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Deep Y-Descent in Right Atrial Waveforms Following Left Ventricular Assist Device Implantation

TERUHIKO IMAMURA, MD, PhD¹, DAISUKE NITTA, MD, PhD², TAKEO FUJINO, MD, PhD², BRYAN SMITH, MD², SARA KALANTARI, MD², ANN NGUYEN, MD², NIKHIL NARANG, MD², LUISE HOLZHAUSER, MD², DANIEL RODGERS, BN², TAE SONG, MD², TAKEYOSHI OTA, MD, PhD², VALLUVAN JEEVANANDAM, MD², GENE KIM, MD¹, GABRIEL SAYER, MD¹, NIR URIEL, MD, MSc¹

¹Department of Medicine, University of Chicago Medical Center, Chicago, Illinois

²Department of Surgery, University of Chicago Medical Center, Chicago, Illinois.

Abstract

Background—Characterization of right heart catheterization (RHC) waveforms provides diagnostic and clinical information in heart failure patients. We aimed to investigate the implication of RHC waveforms, specifically the y-descent, in patients with left ventricular assist device (LVAD).

Methods and Results—Patients underwent RHC and waveforms were quantified prior to and 6 months after LVAD implantation. The impact of a deep y-descent (>3 mmHg) on echocardiographic measures of right heart function and 1-year hemocompatibility-related adverse event rates were investigated. Eighty-nine patients (median 59 years old, 65 male) underwent RHC. RHC waveform showed unique changes following LVAD implantation, particularly an increase in the steepness of the y-descent. A post-LVAD deep y-descent was associated with reduced right ventricular function and enlarged right heart. Patients with post-LVAD deep y-descent had higher rates of gastrointestinal bleeding (0.866 vs 0.191 events/year) and stroke (0.199 vs 0 events/year) compared with those without ($P < .05$ for both).

Conclusion—RHC waveforms characterized by deep y-descent on RHC waveform during LVAD support was associated with impaired right ventricular function and worse clinical outcomes.

Keywords

Heart failure; hemodynamic; hemocompatibility

Reprint requests: Teruhiko Imamura MD, PhD, FAHA, FACC, FESC, FHFSA, FJCC, Department of Medicine, University of Chicago Medical Center, 5841 S Maryland Avenue, Chicago, IL 60637. Tel: 1-773-702-9460; Fax: 1-773-834-1764. te.imamu@gmail.com.

Disclosures

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Supplementary materials

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Despite recent improvement in the technology of continuous-flow left ventricular assist device (LVAD),¹ hemo-compatibility-related adverse events (HRAEs) remain major causes of readmissions.^{2,3}

Our team recently demonstrated that the failure to optimize hemodynamics, particularly with elevated right atrial pressures (RAPs), was associated not only with heart failure recurrence but also with HRAE.⁴ Elevated RAP likely signifies a component of right ventricular (RV) dysfunction, and it has been previously shown that early- and late-onset RV failure (RVF) are associated with worse clinical outcomes during LVAD support.^{5–10}

Although various procedures have been proposed to assess RV function, including physical examination, echo-cardiography,¹¹ and invasive hemodynamics,¹² no easy-to-measure and clinically useful objective index have been defined thus far. Most studies define RVF with clinical signs and symptoms as well as need of inotropes or mechanical support, without any definitive objective criteria that is universally agreed upon.^{5–10}

Right heart catheterization (RHC) is the gold standard to measure intracardiac filling pressures.¹³ Catheter waveform obtained during RHC may provide important physiologic information on cardiac function, although most of them are classical findings.¹⁴ For example, a deep y-descent is classically known to indicate reduced RV function. As such, we hypothesized that detailed RHC waveform analyses, particularly a deep y-descent, might allow for RV functional assessment and provide prediction of prognosis LVAD patients.

In this study, we investigated 1) the change in the RHC waveform before and after LVAD implantation; and 2) the impact of post-LVAD waveforms, particularly by focusing on a deep y-descent, on clinical outcomes.

Methods

Patient Selection

This was a retrospective study of LVAD patients implanted between April 2014 and February 2018 at our institution. Patients underwent hemodynamic waveform assessments from standard RHC tests performed within 1 week prior to and 6 months after LVAD implantation (time zero). Right heart function by transthoracic echocardiography was assessed 6 months post-implantation (time zero). Clinical outcomes, including HRAE, were followed for 1 year from the 6 months post-implantation. The study was approved by the institutional review board at the University of Chicago.

RHC Waveform Assessment—All patients underwent RHC via right internal jugular vein using a 7-French Swan-Ganz catheter,¹³ and standard hemodynamic assessments were performed at end-expiratory setting within 1 week prior and 6 months after LVAD implantation (time zero). In addition, waveform-specific variables were measured:¹⁴ 1) a-wave and v-wave heights from mean RAP (Fig. 1A); 2) x-descent and y-descent depths from mean RAP (Fig. 1A); 3) RV end-systolic and end-diastolic pressures (Fig. 2B); and 4) dP/dt of RV (Fig. 1B).

