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Echocardiographic Predictors of Hemodynamics in Patients Supported With Left Ventricular Assist Devices

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Abstract

Background: The assessment of hemodynamics in patients supported with left ventricular assist devices (LVADs) is often challenging. Physical examination maneuvers correlate poorly with true hemodynamics. We assessed the value of novel transthoracic echocardiography (TTE)–derived variables to reliably predict hemodynamics in patients supported with LVAD.

Methods and Results: A total of 102 Doppler-TTE images of the LVAD outflow cannula were obtained during simultaneous invasive right heart catheterization (RHC) in 30 patients supported with continuous-flow LVADs (22 HMII, 8 HVAD) either during routine RHC or during invasive ramp testing. Properties of the Doppler signal through the outflow cannula were measured at each ramp stage (RS), including the systolic slope (SS), diastolic slope (DS), and velocity time integral (VTI). Hemodynamic variables were concurrently recorded, including Doppler opening pressure (MAP), heart rate (HR), right atrial pressure, pulmonary artery pressure, pulmonary capillary wedge pressure (PCWP), Fick cardiac output (CO) and systemic vascular resistance (SVR). Univariate and multivariate regression analyses were used to explore the dependence of PCWP, CO, and SVR on DS, SS, VTI, MAP, HR, and RS. Multivariate linear regression analysis revealed significant contributions of DS on PCWP ($PCWP_{pred} = 0.164DS + 4.959$; $R = 0.68$). Receiver operating characteristic (ROC) curve analysis revealed that $PCWP_{pred}$ could predict an elevated PCWP ≥ 18 mm Hg with a sensitivity (Sn) of 94% and specificity (Sp) of 85% (area under the

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Disclosures

Dr Uriel is a consultant to Medtronic and Abbott. Dr Jeevanandam is a consultant to Abbott. Dr Burkhoff is a consultant to Medtronic. All of the other authors have no relevant disclosures.

Supplementary materials

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ROC curve 0.88). CO could be predicted by RS, VTI, and HR ($CO_{pred} = 0.017VTI + 0.016HR + 0.12RS + 2.042$; $R = 0.61$). CO_{pred} could predict CO 4.5 L/min with Sn 73% and Sp 79% (AUC 0.81). SVR could be predicted by MAP, VTI, and HR ($SVR_{pred} = 15.44MAP - 5.453VTI - 6.349HR + 856.15$; $R = 0.84$) with Sn 84% and Sp 79% (AUC 0.91) to predict SVR 1200 dyn-s/cm⁵.

Conclusions: Doppler-TTE variables derived from the LVAD outflow cannula can reliably predict PCWP, CO, and SVR in patients supported with LVADs and may mitigate the need for invasive testing.

Keywords

LVAD; hemodynamics; noninvasive

Left ventricular assist devices (LVADs) have become a mainstay therapy for patients with advanced heart failure. More than 2000 durable LVADs are implanted each year in the United States.¹ With improvements in technology and management, survival following LVAD implantation now exceeds 80% at 1 year and 70% at 2 years.^{1,2} Despite improvements in outcomes, inadequately treated heart failure remains a major hindrance for many patients, leading to readmissions for heart failure management. Readmission rates approach 1.64 per patient-year of follow-up, with up to 25% of readmissions occurring because of cardiac or LVAD-related problems.^{3,4}

Invasive assessment of both LVAD performance and intracardiac hemodynamics are often necessary during the index admission or after readmission. Right heart catheterization (RHC) and hemodynamic ramp tests can be performed to guide medical management.^{5,6} Noninvasive methods to reliably estimate intracardiac hemodynamics would allow for optimization of medical therapy and LVAD support without the added inconvenience and risk of invasive monitoring. Transthoracic echocardiography (TTE) in patients supported with LVADs has previously been shown to be effective in assessing right-side flow and pressures and can be used as part of an algorithm to estimate left-side filling pressures.⁷ Attempts to define hemodynamics with the use of TTE have involved time-intensive protocols and heavily rely on the E/e' ratio, which is poorly validated among patients with advanced heart failure and among patients supported with LVADs.^{8,9}

In the present study, we propose TTE parameters derived entirely from Doppler analysis of the LVAD outflow graft that are readily obtainable and can accurately predict pulmonary capillary wedge pressure (PCWP), cardiac output (CO), and systemic vascular resistance (SVR).

