardiography use at this time for troubleshooting device malfunction in HVAD patients.

## Study Limitations

This study has several limitations. First, it is a single-center prospective analysis of a relatively small cohort of patients. Second, the test was based on the same protocol design for the HMII without adding hemodynamics parameters or 3D volumetric assessment that might explain the differences we observed.

## Conclusion

Unloading of the LV, as assessed by changes in LVEDD, are different in axial-flow and centrifugal-flow pumps, which has implications for the device optimization and evaluation of device obstruction in HVAD patients. Furthermore, the relationship between LVEDD and rpm for HVAD patients is different when the aortic valve is open and closed. Different unloading mechanics should be studied with the use of hemodynamics and 3-dimensional echocardiography.

## Disclosures

Dr Yoshifumi Naka, Dr Ulrich Jorde, and Dr Nir Uriel are consultants to Thoratec and Heartware. Dr Burkhoff is an employee of Heartware. The other authors report no potential conflicts of interest.

## Supplementary Data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.cardfail.2015.06.010

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