HVAD Waveform Analysis as a Noninvasive Marker of Pulmonary Capillary Wedge Pressure: A First Step Toward the Development of a Smart Left Ventricular Assist Device Pump

Jonathan Grinstein,* Daniel Rodgers,* Sara Kalantari,* Gabriel Sayer,* Gene H. Kim,* Nitasha Sarswat,* Sirtaz Adatya,* Takeyoshi Ota,† Valluvan Jeevanandam,† Daniel Burkhoff,‡ and Nir Uriel*

Flow waveforms are an important feature of the HVAD left ventricular assist device (LVAD) that provides information about HVAD function and patient hemodynamics. We assessed the properties of one specific aspect of the waveform, the slope of the ventricular filling phase (VFP), and its correlation with pulmonary capillary wedge pressure (PCWP). A total of 101 screenshots from the HVAD monitor and simultaneous hemodynamic measurements were obtained simultaneously during sequential stages of invasive hemodynamic ramp studies. Each screenshot was digitized (IGOR Pro, WaveMetrics Inc., Oswego, OR) and properties of the flow waveforms including instantaneous flow and rate of change of flow were analyzed. Ventricular filling phase slope (VFPS) was calculated for each screenshot and correlated to PCWP. Ventricular filling phase slope was significantly higher in patients with PCWP ≥ 18 mm Hg than in patients with PCWP < 18 mm Hg [6.25 (5.84–7.37) L/min/s *vs.* 3.27 (2.00–4.69) L/min/s, $p \leq 0.0001$]. A VFPS threshold of 5.8 L/min/s predicted a PCWP ≥ 18 mm Hg with a sensitivity of 87% and specificity of 95% (AUC 0.95). Ventricular filling phase slope of the HVAD flow waveform is a novel noninvasive parameter that correlates with PCWP and can discriminate elevated *versus* normal or low PCWP. Automated reporting of this parameter may help clinical assessment and management of patients supported by an HVAD and may serve as the basis of a smart LVAD pump that can adapt in response to changes in a patient's physiology. *ASAIO Journal* 2017; XX:00–00.

Key Words: left ventricular assist device, hemodynamics, flow versus time waveform.

Continuous flow left ventricular assist devices (CF-LVADs) are the most common form of durable support for advanced heart failure patients with nearly 2,000 implants in the United States each year.[1] Continuous unloading of the left ventricle by CF-LVADs reduces myocardial workload and left-sided filling pressures, inducing reverse remodeling and optimizing conditions for myocardial recovery.[2] The HeartWare HVAD (HeartWare International, Inc., Framingham, MA) is a continuous centrifugal flow pump that is approved for bridge to transplantation (BTT)[3] and is being studied for destination therapy (DT).[4,5] Like all CF-LVADs, ventricular unloading by the HVAD is flow-dependent and therefore speed-dependent, with a strong inverse relationship between speed and pulmonary capillary wedge pressure (PCWP).[6]

Optimization of device speed and medical therapy so that PCWP is in a normal range is considered an important aspect of the long-term care of the CF-LVAD patient in order to minimize the risk of numerous adverse events. However, assessment of PCWP generally requires invasive monitoring. Availability of a noninvasive means of estimating PCWP would provide a powerful tool for monitoring patients and adjusting device speed and medical therapy.

The HVAD system has a unique feature among CF-LVADs of calculating and displaying an estimate of instantaneous device flow. Flow is estimated based on the pump's rotational speed, the electrical current drawn by the pump, and the patient's hematocrit that is entered manually into the monitor. The HVAD estimates of pump flow have been shown to be accurate and to correlate well with flow measured by high fidelity probes both *in vitro* and *in vivo* in an ovine model.[7] Flow through the pump is dependent on the pressure gradient between the LV and aorta and the rotary speed (RPMs) of the device. At constant RPMs, HVAD flow variations occur because ventricular pressure varies during each cardiac cycle (**Figure 1**); peak flow occurs at end-systole when left ventricular (LV) pressure peaks and the pressure gradient is at its lowest value. During ventricular diastole, LV pressure drops to a minimum and then rises during filling after mitral valve opening. Because aortic pressure is normally relatively constant, the rate of rise of flow during diastole reflects the rate of rise of ventricular pressure. This rate is largely determined by end-diastolic LV pressure which, in turn, is a reflection of PCWP.