Methods

Patient Population

Consecutive patients undergoing RHC with simultaneous TTE from October 2014 to October 2016 were enrolled in this analysis. To assess the reliability of TTE parameters under different loading conditions, a subset of patients underwent repeated TTE and hemodynamic measurements during the stages of an invasive hemodynamic ramp protocol.

Demographic information was extracted by means of chart review. All patients provided informed written consents, and the Institutional Review Board approved the study.

Right Heart Catheterization and Ramp Testing

RHC was performed via the right internal jugular vein with the use of a 5-F Swan-Ganz catheter (Edwards Lifesciences, Irvine, California). Therapeutic anticoagulation was maintained for the test with a target international normalized ratio between 2 and 3. Measurements included central venous pressure (CVP), systolic, diastolic, and mean pulmonary arterial pressures (SPAP, DPAP, and MPAP), and PCWP. CO was calculated with the use of the indirect Fick equation and an estimated oxygen consumption of $125 \text{ mL} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$. Arterial oxygen saturation was measured from peripheral plethysmography, and hemoglobin was measured from the venous blood gas. Mean arterial pressure (MAP) was defined as the opening pressure recorded with the use of the Doppler technique and a manual sphygmomanometer. SVR was calculated from the MAP, CVP, and CO. Heart rate (HR) was recorded from telemetry. Hemodynamic parameters were measured at each stage of the ramp study in the subset of patients who underwent ramp testing. Real-time echocardiographic imaging was performed simultaneously with hemodynamic image acquisition.

Our ramp protocols have previously been described.^{10,11} In brief, patients underwent hemodynamic assessment at their presenting speeds and then had their speeds reduced to a low speed of 2300 rpm (HVAD) or 8000 rpm (HMII). Speeds were then increased by increments of 100 rpm (HVAD) or 400 rpm (HMII) to a maximum speed of 3200 rpm (HVAD) or 12,000 rpm (HMII). Repeated hemodynamic assessments were performed at each ramp stage (RS; Supplemental Table 1). Ramp testing was terminated early if the patient developed a suction event, ventricular arrhythmia, or MAP was $>120 \text{ mm Hg}$.

Doppler Echocardiographic Analysis

Limited echocardiography, including pulse-wave Doppler acquisition of the outflow graft of the continuous-flow (CF) LVAD, was conducted at the time of RHC and at each RS in the subset of patients who underwent ramp testing. Properties of the Doppler signal through the outflow graft, including diastolic slope (DS), systolic slope (SS), and velocity time integral (VTI), were measured and defined as previously reported.^{12–14} Briefly, DS was measured as the rate of change in velocity during the diastolic portion of the cardiac cycle, and SS was measured as the maximum rate of change in velocity during the systolic portion of the cardiac cycle. VTI of the outflow cannula was measured over the entire cardiac cycle (from R-wave to R-wave on the surface electrocardiogram; Fig. 1). Individuals analyzing the Doppler signal were blinded to the hemodynamic data.

Statistical Methods

Data were recorded with the use of a spreadsheet (Excel 2011; Microsoft Corp, Redmond, Washington) and analyzed with the use of SPSS statistical software v24.0 (IBM, Armonk, New York). Normality was assessed by means of the Shapiro Wilk test. Univariate and multivariate linear regression analyses were used to explore the dependence of PCWP, CO, and SVR on DS, SS, VTI, MAP, HR, and RS. All parameters with a P value $<.05$ on

univariate analysis were included in the multivariate analysis after the confirmation that variance inflation factors of each variable were not significant (<2.0). Pearson correlation testing was performed to compare the measured parameter (PCWP, CO, and SVR, respectively) with the predicted value ($PCWP_{pred}$, CO_{pred} , and SVR_{pred} , respectively) after multiregression analysis.

We also explored the sensitivity (Sn) and specificity (Sp) of each predicted value to discriminate whether PCWP was ≥ 18 mm Hg, CO ≥ 4.5 L/min, or SVR ≥ 1200 dyn·s/cm⁵. True positive (TP), true negative (TN), false positive (FP), and false negative (FN) rates were determined at various thresholds for each parameter. The sensitivity and specificity of these parameters for detecting either an elevated PCWP, reduced CO, or elevated SVR was calculated at each threshold and a receiver operating characteristic (ROC) curve of Sn versus $1 - Sn$ was created. To assess the reproducibility of DS and SS, all measurements were repeated by a second observer and interobserver variability was assessed by means of intraclass correlation measurement.

