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Hemodynamic Ramp Tests in Patients With Left Ventricular Assist Devices

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ABSTRACT

OBJECTIVES This study tested whether combined invasive hemodynamic and echocardiographic ramp tests can help optimize patient management.

BACKGROUND Guidelines for optimizing speed and medications in continuous flow ventricular assist device (cfLVAD) patients are mainly based on expert opinion.

METHODS Thirty-five cfLVAD patients (21 HeartMate II [Thoratec, Pleasanton, California] and 14 HVAD [HeartWare International, Framingham, Massachusetts]) underwent ramp tests with right heart catheterization (including central venous pressure [CVP], pulmonary artery pressure, pulmonary capillary wedge pressure [PCWP], and blood pressure) and echocardiography. Data were recorded at up to 9 speed settings. Speed changes were in steps of 400 revolutions per minute (RPM) for HeartMate II (8,000 to 12,000 RPM) and 100 RPM for HVAD (2,300 to 3,200 RPM) patients.

RESULTS Only 42.9% of patients had normal CVPs and PCWPs at their original RPM settings. Going from lowest to highest speeds, cardiac output improved by 0.16 ± 0.19 l/min/step (total change 1.28 ± 1.41 l/min) and PCWP decreased by 1.23 ± 0.85 mm Hg/step (total change 9.9 ± 6.5 mm Hg). CVP and systolic blood pressure did not change significantly with RPM. RPM were adjusted based on test results to achieve CVPs and PCWPs as close to normal limits as possible, which was feasible in 56% of patients. For the remainder, results indicated which type of medical management should be pursued.

CONCLUSIONS Use of combined hemodynamic and echocardiographic ramp tests in patients provides objective means of optimizing RPM, and has the potential to guide medical management. It remains to be tested whether this strategy has a beneficial impact on quality of life or clinical outcomes. (J Am Coll Cardiol HF 2016;4:208-17)
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Continuous flow left ventricular assist devices (cfLVADs) prolong life in end-stage heart failure (1-3) and are increasingly used as both bridge to transplantation and destination therapy. With increasing duration of cfLVAD support, attention is shifting to enhancing patient quality of life. One important step is optimization of patients' hemodynamic profile, which is dependent on the complex interaction between the individual patient's pathophysiology and pump characteristics. On the patient side, ventricular contractility and volume status, together with pulmonary and systemic vascular properties, are important factors. In contrast, pump characteristics are quantified by speed-dependent pressure-flow relationships. Of the two most widely used cfLVADs, one is a centrifugal flow pump

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(HVAD, HeartWare International, Framingham, Massachusetts) and the second one is an axial flow pump (HeartMate II, Thoratec, Pleasanton, California). Multiple investigators have suggested that fundamental differences exist in the pumping characteristics of these 2 devices (4,5).

Optimizing the hemodynamic profile of a cfLVAD patient requires detailed comprehension of ventricular-vascular-cfLVAD interactions (6). The International Society of Heart and Lung Transplantation guidelines predominantly reflect expert opinion, and there is significant physician variability in the assessment and management of cfLVADs (7). (Revolutions per minute (RPM) are recommended to be adjusted to adequately unload the left ventricle (LV) while maintaining midline interventricular septum and minimizing mitral regurgitation (Class of Recommendation: I; Level of Evidence: C). RPM are recommended to be set low enough to allow intermittent aortic valve (AV) opening (Class of Recommendation: IIb; Level of Evidence: B). Diuretics, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, β-blockers, and mineralocorticoids are considered useful for managing volume status, blood pressure, arrhythmias, and myocardial fibrosis (Class of Recommendation: I; Level of Evidence: C) (8).

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The intent of this study is to develop an evidence-based approach to the management of cfLVAD patients based on the interaction between device function and patient hemodynamics. We applied a standardized hemodynamic ramp protocol in clinically stable cfLVAD patients to assess the impact of acute changes in cfLVAD speed on hemodynamics and LV unloading. We hypothesize that the findings of this study will have important implications for the refinement of management guidelines and establish the role of periodic hemodynamic monitoring in cfLVAD patients.

METHODS

In this prospective study, 35 consecutive cfLVAD patients (14 HVAD and 21 HeartMate II) were enrolled and evaluated with a hemodynamic and echocardiographic ramp test. The test was performed in stable outpatients, ideally between 1 and 3 months following LVAD implantation. Patients implanted prior to the initiation of this protocol were enrolled as they were seen in the outpatient clinic, regardless of time since surgery. This study includes patients undergoing the hemodynamic ramp study for LVAD speed optimization. Patients in whom an LVAD thrombus was suspected were excluded.