We therefore hypothesized that the diastolic slope of the HVAD waveform correlates with and can serve as a surrogate for invasively measured PCWP. Flow waveforms were recorded in conjunction with real-time hemodynamics during invasive right heart catheterization (RHC) and correlations between the diastolic waveform slope and PCWP were analyzed to arrive at noninvasive parameters to predict left-sided filling pressures.

From the *Department of Medicine, University of Chicago Medical Center, Chicago, Illinois; †Department of Surgery, University of Chicago Medical Center, Chicago, Illinois; and ‡Division of Cardiology, Columbia University, New York, New York.

Submitted for consideration March 2017; accepted for publication in revised form April 2017.

Disclosure: Dr. Uriel is a consultant to Medtronic and St. Jude. Dr. Jeevanandam is a consultant to St. Jude. Dr. Burkhoff is a consultant to Medtronic. Drs. Grinstein and Uriel hold a patent on the VFPS. All other authors have no relevant disclosures.

Correspondence: Nir Uriel, Cardiovascular Division, University of Chicago Medical Center, 5841 S Maryland Ave, MC 2016, Chicago, IL 60637. Email: nuriel@medicine.bsd.uchicago.edu.

DOI: 10.1097/MAT.0000000000000604

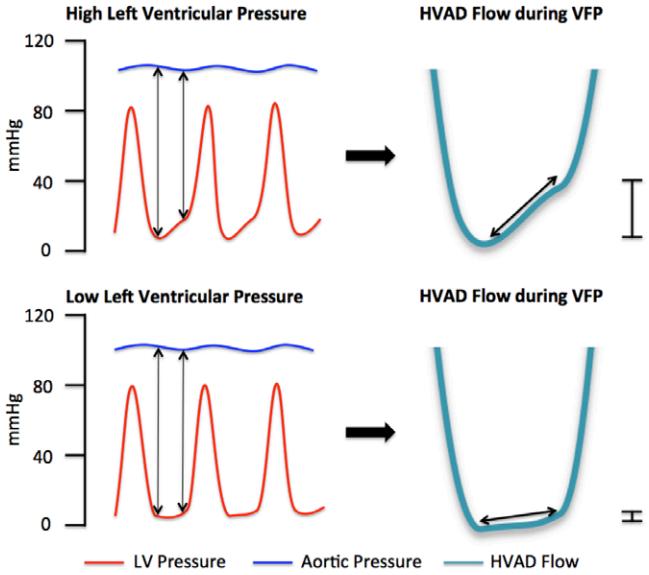

Figure 1. Physiologic principles of the VFP. Instantaneous HVAD flow is dependent on RPMs and the instantaneous difference between aortic ventricular and LV pressure. Under normal HVAD operating conditions, aortic pressure shows relatively little pulsation and is relatively constant. The rate of change of flow during the VFP is therefore largely a reflection of the rate of change of LV pressure during diastole. With higher values of LV end-diastolic pressure (top) a greater rate of rise of flow is expected during VFP. With a lower LV EDP (bottom) a low slope is expected. In turn, LV EDP is expected to correspond to PCWP. PCWP, pulmonary capillary wedge pressure; LV, left ventricular; VFP, ventricular filling phase.

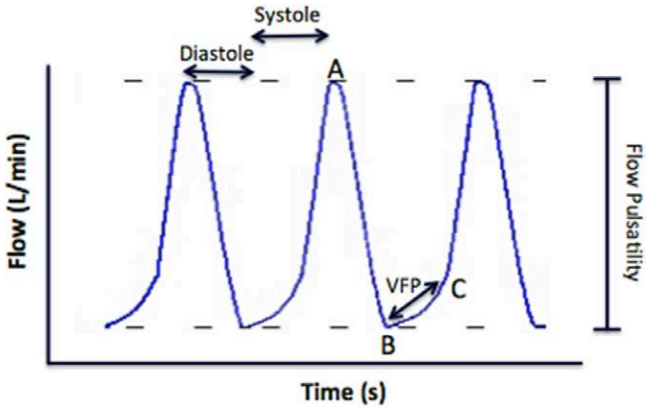

Figure 2. Digitally converted flow *versus* time curve from a HeartWare HVAD screenshot. Flow pulsatility is represented as the difference between peak flow (A) and minimal flow (B). The VFP is the time period between B and C. The VFPS is the rate of change of flow between points B and C. VFP, ventricular filling phase. VFP, ventricular filling phase; VFPS, ventricular filling phase slope.