Echocardiographic Assessment—Standard transthoracic echocardiography was performed at the time of hemodynamic assessment 6 months postimplantation (time zero) per the current American Society of Echocardiography guidelines, as detailed in the Supplementary materials.¹¹

Hemocompatibility-Related Adverse Events

Clinical adverse events attributable to gastrointestinal bleeding (GIB), stroke (disabling or non-disabling), or pump thrombosis (medically or surgically treated) were classified as HRAEs as detailed previously.² Data of deaths and hospital readmissions due to HRAEs for 1 year starting 6 months postimplantation (time zero) were collected and validated by 2 independent researchers (T.I. and D.R.).

Statistical Analyses

Statistical analyses were performed with SPSS Statistics 22 (SPSS Inc, Armonk, IL). Two-sided P values $< .05$ were considered statistically significant. Continuous variables were expressed as mean and standard deviation or median (25% quartile, 75% quartile), considering their distribution.

A y-descent of >3 mmHg on the waveform was defined as depth based on receiver operation characteristics analysis. Patients were divided into 2 groups: a deep y-descent group (>3 mmHg) and a normal y-descent group (≤ 3 mmHg).

The impact of a deep y-descent at 6 months post-implantation (time zero) on HRAE for 1 year (from 6 to 18 months postimplantation) was investigated as a primary endpoint. HRAE-free survival rates were assessed by using Kaplan–Meier analysis and compared between groups using the log rank test. Event rates were expressed as event per patient-year. Cox proportional hazard ratio regression analyses were performed to investigate the impact of deep y-descent on 1-year development of HRAE by adjusting for other variables. Variables with $P < .05$ of significance in the univariate analyses were enrolled in the multivariate model using a simultaneous forced-entry method.

Results

Preoperative Baseline Characteristics

In total, 89 patients were investigated. Median age was 59 years old and 65 (73%) were male. Most patients (71%) received LVAD implantation as destination therapy (Table 1). No patients received pulmonary vasodilators at time of enrollment.

Waveform Changes Following LVAD Implantation

Following LVAD implantation, some RHC waveform features showed unique changes (Table 2). Mean RAP remained unchanged ($P = .16$). The a-wave height decreased, whereas the magnitude of the y-descent increased ($P < .05$ for both). Systolic RV pressure, RV end-diastolic pressure, and RV dP/dt decreased significantly ($P < .05$ for all). Composite waveforms were created to represent each variable (Fig. 2A–D).

Post-LVAD Deep y-Descent

The range of the depth of post-LVAD y-descents is shown in Supplementary Fig. S1. Thirty-four of 89 patients (38%) had a deep y-descent (>3 mmHg), which is a cutoff statistically calculated by the receiver operating characteristic analysis for the development of any HRAE (Supplementary Fig. S2).

Preoperative Baseline Characteristics Stratified by Post-LVAD Deep y-Descent

There were no statistical differences in the preoperative baseline characteristics between the post-LVAD deep y-descent and post-LVAD normal y-descent groups, except for a lower rate of male patients in the post-LVAD deep y-descent group (61% vs 81%, $P = .033$; Table 1). Of note, the prevalence of patients with a deep y-descent “pre-LVAD” were comparable between the 2 groups (11% vs 11%, $P = .98$).

Post-LVAD Hemodynamic Variables

Post-LVAD hemodynamic variables (at time zero) were statistically comparable between the 2 groups, although RAP tended to be higher and pulmonary artery pulsatility index tended to be lower in the post-LVAD deep y-descent group ($P > .05$ for all; Supplementary Table S1). With regard to RHC waveform variables, the v-wave was higher in the post-LVAD deep y-descent group (2.8 ± 2.1 vs 1.9 ± 0.7 mmHg, $P = .021$). LVAD flow was lower in the post-LVAD deep y-descent group (4.51 ± 0.91 vs 5.00 ± 1.14 L/min, $P = .044$).

Post-LVAD Echocardiographic Right Heart Function

Patients in the post-LVAD deep y-descent group had worse RV function and larger right heart size compared with the post-LVAD normal y-descent group at time zero ($P < .05$ for all), although differences in the grade of tricuspid regurgitation and RV fractional area change did not reach statistical difference (Table 3).

Freedom from HRAEs Stratified by Deep y-Descent

One-year survival free from HRAEs (from 6 months postimplant [time zero]) was significantly lower in the post-LVAD deep y-descent group compared with the post-LVAD normal y-descent group (40% vs 84%, $P < .001$; Fig. 3A).

During the study period, antiplatelet and anticoagulation therapies were statistically not different between groups (Supplementary Table S2). Hemoglobin remained lower and lactate dehydrogenase level remained higher in the post-LVAD deep y-descent group throughout the study period. Total bilirubin levels remained unchanged between 2 groups, whereas creatinine levels tended to be higher in the post-LVAD deep y-descent group.