RAMP TEST PROTOCOL. In the catheterization laboratory, patients underwent an echocardiographic ramp study using previously reported methods (8,9). Simultaneously, we assessed hemodynamics with right heart catheterization. The complete protocol is described in the Appendix. The hemodynamic parameters recorded included opening Doppler blood pressure (oD-BP) (9); central venous pressure (CVP); systolic, diastolic, and mean pulmonary artery pressures (PAP); and pulmonary capillary wedge pressure (PCWP). Cardiac output (CO) and cardiac index (CI) were calculated by the indirect Fick method. Two-dimensional echocardiographic parameters were collected as detailed previously (10,11). At the conclusion of each test, the attending cardiologist reviewed the data and the device was set at the speed wherein hemodynamic normalization was achieved, that is, PCWP <18 mm Hg and CVP <12 mm Hg, with the secondary goals of intermittent AV opening and minimal mitral regurgitation.

DATA ANALYSIS AND STATISTICAL METHODS. Ramp test parameter recordings at different speeds were entered into a spreadsheet (EXCEL 2010 Microsoft Corporation, Redmond, Washington) and plotted with either EXCEL or Origin (OriginLab Corporation, Northampton, Massachusetts) software. All statistical analyses were performed using SPSS (version 22, IBM, Armonk, New York). Normality was tested with the Shapiro-Wilk test. Normally distributed continuous variables were reported as mean ± SD, and skewed continuous data are reported as median (interquartile range). Categorical variables were summarized using frequencies and percentages. Continuous variables were compared using the Student's *t* test or Mann-Whitney *U* test, as appropriate. Categorical values were compared with the chi-square or Fisher's exact test. A p value of 0.05 was considered statistically significant. Slopes were calculated using linear regression (10), which is described in detail in the Online Appendix. The University of Chicago's Institutional Review Board committee approved this study and all patients signed informed consent.

RESULTS

BASELINE CHARACTERISTICS. Patient characteristics are summarized in Table 1. Patients were

ABBREVIATIONS AND ACRONYMS

AV = aortic valve

cfLVAD = continuous flow left ventricular assist device

CI = cardiac index

CO = cardiac output

CVP = central venous pressure

LV = left ventricle/ventricular

oD-BP = opening Doppler blood pressure

PAP = pulmonary artery pressure

PCWP = pulmonary capillary wedge pressure

RPM = revolutions per minute

RV = right ventricle/ventricular

TABLE 1 Baseline Characteristics

	All (N = 35)	HeartMate II (n = 21)	HVAD (n = 14)	p Value
Age, yrs	58.5 ± 9.4	59.9 ± 9.2	56.4 ± 9.5	0.28
Male	62.9 (21)	61.9 (13)	64.3 (9)	0.89
Ischemic etiology	40.0 (14)	28.6 (6)	57.1 (8)	0.09
Destination therapy	71.4 (25)	90.5 (19)	42.9 (6)	0.006
Diabetes mellitus	38.2 (13)	35.0 (7)	42.9 (6)	0.65
Hypertension	48.6 (17)	57.1 (12)	35.7 (5)	0.23
Prior stroke	5.7 (2)	4.8 (1)	7.1 (1)	0.77
NYHA functional class I/II	74.2 (26)	71.4 (15)	78.6 (11)	0.64
Implant to ramp study, days	321 (121–644)	373 (166–644)	173 (86–510)	0.27
Hemodynamics at baseline				
cfLVAD speed, RPM		9,094 ± 417	2,704 ± 147	
oD-BP, mm Hg	89.1 ± 11.6	89.1 ± 12.0	89.0 ± 11.5	0.83
CVP, mm Hg	9.5 ± 6.0	10.1 ± 6.1	8.5 ± 6.0	0.45
Systolic PAP, mm Hg	37.5 ± 11.2	37.6 ± 12.1	37.4 ± 10.0	0.95
Diastolic PAP, mm Hg	19.1 ± 7.0	19.0 ± 7.4	19.2 ± 6.6	0.91
Mean PAP, mm Hg	25.4 ± 8.1	25.8 ± 8.6	24.9 ± 7.5	0.75
PCWP, mm Hg	13.8 ± 6.9	14.4 ± 7.8	12.9 ± 5.4	0.51
CO, l/min	4.3 ± 1.2	4.2 ± 1.0	4.5 ± 1.4	0.54
CI, l/min/m^2	2.1 ± 0.5	2.0 ± 0.4	2.3 ± 0.5	0.09
Flow, l/min	4.6 ± 0.7	4.9 ± 0.5	4.2 ± 0.9	0.04

Values are mean ± SD, n (%), or median (interquartile range).

cfLVAD = continuous flow left ventricular assist device; CI = cardiac index; CO = cardiac output; CVP = central venous pressure; NYHA = New York Heart Association; oD-BP = opening Doppler blood pressure; PAP = pulmonary artery pressure; PCWP = pulmonary capillary wedge pressure.

58.5 ± 9.4 years old and mostly male (62.9%). The majority of patients were implanted for destination therapy (71.4%). The median time between the ramp test and device implantation was 321 days (range 13 to 1,954 days). There were more patients implanted as destination therapy in the HeartMate II group and the median interval between implantation and the ramp test tended to be longer (median 373 vs. 173 days for HeartMate II and HVAD, respectively; p = 0.27).