METHODS

Patient Population

Fifteen consecutive HVAD patients were prospectively enrolled into this study between June 2014 and April 2016. After informed consent, all patients underwent RHC followed by an invasive hemodynamic ramp study.[8] Our HVAD ramp protocol was previously published.[9] In brief, patients had HVAD speeds increased by 100 rpm from 2,300 rpm to a maximum speed of 3,200 rpm. The study was prematurely terminated if a patient developed a suction event, elevated mean arterial pressure above 120 mm Hg or if they developed ventricular arrhythmia. Two patients underwent a reverse ramp protocol with HVAD speed reduction from their baseline speed by 100 rpm increments to a low speed of 1,800 rpm. Screenshots of the HVAD flow *versus* time curves were obtained at each stage of the ramp test. A total of 101 screenshots were obtained. Screenshots of the waveforms were digitally converted for analysis. Waveform parameters were compared with simultaneously measured PCWP. Demographic information and duration of LVAD implantation were obtained by chart review. This study was approved by the institutional review board at the University of Chicago and all subjects provided informed consent.

Right Heart Catheterization

All patients underwent RHC *via* the right jugular vein using a 7 French Swan-Ganz catheter (Edwards Lifesciences, Irvine, CA). Therapeutic anticoagulation was maintained for the test. Measurements included central venous pressure (CVP), systolic, diastolic, and mean pulmonary artery pressures (SPAP, DPAP, and MPAP), PCWP, and pulmonary artery oxygen saturation (PAO2sat). Cardiac output (CO) and cardiac index (CI) were calculated by the indirect Fick equation with estimated oxygen consumption of 125 ml/min/m^2. Hemoglobin was measured from the venous blood gas and arterial oxygen saturation was measured by noninvasive pulse oximetry. Arterial pressure was indexed by the opening pressure recorded using the Doppler technique and a manual sphygmomanometer. Hemodynamic parameters were measured at each stage of the ramp study.

Waveform Analysis

Screenshots of the flow *versus* time waveforms of the HVAD System were obtained using a digital camera (iPhone 6, Apple Inc., Cupertino, CA) at each stage of the ramp study when available. Calibration of the HVAD system using the patients hematocrit was performed before waveform analysis began. A total of 101 screenshots were obtained. The flow waveform recorded from each screenshot was converted into a digital signal using a commercially available wave analyzer (IGOR Pro, WaveMetrics Inc., Oswego, OR). An (X,Y) plot of the waveform was created by using reference points from the flow *versus* time screenshot (*i.e.* zero time was demarcated as X = 0; zero flow was demarcated as Y = 0). Properties of the flow waveforms, including instantaneous flow and rate of change of flow during all stages of the cardiac cycle were analyzed as summarized in **Figure 2**. Image acquisition was standardized by a single operator and data filtering was not performed. Measurements were performed by two operators. Flow pulsatility was defined as the difference between maximum and minimum flow (**Figure 2**, A minus B). The systolic upslope was defined as the rate of change of flow during peak systolic contraction (after point C) and the diastolic downslope was defined as the rate of change of flow during early diastole (period of time between A and B in **Figure 2**). The early VFP flow which begins just after mitral valve opening is represented by the period of time between points B and C in **Figure 2**. The ventricular filling phase slope (VFPS) was calculated as the

difference in flow between points B and C divided by the time difference between those two points.

Statistical Methods

Data were entered into a spreadsheet (EXCEL 2011, Microsoft Corp, Redmond, WA) and analyzed using SPSS Statistical software v.24.0 (SPSS, IBM, Armonk, NY). The Shapiro–Wilk test for normal distribution was used to assess for normality of continuous variables and the Student *t*-test to determine differences in the means of normally distributed data. The Mann–Whitney test was used to compare medians for non-parametric variables. The Fisher's exact test was used to analyze categorical variables. To test whether VFPS could discriminate normal or low PCWP from elevated PCWP, we compared waveform and hemodynamic parameters recorded when PCWP was ≤18 mm Hg to those recorded when PCWP was >18 mm Hg.