Results

Baseline Characteristics

Thirty patients (22 HMII, 8 HVAD) underwent simultaneous RHC and TTE from October 2014 to October 2016. Baseline characteristics of the cohort are summarized in Table 1. A subset of 10 patients underwent repeated measurements during stages of a hemodynamic ramp study after the baseline RHC. In total, 102 measurements were obtained. Average age was 59.5 (range 44–76) years, and 73% were male. Patients who underwent hemodynamic ramp testing had similar characteristics as those who underwent isolated RHC, although there was a trend toward a shorter duration of LVAD support among those who underwent ramp testing (10.4 ± 11.3 mo vs 24.4 ± 21.3 mo; $P = .06$). Descriptive statistics of the variables used to predict hemodynamics are summarized in Supplemental Table 2.

Doppler Waveform Analysis and Hemodynamics

Univariate and multivariate analyses of variables predictive of PCWP, CO, and SVR are presented in Tables 2–4, respectively. A multivariate linear regression model showed significant contributions of DS to PCWP ($PCWP_{pred} = 0.164DS + 4.959$; $R = 0.68$; Fig. 2A, left). ROC curve analysis revealed that $PCWP_{pred}$ could predict an elevated PCWP ≥ 18 mm Hg with Sn 94% and Sp 85% (area under the ROC curve [AUC] 0.88; Fig. 2A, right). Multivariate linear regression modeling revealed that CO could be predicted by RS, VTI, and HR ($CO_{pred} = 0.017VTI + 0.016HR + 0.12RS + 2.042$; $R = 0.61$; Fig. 2B, left). ROC analysis revealed that CO_{pred} could predict a CO ≥ 4.5 L/min with Sn 73% and Sp 79% (AUC 0.81; Fig. 2B, right). SVR could be predicted by MAP, VTI, and HR ($SVR_{pred} = 15.44MAP - 5.453VTI - 6.349HR + 856.15$; $R = 0.84$; Fig. 2C, left). ROC analysis revealed that SVR_{pred} could predict an SVR ≥ 1200 dyn·s/cm⁵ with Sn 84% and Sp 79% (AUC 0.91; Fig. 2C, right). The interobserver variability was low for DS and SS as indicated by a high intraclass correlation coefficient for both variables ($r = 0.94$ and $r = 0.92$, respectively).

Discussion

In this study we evaluated the accuracy of echocardiographic parameters to predict invasive hemodynamics. Our main findings are as follows: 1) PCWP can be assessed with the use of the DS of the outflow cannula; 2) CO can be assessed with the use of the RS, HR, and the VTI of the outflow cannula; and 3) SVR can be assessed with the use of the MAP, HR, and VTI of the outflow cannula.

Hemodynamic assessment of patients supported with LVADs allows for optimization of pump performance and guidance of medical management.⁵ Tailoring LVAD speed to the physiologic needs of the patients, as assessed by invasive hemodynamic testing, leads to improved survival and reduced readmission rates.¹⁵ Although invasive hemodynamic assessment can be safely performed in the majority of LVAD patients, it remains an invasive test that carries risk and is inconvenient to the patients.¹⁶ Physical examination poorly predicts LVAD hemodynamics, because traditional auscultatory and visual examination techniques are unpredictable and unstudied in the setting of continuous unloading of the left ventricle.¹⁷ Supplemental and accurate noninvasive methods of assessing LVAD hemodynamics are therefore necessary to maximize LVAD performance while at the same time mitigating risk to the patient.