Hemodynamic parameters at baseline speeds (9,094 ± 417 RPM for HeartMate II and 2,704 ± 147 RPM for HVAD) were similar between devices. In terms of optimal hemodynamics, 42.9% of patients had both CVP and PCWP in the defined normal range.

Fick CO values were similar between devices; however device-estimates of cfLVAD flow differed between groups. The correlation between device flow and Fick CO when the AV was closed (i.e., total flow provided by the device) differed between devices: Fick CO = 0.11 + Flow 1.09 for HVAD (r^2 = 0.43) and Fick CO = 2.70 + 0.38·Flow for HM II (r^2 = 0.07). Accordingly, comparisons will be based on ramp step numbers and Fick CO, not device-estimated flows.

RAMP STUDY RESULTS. The slopes of the relationships between RPM steps and each of the hemodynamic and echocardiographic parameters are summarized in Table 2.

Cardiac output. Increases in device speed were associated with increases in pulmonary artery oxygen saturations (Figures 1A and 1B) indicative of increased CO (Figures 1C and 1D). In HVAD patients, Fick CO averaged 4.2 l/min at 2,300 RPM and increased by an average 0.09 l/min for each 100 RPM increase such that at RPM step 9 (or highest RPM achieved), flow increased to 5.1 l/min. In HeartMate II patients, Fick CO averaged 3.7 l/min at 8,000 RPM and increased by an average of 0.21 l/min for each 400 RPM increase such that at RPM step 10 (or highest RPM achieved), flow was increased to 5.2 l/min. There was considerable interpatient variability (ranging from 2.4 l/m to 7.0 l/m at the lower speed), and patients with low levels of CO tended to have lower slopes, irrespective of device.

PCWP, CVP, PAP, and oD-BP. Figure 2 shows the impact of RPM changes on PCWP for HVAD (Figure 2A) and HeartMate II (Figure 2B) patients. At any given RPM step, PCWP varied widely between patients. For example, at RPM step 0, PCWP ranged between 4 and 38 mm Hg among the 2 cohorts. In all patients and for both devices, PCWP decreased with increasing device speed (Table 2). On average, there was a 1.23 mm Hg reduction in PCWP with each RPM step. In addition, there was a strong inverse relationship between PCWP and in all patients (Figures 2C and 2D). The slope of these relations did not differ between HVAD (-6.3 ± 4.9 mm Hg·min/l) and HeartMate II (-5.5 ± 4.3 mm Hg·min/l; p = 0.65).

Similar to PCWP, CVP varied widely between patients (Figures 2E and 2F). At step 0, CVP ranged between 3 and 30 mm Hg. However, in sharp contrast to PCWP, CVP did not vary significantly with changing

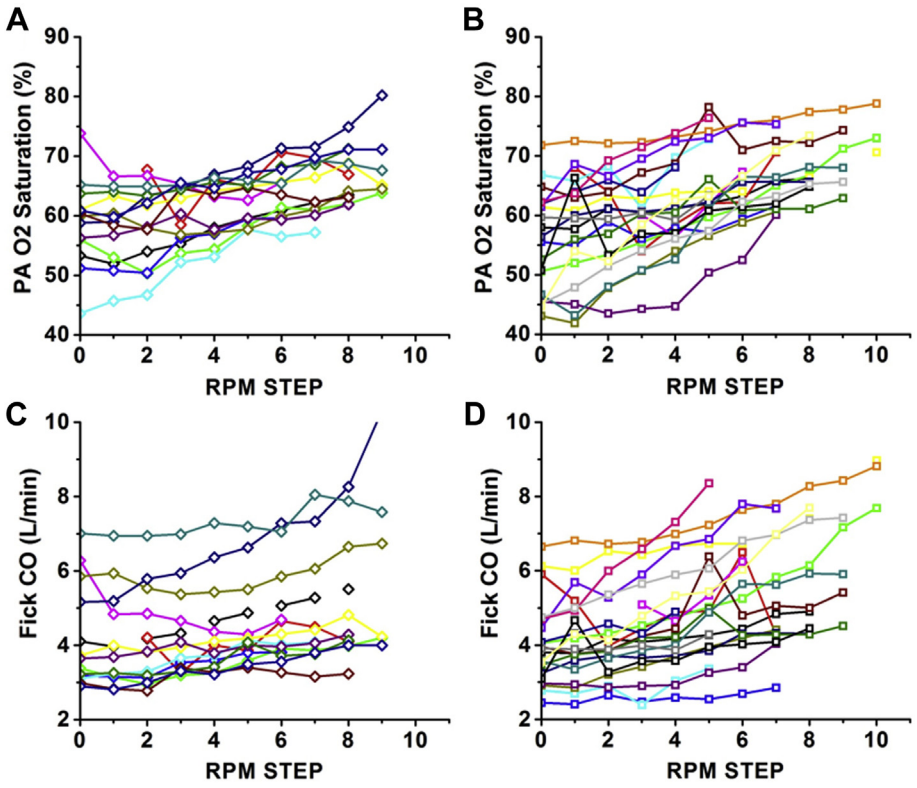
TABLE 2 Hemodynamics and Echocardiographic Changes in Response to Speed Changes as Represented by the Slope of the Overall Change