In addition, multivariable regression analysis was used to explore the dependence of VFPS on PCWP, heart rate, HVAD RPMs, HVAD mean flow (Flow), and arterial blood pressure (BP). The goal was to arrive a formula to adjust the VFPS to provide the best correlation to PCWP from the other, readily available, noninvasively determinable clinically parameters: $VFPS_{adjusted}$ = a0 + a1*VFPS + a2*HR + a3*RPM + a4*BP +a5*Flow. Parameters with associated p values > 0.15 were removed serially from the multi-regression analysis until all the remaining parameters had $p < 0.05$. Ventricular filling phase slope adjusted according to the final regression equation was designated $VFPS_{adjusted}$.

We also explored the sensitivity and specificity of VFPS alone and $VFPS_{adjusted}$ to discriminate whether PCWP was ≥18 mm Hg. True positive, true negative, false positive, and false negative rates were determined at various thresholds for each parameter. The sensitivity and specificity of these parameters for detecting elevated PCWP was calculated at each threshold and a receiver operator curve (ROC) was constructed as a plot of sensitivity *versus* 1-specificity. Intra-observer variability and inter-observer variability in measurements of the VFPS was assessed in a subset of 15 screenshots by measuring intraclass correlation.

RESULTS

Baseline Characteristics

Right heart catheterization was performed in 15 patients and the baseline characteristics of the cohort are summarized in **Table 1**. In total, there were 101 unique screenshots with corresponding hemodynamic data (**Table 2**). The patients' age ranged from 24 to 76 (mean 54.9) and 47% were male. The majority of patients were implanted as BTT (60%). Data obtained with PCWPs either ≤18 or >18 mm Hg are summarized in **Table 2**. Overall, PCWPs ≥ 18 mm Hg were observed on similar degrees of HVAD RPMs [2,700 (2,420–2,900) rpm *vs.* 2,600 (2,400–2,680) rpm, $p = 0.11$] and with similar Doppler opening pressures [95 (86–102) mm Hg *vs.* 90 (87–100) mm Hg, $p = 0.88$] compared with screenshots associated with PCWPs < 18 mm Hg. Recordings obtained at the higher range of PCWPs were also associated with higher values of CVP, MPAP, and heart rates.

Table 1. Baseline Characteristics

	All Patients (n = 15)
General characteristics	
Age (years), mean ± SD	54.9 ± 19.9
Male, n (%)	7 (46.7)
LVAD characteristics	
Duration of LVAD, months ± SD	18.2 ± 18.5
Destination, n (%)	
BTT	9 (60)
DT	6 (40)
Origin of cardiomyopathy	
Ischemic, n (%)	4 (26.7)
Nonischemic, n (%)	11 (73.3)
Medical history	
Hypertension, n (%)	6 (40)
Hyperlipidemia, n (%)	5 (33.3)
Atrial Fibrillation, n (%)	6 (40)
DM, n (%)	6 (40)
COPD, n (%)	2 (13.3)
PAD, n (%)	0 (0)
CVA, n (%)	4 (26.7)
S/p Sternotomy, n (%)	5 (33.3)

LVAD, left ventricular assist device; BTT, bridge to transplantation; DT, destination therapy.

There was a strong correlation between VFPS and PCWP ($p < 0.001$) as shown in **Figure 3A**, although there was significant scatter around the regression ($r^2 = 0.306$). Nevertheless, VFPS was significantly higher in patients with PCWP ≥ 18 mm Hg than in patients with PCWP < 18 mm Hg [6.25 (5.84–7.37) L/min/s *vs.* 3.27 (2.00–4.69) L/min/s, $p \leq 0.0001$] (**Table 2**, **Figure 3B**). Receiver operator curve analysis revealed a VFPS threshold of 5.8 L/min/s, predicted a PCWP ≥ 18 mm Hg with a sensitivity of 87% and specificity of 95% (AUC 0.95) (**Figure 4**). In other exploratory analyses, a threshold value of 6.0 provides a sensitivity of 89% and specificity of 92% to detect a PCWP ≥ 20 mm Hg. Intra-observer variability (r = 0.995, 95% CI 0.980–0.999) and inter-observer variability (r = 0.991, 95% CI 0.966–0.998) between measurements of VFPS were low.