Doppler-TTE can be used to noninvasively assess flow patterns in both the native heart and LVAD circuit and can indirectly be used to assess intracardiac pressures and CO. Estep et al showed that Doppler-TTE can accurately predict right atrial pressure, right ventricular (RV) stroke volume, and pulmonary vascular resistance. They also showed that a complex algorithm involving measurements of mitral inflow velocities, right atrial pressure, SPAP, and indexed left atrial volumes could accurately predict left-side filling pressures.⁷ The complexity of their algorithm, and the need for repeated measurements, has limited widespread adoption of this technique.⁹ Flow through the LVAD outflow graft can similarly be assessed with the use of Doppler TTE. Stainback et al showed that the VTI of the outflow graft in patients supported with the Jarvik 2000 (Jarvik Heart, New York, New York) measured with the use of pulsed-wave Doppler correlated with a noninvasive assessment of cardiac output from TTE-derived RV and left ventricular CO.¹⁸ To date, no group has validated outflow graft VTI with the use of invasively measured cardiac output. With sonographer experience and dedicated training, our group has reported that the outflow graft can be successfully imaged in up to 95% of patients.¹⁹

In the present paper, we report echocardiographic parameters that can reliably predict elevated PCWP, elevated SVR, and reduced CO. Unlike previous methods which require multiple different image acquisitions from various chambers of the heart, our parameters can be obtained with the use of a single pulsed-wave Doppler TTE image of the CF-LVAD outflow cannula which can be analyzed to provide DS, SS, and VTI. Together with readily available clinical information, such as HR, MAP, and LVAD speed (RS), we report new equations to predict absolute PCWP, CO, and SVR. We also show that simplified equations that can be rapidly analyzed can quickly dichotomize high from low PCWP, CI, and SVR.

Previously, our group used outflow graft VTI and DS as a marker of LVAD flow in the development of novel echocardiographic parameters to quantify aortic insufficiency.¹³ With the present study, we further enrich the use of these echocardiographic parameters to assess LVAD patients' hemodynamics to permit further optimization of medical therapy in the form of diuretics and afterload reduction.

Study Limitations

This was a single-center study and therefore open to institutional and operator bias. Although our cohort size was modest at 30 patients, repeated measurements during sequential stages of invasive hemodynamic ramp testing was available for a subset of 10 patients, which allowed for a more robust sample size (102 measurements) as well as allowed for assessment of the parameters under variable loading conditions. Given that patients undergoing invasive ramp testing may have a unique clinical indication for this detailed testing, the possibility of a selection bias exists. Hemodynamic assessments used the indirect Fick equation, which may be less accurate in LVAD patients owing to reliance on an assumed oxygen consumption and not a directly measured oxygen consumption.²⁰ Unlike previous noninvasive assessments of hemodynamics in LVAD patients, our parameters are unique to LVAD physiology and validated in this patient population. A prospective validation study is needed to better assess these novel parameters.

Conclusions

TTE variables derived from pulsed-wave images from the LVAD outflow graft can reliably predict PCWP, CO and SVR in patients supported with LVAD. These parameters may mitigate the need for routine invasive testing and may be used, together with clinical assessment, to tailor medical therapy in LVAD patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1. Measurement of velocity time integral (VTI) from R-wave to R-wave, systolic slope (SS), and diastolic slope (DS) from pulsed-wave Doppler transthoracic echocardiography signal.

Fig. 2.

(A) *Left:* Performance of predicted pulmonary capillary wedge pressure (PCWP) derived from the diastolic slope (DS) compared with measured PCWP. *Right:* Receiver operating characteristic (ROC) curve of predicted PCWP to predict PCWP 18 mm Hg. (B) *Left:* Performance of predicted cardiac output (CO) derived from the ramp stage (RS), velocity time integral (VTI), and heart rate (HR) compared with measured CO. *Right:* ROC of predicted CO to predict CO 4.5 L/min. (C) *Left:* Performance of predicted systemic vascular resistance (SVR) derived from the mean arterial pressure (MAP), velocity time

integral (VTI), and heart rate (HR) compared with measured SVR. *Right:* ROC of predicted SVR to predict SVR $> 1200 \text{ dyn}\cdot\text{s}/\text{cm}^5$.

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Table 1.