	HeartMate II (n = 21)	HVAD (n = 14)
CVP slope	-0.29 ± 0.36	-0.24 ± 0.29
Systolic PAP slope	-1.19 ± 0.83	-0.76 ± 0.65
Diastolic PAP slope	0.79 ± 0.50	-0.69 ± 0.51
Mean PAP slope	-1.01 ± 0.56	-0.64 ± 0.50
PCWP slope	-1.42 ± 0.76	-1.01 ± 0.68
CO slope	0.23 ± 0.17	0.10 ± 0.13
CI slope	0.11 ± 0.09	0.06 ± 0.07
oD-BP slope	1.05 ± 3.65	0.21 ± 1.34
Flow slope	0.38 ± 0.72	0.16 ± 0.05
PA O_2 Sat	1.55 ± 0.95	0.97 ±.0.88
LVEDD 2D	-0.20 ± 0.14	-0.11 ± 0.05

Values are mean ± SD.

LVEDD = Left ventricular end diastolic diameter; PA O_2 Sat = pulmonary artery oxygen saturation; other abbreviations as in Table 1.

FIGURE 1 Changes in PA O_2 Saturation and Fick CO During Ramp Studies



Pulmonary artery oxygen saturation and Fick cardiac output (CO) increased in both HVAD (HeartWare International, Framingham, Massachusetts) **(A and C)** and HeartMate II (Thoratec, Pleasanton, California) **(B and D)** patients. For HVAD patients, revolutions per minute (RPM) ranged between 2,300 and 3,200 RPM, with 100-RPM steps. For HeartMate II patients, RPM ranged between 8,000 to 12,000 RPM with 400-RPM steps. PA O_2 = pulmonary artery oxygen.

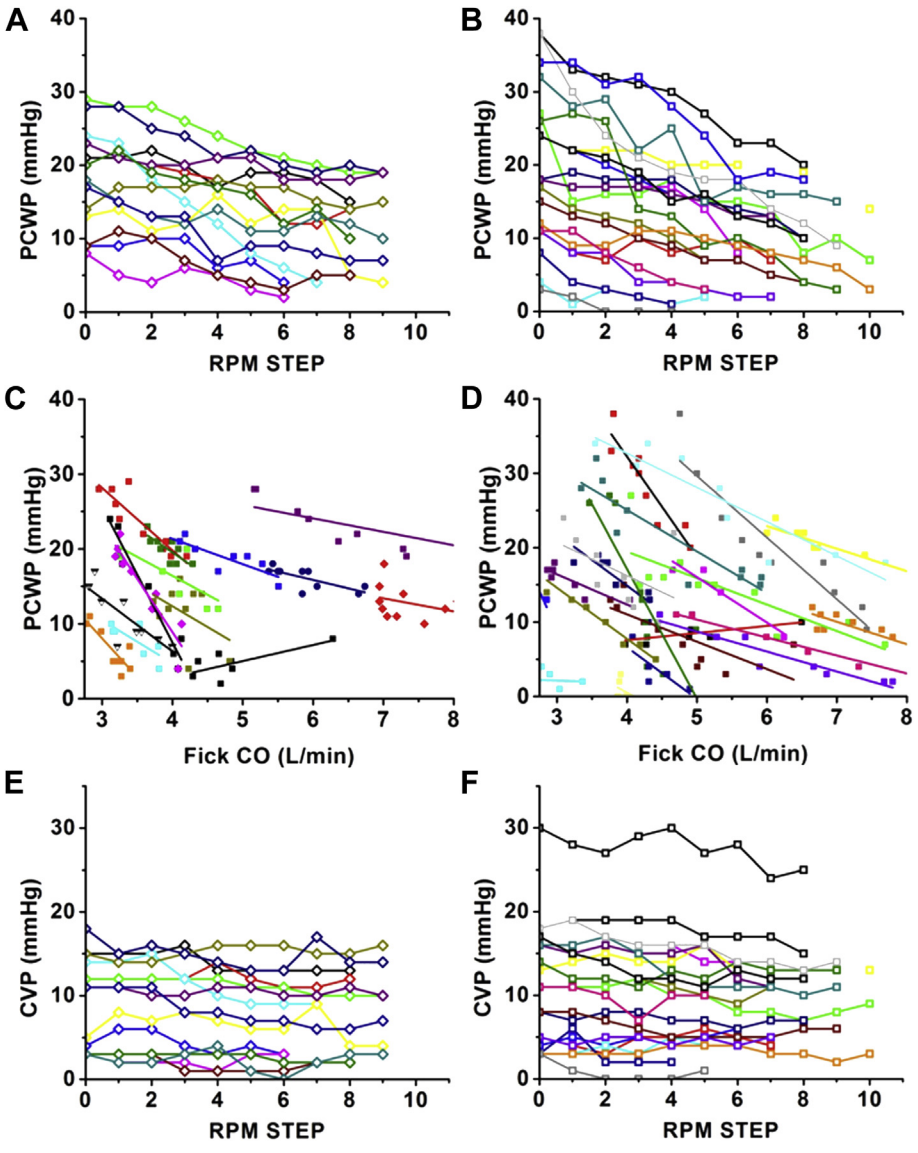
RPM's with either device. The slope of these relations averaged -0.3 ± 0.3 mm Hg.min/l, indicating the overall trend for CVP to decrease with increasing RPM.