Multiple regression analysis revealed significant contributions of device RPMs and mean HVAD flow to the correlation between VFPS and PCWP (**Figure 3C**):

$VFPS_{adjusted} = 3.448 + 0.239*\ln(VFPS) - 0.001*RPM + 0.450*\ln(Flow)$,

which improved the correlation coefficient (r^2) to 0.349. $VFPS_{adjusted}$ was significantly lower for PCWP < 18 mm Hg compared with PCWP ≥ 18 mm Hg [1.44 (1.58–1.78) *vs.* 1.90 (1.85–2.08) mm Hg, $p < 0.0001$] (**Table 2**). Receiver operator curve analysis revealed an optimal cutoff of 1.8, which yielded a sensitivity of 80% and a specificity of 76%, not better than results obtained with VFPS alone. Accordingly, despite the improved correlation, the area under the ROC curve (0.82) was not better than what was observed with VFPS alone (0.95).

DISCUSSION

Pulmonary capillary wedge pressure is an important clinical parameter for management of medical therapies and speed optimization in patients supported by LVADs. Specifically, this parameter is key in the assessment and management of volume status. Studies have shown that PCWP is difficult to assess based on clinical methods normally applied in non-LVAD

Table 2. Median LVAD Parameters, Hemodynamics and Flow Characteristics (Interquartile Range) Stratified by Pulmonary Capillary Wedge Pressure

	All screenshots (n = 101)	PCWP < 18 (n = 86)	PCWP ≥ 18 (n = 15)	*p* Value*
LVAD characteristics				
Pulsatility, L/min ± SD	4.44 (3.51 to 4.92)	4. 37 (3.39 to 4.92)	4.53 (4.05 to 4.63)	0.26
Flow (mean), L/min ± SD	3.50 (2.7 to 4.65)	3.50 (2.70 to 4.40)	4.50 (2.20 to 5.00)	0.34
Power, Watts ± SD	3.70 (2.90 to 4.70)	3.90 (2.90 to 4.80)	3.50 (2.90 to 4.00)	0.26
Speed, RPM ± SD	2,680.00 (2,400.00 to 2,890.00)	2,700.00 (2,420.00 to 2,900.00)	2,600.00 (2,400.00 to 2,680.00)	0.11
Hemodynamics				
RAP, mm Hg ± SD	7.00 (4.00 to 10.00)	6.00 (4.00 to 9.00)	12.00 (6.00 to 13.00)	0.001
MPAP, mm Hg ± SD	25.00 (17.00 to 32.00)	23.00 (16.00 to 29.00)	35.00 (32.00 to 41.00)	<0.0001
PCWP, mm Hg ± SD	12.00 (8.50 to 15.00)	11.00 (8.00 to 14.00)	20.00 (18.00 to 23.00)	<0.0001
CO, L/min ± SD	4.70 (3.99 to 5.78)	4.76 (4.12 to 5.57)	3.84 (3.33 to 6.74)	0.37
CI, L/min/m^2 ± SD	2.67 (2.39 to 3)	2.68 (2.41 to 3.02)	2.25 (2.03 to 2.83)	0.01
HR, bpm ± SD	80.00 (75.00 to 92.00)	80.00 (75.00 to 89.50)	99.00 (88.00 to 100.00)	0.01
Doppler opening pressure, mm Hg ± SD	94.00 (86.50 to 101.50)	95.00 (86.00 to 102.00)	90.00 (87.00 to 100.00)	0.88
Flow analysis				
Maximum flow, L/min ± SD	6.00 (4.60 to 7.00)	5.90 (4.70 to 6.90)	6.50 (4.10 to 7.30)	0.46
Minimum flow, L/min ± SD	1.55 (0.53 to 2.80)	1.40 (0.60 to 2.70)	2.40 (–0.50 to 3.10)	0.74
Systolic upslope, L/min/s ± SD	18.40 (13.83 to 24.34)	17.62 (12.32 to 24.34)	18.61 (17.71 to 29.88)	0.16
Diastolic downslope, L/min/s ± SD	–22.84 (–33.93 to 16.28)	–22.68 (–32.68 to 16.51)	–29.48 (–36.89 to 16.23)	0.52
VFPS, L/min/s ± SD	3.71 (2.32 to 5.10)	3.27 (2.00 to 4.69)	6.25 (5.84 to 7.37)	<0.0001
$VFPS_{adjusted}$	1.45 (1.66 to 1.88)	1.44 (1.58 to 1.78)	1.90 (1.85 to 2.08)	<0.0001

Data are median (interquartile range). PCWP, pulmonary capillary wedge pressure; LVAD, left ventricular assist device; VFPS, ventricular filling phase slope; CO, Cardiac output; CI, cardiac index; MPAP, mean pulmonary artery pressure.
*Mann–Whitney Rank Sum test.

heart failure patients, such as auscultation, assessment of lower extremity edema, and review of clinical symptoms.[10] Implantable pulmonary artery pressure sensors are invasive and may also be limited to assess PCWP in this patient population owing to decoupling between the pulmonary artery diastolic pressure and PCWP in many patients.[11] Accordingly, availability of a noninvasive means of assessing PCWP has the potential to offer significant advantages for management of LVAD patients.