Baseline Characteristics Stratified by Procedure Type (Ramp Study vs Isolated Right Heart Catheterization)

Characteristic	All Patients (n = 30)	Right Heart Catheterization (n = 20)	Hemodynamic Ramp (n = 10)
General characteristics			
Age, y, mean $\pm$ SD	59.5 $\pm$ 9.4	59.8 $\pm$ 10.3	59.1 $\pm$ 7.9
Male, n (%)	22 (73)	16 (80.0)	6 (60)
Duration of LVAD, mo, mean $\pm$ SD	19.8 $\pm$ 19.6	24.4 $\pm$ 21.3	10.4 $\pm$ 11.3
Destination, n (%)			
BTT	13 (43)	9 (45)	4 (40)
DT	17 (57)	11 (55)	6 (60)
Type of LVAD			
HMII	22 (73)	15 (75)	7 (70)
HVAD	8 (27)	5 (25)	3 (30)
Presenting speed, rpm, mean $\pm$ SD			
HMII	9127 $\pm$ 430	9173 $\pm$ 471	9029 $\pm$ 335
HVAD	2700 $\pm$ 128	2740 $\pm$ 152	2633 $\pm$ 31
Origin of cardiomyopathy, n (%)			
Ischemic	15 (50)	11 (55)	4 (40)
Nonischemic	15 (50)	9 (45)	6 (60)
Hypertension	18 (60)	12 (60)	6 (60)
Hyperlipidemia	10 (33)	9 (45)	1 (10)
Atrial fibrillation	9 (30)	8 (40)	1 (10)
DM	13 (43)	7 (35)	6 (60)
COPD	6 (20)	2 (10)	4 (40)
PAD	3 (10)	3 (15)	0 (0)
CVA	5 (17)	5 (25)	0 (0)
Sternotomy	6 (20)	4 (20)	2 (20)

LVAD, left ventricular assist device; BTT, bridge to transplant; DT, destination therapy; HMII, Heartmate II; HVAD, Heartware LVAD; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; PAD, peripheral artery disease; CVA, cerebrovascular accident.

Table 2.

Linear Regression Analyses to Predict Pulmonary Capillary Wedge Pressure

Variable	Univariate Analysis		Multivariate Analysis		VIF
	B (95% CI)	P Value	B (95% CI)	P Value	
Diastolic slope	0.164 (0.129 to 0.199)	<.001*	0.159 (0.119 to 0.200)	<.001*	1.32
Systolic slope	−0.05 (−0.008 to 0.002)	.005*	−0.001 (−0.004 to 0.001)	.32	1.10
Outflow VTI	0.072 (0.022 to 0.123)	.006*	−0.003 (−0.046 to 0.040)	.89	1.21
MAP	0.103 (−0.002 to 0.209)	.055			
HR	0.073 (−0.014 to 0.160)	.099			
Ramp stage	−0.236 (−0.865 to 0.392)	.46			

VTI, velocity time integral; MAP, mean arterial pressure; HR, heart rate; VIF, variance inflation factor

* $P < .05$.

Table 3.

Linear Regression Analyses to Predict Cardiac Output

Variable	Univariate Analysis		Multivariate Analysis		VIF
	B (95% CI)	P Value	B (95% CI)	P Value	
Diastolic slope	−0.005 (−0.012 to 0.002)	.17			
Systolic slope	0.000 (−0.001 to 0.000)	.55			
Outflow VTI	0.021 (0.014 to 0.028)	<.001*	0.017 (0.009 to 0.024)	<.001*	1.16
MAP	−0.008 (−0.024 to 0.009)	.36			
HR	0.019 (0.006 to 0.032)	.005*	0.016 (0.005 to 0.027)	.004*	1.01
Ramp stage	0.20 (0.110 to 0.289)	<.001*	0.120 (0.036 to 0.204)	.006*	1.16

Abbreviations as in Table 2.

* $P < .05$.

Table 4.

Linear Regression Analyses to Predict SVR

Variable	Univariate Analysis		Multivariate Analysis		VIF
	B (95% CI)	P Value	B (95% CI)	P Value	
Diastolic slope	0.213 (−1.989 to 2.414)	.85			
Systolic slope	0.043 (−0.119 to 0.204)	.60			
Outflow VTI	−6.034 (−8.154 to 3.914)	<.001 [*]	−5.453 (−6.792 to 4.115)	<.001 [*]	1.01
MAP	15.74(11.86–19.62)	<.001 [*]	15.44 (12.70to 18.18)	<.001 [*]	1.00
HR	−6.427 (−10.29 to 2.570)	.001 [*]	−6.349 (−8.580to4.118)	<.001 [*]	1.00
Ramp stage	−8.657 (−37.70 to 20.39)	.56			

Abbreviations as in Table 2.

^{*} $P < .05$.