Systolic and mean PAP decreased with increasing RPM by similar values as PCWP (Table 2). However, diastolic PAP did not change significantly. oD-BP increased from 86 ± 18 mm Hg to 96 ± 18 mm Hg with a slope of 0.7 ± 2.8 mm Hg/step. The change in oD-BP may have underestimated changes in mean blood pressure, as this value is more likely to represent systolic blood pressure at lower ramp stages and mean blood pressure at higher stages, due to changes in pulsatility.

CVP-PCWP correlations. To test whether patients with high PCWP also had high CVP, we plotted these 2 variables versus each other (Figure 3). This graph was divided into 5 zones depending on reduced, normal, *or* elevated PCWP (normal range set between 8 and 18 mm Hg) and reduced, normal or elevated CVP (normal range set between 3 and 12 mm Hg). The line depicting the CVP-PCWP ratio of 0.63 (considered by some investigators as an index of right heart failure) is illustrated in Figure 3A (11). The different zones are labeled normal, hypovolemic, volume overload, right heart failure, and left heart failure, as shown, depending on the combination of PCWP and CVP (discussed further subsequently). At baseline (i.e., at the originally set speed) (Figure 3A), 20 (57%) patients were outside the normal zone, with several in the volume overload, hypovolemic, and right heart failure zone. Note that there were multiple patients with CVP/PCWP >0.63, but most of these patients were not considered on a clinical basis to have right heart failure.

At RPM step 0 (Figure 3C) the points shifted upward and rightward, with more patients moving into the left heart failure and volume overload zones. In contrast, at RPM step 9, the points shifted downward and leftward, with some shifting to the right heart failure and hypovolemic zones. These data show that

FIGURE 2 Changes in PWCP and CVP During Ramp Studies

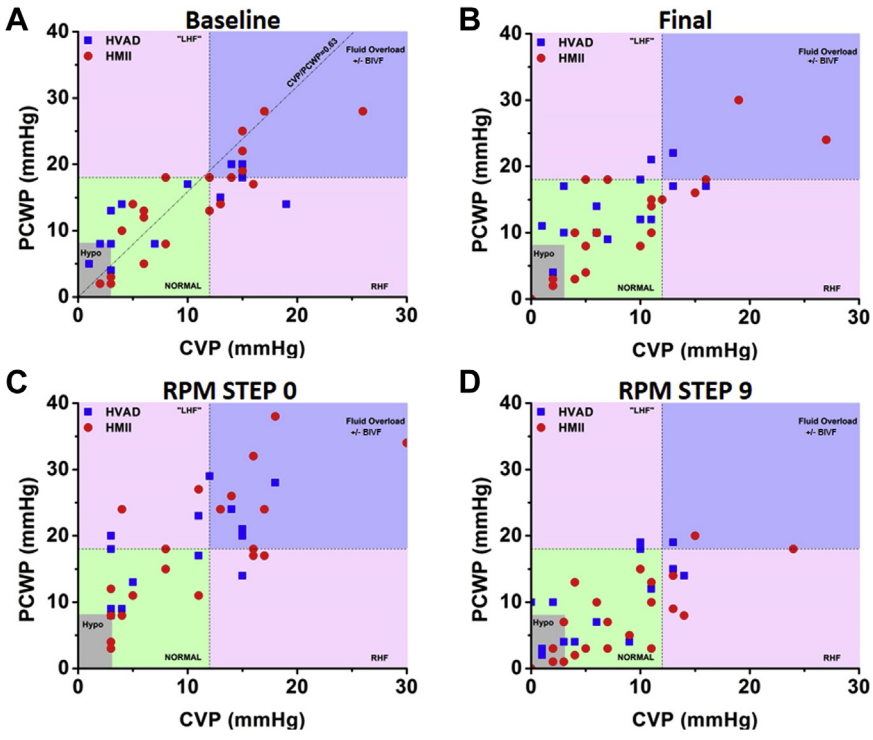


Pulmonary capillary wedge pressure (PCWP) decreased with increasing revolutions per minute (RPM) for both HVAD (HeartWare International, Framingham, Massachusetts) **(A)** and HeartMate II (Thoratec, Pleasanton, California) **(B)** patients. The reduction in PCWP was linearly related to Fick cardiac output (CO) in both HVAD **(C)** and HeartMate II **(D)** patients. Central venous pressure (CVP) did not vary significantly in either HVAD **(E)** or HeartMate II **(F)** patients.

the PCWP-CVP working point can be manipulated by changing RPM, but that it cannot always be positioned for both parameters within the normal limits.