Theory predicted and our observations confirmed that there is a high correlation between PCWP and the slope of the HVAD waveform during the VFPS. In view of the fact that there are many factors that influence VFPS, this parameter alone is not sufficient to quantify PCWP in absolute terms. However, in this pilot study, the data would suggest that the VFPS may be a useful tool to aid in the assessment of PCWP. It was demonstrated that using a cutoff value of 5.8 L/min/s, VFPS can discriminate between PCWP < 18 and PCWP ≥ 18 mm Hg with a high degree of sensitivity and specificity. This approach may therefore offer the clinician a means of determining whether the wedge pressure is above a generally accepted value suggestive of relative fluid overload. Despite improved correlation to PCWP after adjusting VFPS for noninvasively available clinical parameters, $VFPS_{adjusted}$, it was still not sufficient for prediction of absolute values of PCWP and did not improve the sensitivity or specificity in detecting elevated values of this parameter. VFPS, therefore, can be used as a rapid screening tool to assess actionable volume overload. Caution should be taken in interpreting low VFPS given the significant scatter around the mean at lower values. Despite the current limitations, clinical symptoms of congestion should not exist for PCWP less than 18 mm Hg and thus, use of the VFPS as a threshold detector at a value of 18 mm Hg will allow for a clinically meaningful intervention.

Although digital conversion of screenshots and waveform analysis as performed in the current study is laborious and can

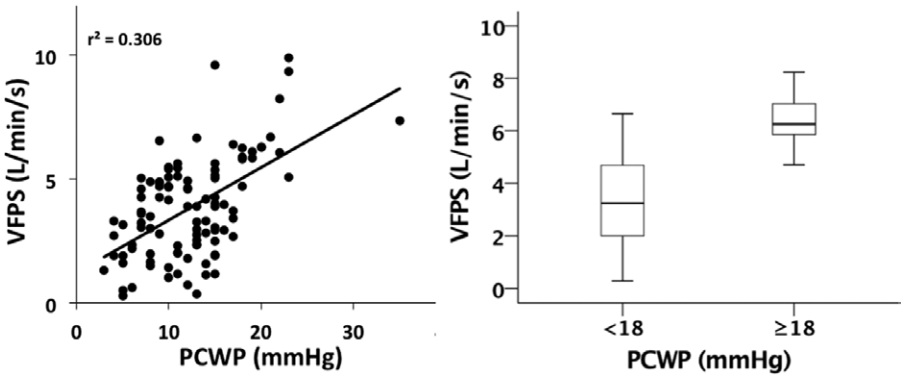

Figure 3. A: Correlation between PCWP and VFPS. B: VFPS in greater when PCWP ≥ 18 mm Hg. C: The correlation between PCWP and VFPS can be improved by adjusting VFPS for covariates as indicated in the text. D: VFPS adjusted is greater when PCWP ≥ 18 mm Hg. PCWP, pulmonary capillary wedge pressure; VFPS, ventricular filling phase slope.