Speed changes as a result of the ramp study. The ramp studies guided cfLVAD speed adjustments and changes in medical therapy. Examples of individual test results are shown graphically in Figures 4A to 4D. For each patient, PCWP is plotted as a function of CVP at each of the RPM tested. Furthermore, points are color coded for whether CI was ≥2.0 l/min/m^2 (blue) or <2.0 l/min/m^2 (red). Patient A was able to achieve normal CVP, PCWP, and CI. Patient B remained with elevated CVP and PCWP over the entire range of RPM, suggestive of the need for diuresis. Patient C had low CVP, PCWP, and CI, suggestive of volume depletion. Patient D remained with elevated CVP and low PCWP

FIGURE 3 Relationship of CVP and PCWP in Individual Patterns at Baseline, Final Set Speed, Ramp Stage 0, and Final Ramp Stage



Plots of individual patients' CVP versus PCWP. Plots are divided into 5 zones based on hemodynamic profiles: normal, left heart failure (LHF), fluid overload, right heart failure (RHF), and hypovolemia (Hypo). **(A)** Baseline results at the original, pre-ramp test speed. **(B)** Results at the post-test speed showing a migration of the points toward the normal zone. **(C)** CVP-PCWP relations at the lowest RPM (step 0: 2,300 RPM for HVAD [HeartWare International, Framingham, Massachusetts] and 8,000 RPM for HeartMate II [Thoratec, Pleasanton, California]). **(D)** CVP-PCWP relations at the highest RPM (step 9: 3,200 RPM for HVAD and 12,000 RPM for HeartMate II). Abbreviations as in Figure 2.

over the entire range of RPM, suggesting persistent right heart failure.

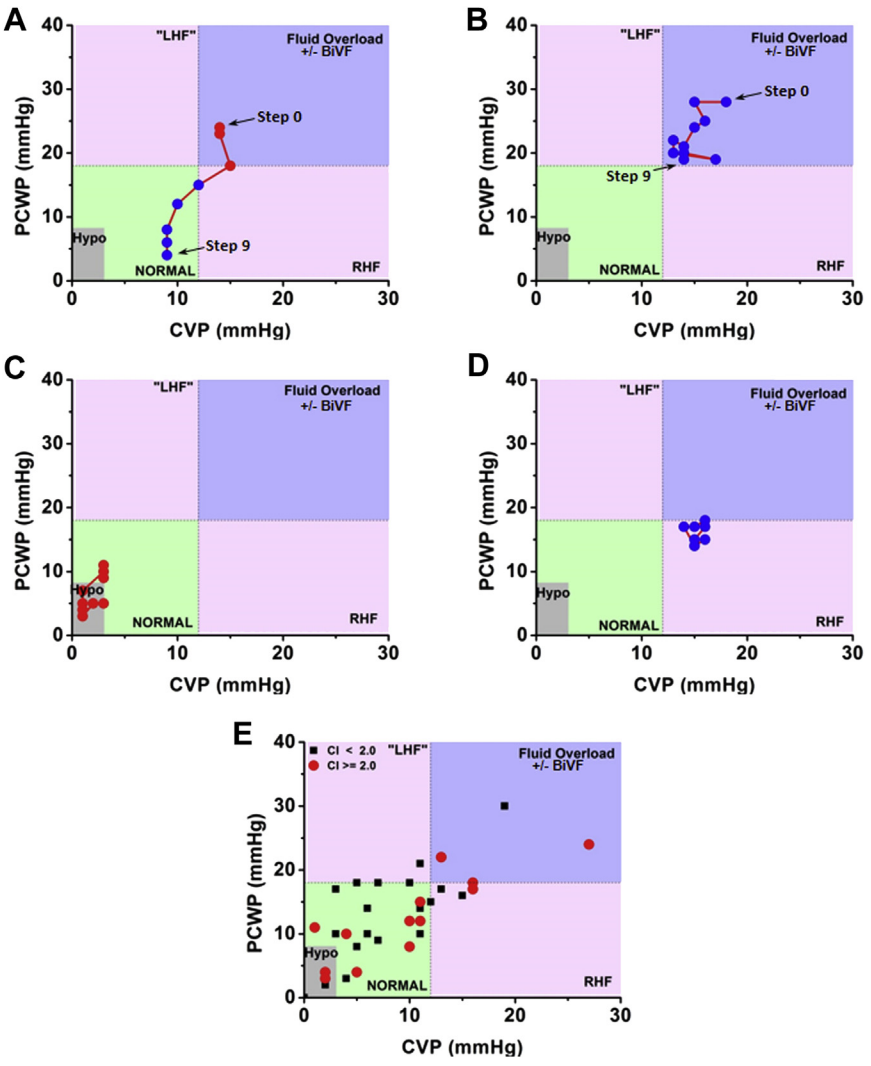
Overall, 12 (34%) patients had their speed changed by ≥100 RPM in HVAD or ≥400 RPM in HeartMate II as a result of the ramp test (5 HVAD and 7 HeartMate II); speed was increased in some and decreased in others. The mean new speeds were 2,750 ± 158 for HVAD and 9,313 ± 416 for HeartMate II. Overall, there were no differences in average hemodynamic parameters when comparing baseline values to those obtained with the final set values. However, the percent of patients with both CVP and PCWP within the normal zone increased from 40% at baseline to 56% at the final set speed. Plotting PCWP versus CVP provides an overview of the improvements in hemodynamics before the ramp test (at baseline) and at the final set speed at the end of the ramp test. This plot is further refined to code for CI as shown in Figure 4E.

Finally, at the new set speed, 33% of the patients (30% of HeartMate II and 38% of HVAD patients) had at least intermittent AV opening at the optimized hemodynamics.

DISCUSSION

We performed hemodynamic and echocardiographic ramp tests in patients supported by cfLVADs. There are 3 main findings. First, there was an unexpectedly wide variability in baseline (i.e., pre-ramp test) hemodynamics in our patients managed according to clinical standards. Second, only 43% of the patients had "normal" hemodynamic profiles at their baseline speeds; this improved to 56% after speed adjustments based on test results. Third, both axial and centrifugal cfLVADs provided significant unloading of the LV, manifested as decreases in PCWP. These changes were flow dependent, not device dependent.

FIGURE 4 Examples of Change in CVP-PCWP Relationship During Ramp Studies and Final CVP-PCWP Relationship of All Patients at Set Speed



Examples of CVP-PCWPs from 4 individual ramp tests **(A to D)**. **Dots** are coded for cardiac index (CI) ≥2.0 l/min/M2 in **blue**, and CI <2.0 l/min/M2 in **red**. **(A)** Patient moves from fluid overload zone at step 0 to normal zone with increased RPM. **(B)** Patient remains in fluid overload zone independent of RPM. **(C)** Patient remains in the hypovolemic zone independent of RPM. **(D)** Patient remains in RHF zone with elevated CVP and normal PCWP. **(E)** Results of all tests at the final set RPM, with color coding of CI. Abbreviations as in Figure 2.

Our population of outpatients managed according to current International Society of Heart and Lung Transplantation guidelines, which was seemingly well compensated from a heart failure perspective had a wide spectrum of hemodynamic profiles. Multiple patients had PCWPs and CVPs that were well outside the normal ranges, suggestive of fluid overload, hypovolemia, or right ventricular (RV) failure. Only 43% of the patients had PCWPs and CVPs within the normal range and significantly fewer (23%) had concomitant CIs above a lower cutoff of 2.0 l/min/m^2. After speed adjustments based on the results of the ramp test, the number of patients attaining normal values of PCWP and CVP increased to 56%, while the remaining patients reached improved filling pressures compared to pretest conditions.

The average new optimal set speeds were generally higher than their pre-test values. Most prior publications do not report average cfLVAD speeds (only ranges), making it difficult to compare results between studies. However, the final set speeds achieved in the present study are significantly higher than we

have reported in our prior studies (8,12). Even at these speeds, some of the patients remaining outside the normal hemodynamic boundaries had balanced CVP and PCWP elevations (volume overload state, ~12%), some had mainly isolated CVP elevation (right heart failure, ~9%) and some had low CVPs and PCWPs (hypovolemia, ~9%) suggesting the need for adjustment of medical management.

Our data, when displayed on the CVP-PCWP diagram with color coding for CI (as in **Figure 4**) and regional shading for normal and different types of abnormalities provides an assessment of hemodynamic status that is useful to guide optimization of both device settings and medical therapy. The boundaries between the different regions are somewhat arbitrary and should be considered to provide only a sense of overall status at the time measurements were obtained. Nevertheless, these diagrams emphasize the wide variety of hemodynamic states existing between patients and the need for treating physicians to customize management strategies for the individual patient. For example, the patient depicted in **Figure 4C** suggests that an important contributing factor is hypovolemia. Similarly, the patient illustrated in **Figure 4D** suggests that right heart failure should be investigated. The average slope values summarized in **Table 2** may provide general guidance on how different hemodynamic parameters vary with the different RPM settings for a given cfLVAD device but are not likely to be useful to predict effects in individual patients.

An important additional finding of our study was an unexpected lack of CVP increase with increasing RPM (**Figures 2E and 2F**), which can be explained by several factors. Firstly, a major effect of increasing RPM was a reduction in systolic and mean pulmonary artery pressures. Reductions in these pressures result in a reduction in RV afterload, which, in turn, will augment RV performance. Second, multiple aspects affecting the interaction between the LV and RV can be impacted by increasing RPM, including shifts in the position of the interventricular septum as well as the overall RV geometry (13–15). These and other potential factors contributing to RV function during cfLVAD speed changes require further investigation. Interestingly, independent of RPM settings, LVAD support has been shown to improve RV function and to decrease CVP in the long term (15).