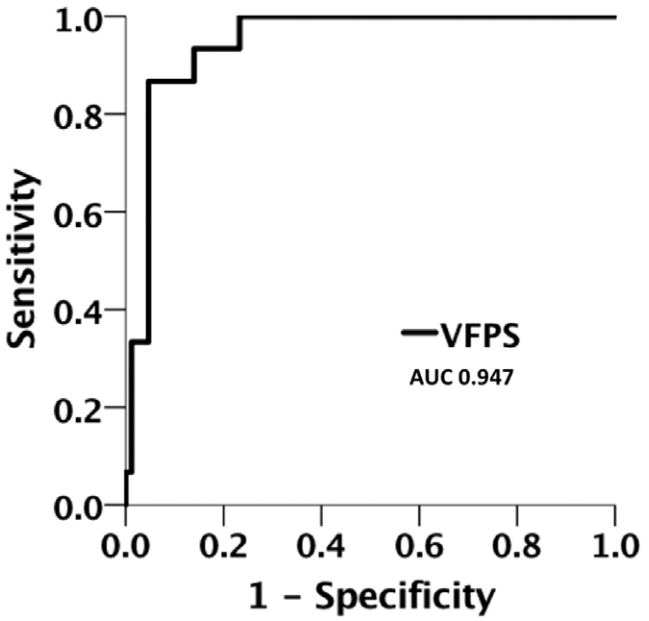

Figure 4. Receiver operator characteristic curve for VFPS, $VFPS_{adjusted}$. Despite a slightly better correlation between PCWP and $VFPS_{adjusted}$, the area under the curve for sensitivity and specificity for detecting a PCWP ≥ 18 mm Hg was for VFPS alone. PCWP, pulmonary capillary wedge pressure; VFPS, ventricular filling phase slope.

be associated with low resolution, real-time automatic waveform analysis of the VFPS could easily be programmed into the HVAD monitor and provide the clinician with useful, noninvasive estimates of the left ventricular filling pressure. Physician will be able to adjust HVAD speed at the bedside base on the VFPS slope that will be provide on the screen. Furthermore, automated interpretation of the VFPS, or a more robust adjustment based on other noninvasive measurements, could serve as a key feedback signal in a "smart" LVAD pump that can adjust speed based on the physiologic needs of the patient (**Figure 5A–F**). For example, if a smart pump detects an elevation in VFPS (5B) signifying an elevated PCWP (5A) rotor speed could be automatically increased to decompress the left ventricle (5C). This would reduce PCWP and VFPS, respectively (5D and 5E). To minimize complications from over-decompression, such as suction events, a smart LVAD pump would then recognize a flat VFPS and reduce the rotor speed to allow an intermediate filling pressure (5F). Given the significant scatter around the mean using VFPS in isolation, eventually, additional clinical variables will need to be incorporated to improve the accuracy of the model.

Although, those results are device specific (HVAD), the concept of flow waveform generated from device power as a surrogate marker for PCWP may be applicable to other pumps, if such waveform will be available for our analysis.

LIMITATIONS

This is a single-center study and thus is open to institutional biases. For each patient, serial measurements and screenshots during sequential stages of an invasive hemodynamic ramp were obtained and thus the total number of data points that were obtained, despite the small cohort is reasonably large. Nevertheless, additional multicenter studies with a larger patient population spanning an even wider range of PCWPs is still needed for further validation. Ventricular filling phase slope was quantified by manually digitizing photographic images of the HVAD waveform. This represents a low resolution approach that can be prone to error. A more optimal approach would be to obtain high resolution digital recordings of the waveform directly from