Patients with both centrifugal and axial flow pumps were included in this study to determine if device-specific differences impacting hemodynamics at baseline and with altered RPM exist. No significant differences in baseline hemodynamics were noted between devices. Furthermore, prior studies based solely on LV end-diastolic dimension measurements suggested that centrifugal flow pump would result in decreased LV unloading compared to axial flow pumps (9,16). The data of the present study contradicts these previous conclusions by demonstrating that unloading, indexed by PCWP (**Figures 2C and 2D**) is flow dependent, not device dependent. Our conclusion is similar to that obtained in an independent head-to-head comparison of the 2 types of devices in a mock circulation model and in a bovine model of acute ischemic heart failure (17). The previously reported differences in unloading characteristics were based on linear measurements of LV end-diastolic dimension, which do not take into account changes in LV shape (9,16). At baseline and during a ramp test, changes in LV and RV shape are likely to differ between devices in which the pump is placed within the thorax at the LV apex (HVAD) and devices where the apical inflow conduit pulls the apex inferiorly with the pump in a subdiaphragmatic position. Investigations into such geometric differences are ongoing.

In an echocardiographic ramp study, septal position, AV opening, and mitral regurgitation are used as surrogates for LV unloading (8). Whether these parameters are useful for determining hemodynamic optimization has not been previously reported. We have found that the majority of our cfLVAD population had elevated filling pressures, reduced CO, or both, despite having had speed set based on clinical judgment and the echocardiographic markers noted previously. Invasive hemodynamics provide a more complete understanding of the interface between patient and pump and foster a more sophisticated approach to setting cfLVAD speed.

STUDY LIMITATIONS. This is a single-center study with a small sample size. Because medical management practices vary significantly between sites, it is uncertain whether the same hemodynamic variability would be encountered at all centers. It is noteworthy, however, that in most LVAD studies, >20% of mortality and morbidity is attributed to worsening heart failure (including right heart failure) (2,18). This might be an unrecognized clue that fluid overload may be present in more patients than previously appreciated.

Perhaps most importantly, this study only addressed the impact of acute changes in RPM on hemodynamics. The long-term effects associated with RPM-dependent changes in renal perfusion, modulation of autonomic reflex activity, right heart function, and other factors will also likely have an impact on how RPM settings will affect long term hemodynamics and clinical outcomes.

Technical limitations should also be considered. First, patient COs were estimated using the indirect Fick method, which is known to have limited accuracy. Second, we noted that the correlation between Fick-estimated COs and device-estimated flows differed between devices. This reinforces the use of step sizes for standardizing ramp tests instead of device flow. Limitations of the accuracy of the HeartMate II flow estimator have been suggested in prior reports (19,20). To date there are no published data describing the accuracy of the HVAD flow estimator. Accordingly, the slopes of the relations based on flows and COs should be considered with these limitations in mind.

Finally, while the HVAD step size of 100 RPM was considered to be comparable to an HeartMate II step size of 400 RPM, these are only estimates. Because the shapes of the pressure-flow curves differ significantly over a wide range of RPM, it is not possible to derive a strict relationship between RPM for the 2 devices. Thus, direct comparisons between RPM steps slopes (**Table 2**) should not be made; slope values should be interpreted separately for each device.

CONCLUSIONS

In this study, an unexpectedly high proportion of clinically stable, seemingly well-compensated heart failure patients supported by cfLVAD had abnormal hemodynamic profiles. This suggests that it is clinically challenging to assess volume status and hemodynamic profile in cfLVAD patients based on routine clinical evaluation. We hypothesize that patient outcomes and quality of life could be improved by periodic evaluations of RPM settings to achieve optimal hemodynamics and guide medical therapy. The current results suggest that combined hemodynamic-echocardiographic ramp tests have the potential of providing objective means of guiding management decisions. Importantly, no fundamental differences in findings or conclusions are based on the type of device (axial or centrifugal flow pump).

Overall, a high interpatient hemodynamic variability in response to a ramp test was noted, indicating the need to understand the responses of each patient to adjust medical therapies and RPM settings. Importantly, there were limits to how much an abnormal hemodynamic profile could be "normalized" by modifying RPM settings, which reinforces the value of optimizing medical therapy. These findings highlight the need for development of clinical tools to help clinicians customize patient-specific management strategies. The CVP-PCWP graph is a simple visual aid that yields clinically relevant insights into individual patient's physiology for guiding therapeutic strategies. However, prior to suggesting widespread adoption of the proposed method, it is necessary to demonstrate that this approach improves patient outcomes (i.e., reduced adverse events), exercise tolerance and quality of life. Until then, the present results provide a foundation for future studies aimed at developing objective and evidence-based management guidelines of these challenging patients. In the future, reliance on noninvasive techniques would be desirable. However, the first step should be to test the specific hypotheses regarding the potential benefits of hemodynamically guided patient management.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Ramp studies that incorporate right heart catheterization and 3-dimensional echocardiography can be used to optimize the speed setting for cfLVAD.

TRANSLATIONAL OUTLOOK: Further studies are needed to determine whether using hemodynamic ramp studies to optimize cfLVAD speed leads to improved survival and a reduction in complications.

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KEY WORDS 3D echocardiography, hemodynamics, left ventricular assist device, ramp, unloading

APPENDIX For expanded Methods section, please see the online version of this article.