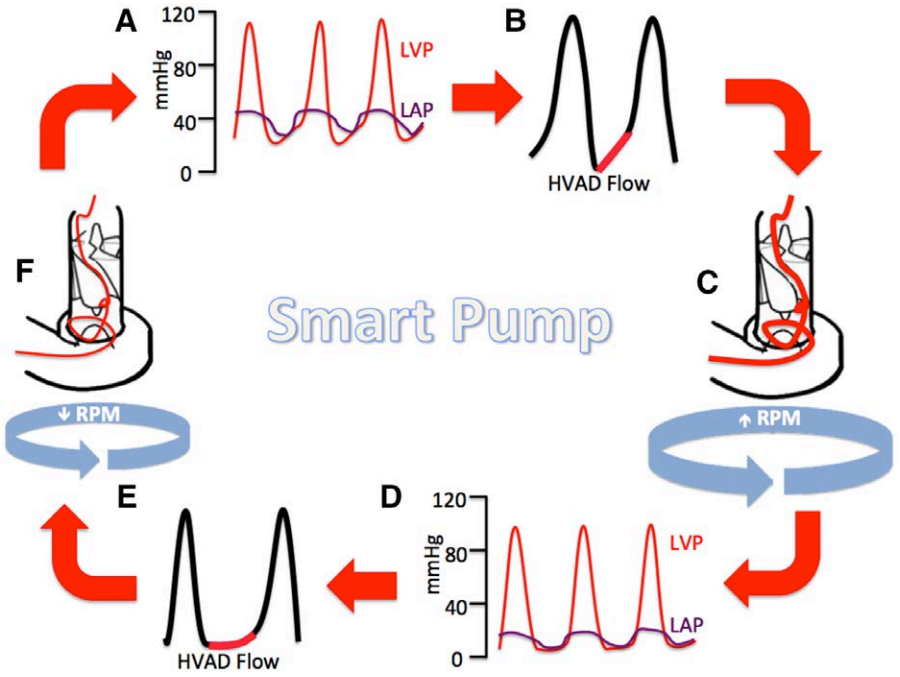

Figure 5. A smart LVAD pump based on the VFPS. An elevated PCWP (A) is recognized as an elevation in the VFPS (B). A smart pump increased the rotor speed (C) which reduced the PCWP (D) and VFPS (E). To avoid complications from high rotor speeds, the smart pump reduces the rotor speed (F) to allow for more intermediate filling pressures. PCWP, pulmonary capillary wedge pressure; LVAD, left ventricular assist device; VFPS, ventricular filling phase slope.

the HVAD controller with automated signal processing for slope quantification. However, such a digital interface with the controller is not commercially available, although a custom device has been described previously. Accordingly, the present results should be viewed as proof of concept. Details of the analysis, especially optimal threshold values for VFPS to optimally detect elevated PCWPs are likely to be refined with availability larger, high resolution data. Similarly, more robust adjustments of VFPS based on noninvasive clinical measurements may improve VFPS-based noninvasive estimation of absolute PCWP. For example, one of the main assumptions of the analysis is that aortic pressure is relatively constant during diastole which may not be the case in all patients. When aortic valve opening occurs, there is increased aortic pressure pulsatility. In such cases, including aortic pulse pressure into the multivariate analysis may improve the correlation between PCWP and $VFPS_{adjusted}$. In the current iteration, VFPS seems to perform most robustly at higher filling pressures.

CONCLUSIONS

HVAD waveform analysis provides useful information that provides a noninvasive means to predict PCWP elevation. Automated reporting of this parameter may help clinical assessment of patients supported with HVAD and may serve as the basis of a "smart" pump that can adjust LVAD support based on the physiologic needs of the patient.

REFERENCES

1. Kirklin JK, Naftel DC, Pagani FD, *et al*: Seventh INTERMACS annual report: 15,000 patients and counting. *J Heart Lung Transplant*, 2015.
2. Burkhoff D, Sayer G, Doshi D, Uriel N: Hemodynamics of mechanical circulatory support. *J Am Coll Cardiol* 66: 2663–2674, 2015.
3. Aaronson KD, Slaughter MS, Miller LW, *et al*: Use of an intrapericardial, continuous-flow, centrifugal pump in patients awaiting heart transplantation. *Circulation* 125: 3191–3200, 2012.
4. Pagani F, Rogers J. A Prospective, Randomized, Controlled, Un-blinded, Multi-Center Clinical Trial to Evaluate the HeartWare® Ventricular Assist System (VAS) for Destination Therapy of Advanced Heart Failure (ENDURANCE). ClinicalTrials.gov identifier: NCT01166347.
5. Pagani FD, Milano CA, Tatooles AJ *et al*: HeartWare HVAD for the treatment of patients with advanced heart failure ineligible for cardiac transplantation: Results of the ENDURANCE destination therapy trial. *J Heart Lung Transplant* 34:S9, 2015.
6. Uriel N, Sayer G, Addetia K, *et al*: Hemodynamic ramp tests in patients with left ventricular assist devices. *JACC Heart Fail* 4: 208–217, 2016.
7. Reyes C, Voskoboynikov N, Chorpenning K, *et al*: Accuracy of the HVAD pump flow estimation algorithm. *ASAIO J* 62: 15–19, 2016.
8. Uriel N, Morrison KA, Garan AR, et al: Development of a novel echocardiography ramp test for speed optimization and diagnosis of device thrombosis in continuous-flow left ventricular assist devices: The Columbia ramp study. *J Am Coll Cardiol* 60: 1764–1775, 2012.
9. Uriel N, Levin AP, Sayer GT, et al: 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. *J Card Fail* 21: 785–791, 2015.
10. Devore AD, Mentz RJ, Patel CB: Medical management of patients with continuous-flow left ventricular assist devices. *Curr Treat Options Cardiovasc Med* 16: 283, 2014.
11. Imamura T, Sayer G, Adatya S, *et.al*: Decoupling between diastolic pulmonary artery pressure and pulmonary capillary wedge pressure is the strongest negative prognostic factor post continuous flow ventricular assist device implantation. *JHLT* 36:S328–S329, 2017.