Impact of Deep y-Descent on HRAE Adjusted for Other Variables

Among the preoperative and postoperative characteristics, a post-LVAD deep y-descent was a significant predictor of the 1-year HRAE with a nonadjusted hazard ratio 4.85 (95% confidence interval [CI]: 2.04–11.6) and an adjusted hazard ratio 4.95 (95% CI: 2.12–10.4; $P < .001$ for both; Table 4). As a continuous variable, a y-descent had hazard ratio 1.55 (95% CI: 1.24–1.94) per 1 mmHg increase in the depth.

Impact of Deep y-Descent on Individual HRAE

Rates of GIB and stroke were significantly higher in the post-LVAD deep y-descent group ($P = .005$ and $P = .014$, respectively), whereas pump thrombosis rates were statistically comparable ($P = .35$; Fig. 3B).

Changes in the Depth of y-Descent and Clinical Outcomes

Before LVAD implantation, most patients (79/89) had normal y-descent. Of them, 47 had persistently normal y-descent post-LVAD, whereas 32 had de novo deep y-descent post-LVAD. Post-LVAD de novo y-descent was associated with lower freedom from HRAE (46% vs 82%, $P = .003$; Supplementary Fig. S3). Among baseline characteristics, no variables were predictors of post-LVAD de novo deep-descent except for female gender (odds ratio 2.93 [95% CI: 1.03–8.31]; $P = .044$).

Discussion

In this study, we investigated 1) the change in RHC waveform parameters, including the depth of y-descent before and after LVAD implantation; 2) and analyzed implications of a post-LVAD deep y-descent (>3 mmHg) on clinical outcomes. Our major findings are as follows: 1) after LVAD implantation, RHC waveforms showed unique and drastic changes; 2) ~40% of patients had a deep y-descent (>3 mmHg) at 6 months following LVAD implantation (time zero); 3) a post-LVAD deep y-descent was associated with worse RV function and reduced LVAD flow; and 4) among all investigated clinical variables including hemodynamic parameters, a post-LVAD deep y-descent was an independent predictor of HRAE, which was predominantly driven by higher event rates of GIB and stroke.

Assessment of RVF During LVAD Support

The definition of RVF during LVAD support is controversial. Most studies define RVF as a spectrum of clinical symptomatology or need for inotropes or mechanical support.^{5–10} Our team recently demonstrated that even subclinical RVF, defined as RAP > 12 mmHg, was major determinant of worse clinical outcomes during LVAD support.⁴ A more objective and easy-to-measure index to assess subclinical RVF has been warranted.

There are several objective methods to assess right heart function, volume, and pressure including echocardiography and intracardiac pressure measurement.^{11,13} However, none of these methods have been validated as a clinical gold-standard technique to accurately assess RV function. Although the absolute value of RAP is a good marker to assess the hemodynamic status of the right heart, it is largely dependent on instantaneous volume status and may not accurately represent RV function.

It is classically known that RHC waveform, particularly a deep y-descent, represents impaired RV function, reflecting rapid early ventricular filling due to reduced RV function.¹⁵ In this study, we measured the height and depth of each waveform from the mean RAP to qualify the waveform.

A deep y-descent (>3 mmHg) was associated with impaired RV function, which was further validated by hemodynamic and echocardiographic assessments. The association with other

more advanced methods including 3-dimensional echocardiographic volume assessment and speckle tracking technique would be potentially useful next steps to better clarify the implications of a deep y-descent.^{16,17}

Changes in RHC Waveform Following LVAD Implantation

We showed for the first time unique changes in RHC waveform following LVAD implantation. These findings may indicate a trend toward worsening RV function with deepening y-descent and reduced RV pressure in LVAD patients, irrespective of clinical symptoms.

Several mechanisms are proposed. Preexisting subclinical RVF may worsen when systemic LVAD flow increases the degree of preload experienced by the RV. Increased LV unloading with the LVAD may cause a leftward shift of the intraventricular septum and change the geographic construct of the RV, leading to enlargement of the RV cavity and lack of tricuspid annulus coaptation.¹⁸

Deep y-Descent and GIB

Causes of GIB during LVAD supports are multifactorial. In addition to the use of anticoagulation and antiplatelet agents as well as acquired von Willebrand disease because of device–blood interaction,¹⁹ inappropriate activation of abnormal angiogenesis has recently been considered as a dominant cause of GIB because of the development of arteriovenous malformation on the GI tract.²⁰

Impaired RV function is associated with GIB.^{21,22} Although the true mechanisms remain unknown, chronically worsening passive congestion in the mesenteric venous system may contribute to the development of arteriovenous malformation (AVM) in the GI tract.²³ Passive congestion in submucosal vessels likely causes relative blood flow obstruction, which theoretically may drive the proposed pathogenesis of AVM formation. Also, systemic congestion may stimulate inflammatory and angiogenesis systems that contribute to the development of AVM.²⁰

Deep y-Descent and Thromboembolic Events

A deep y-descent was also associated with thromboembolic events. Impaired RV function would reduce cardiac forward flow and LVAD filling, lower LVAD flow, and cause pump stasis. Adequate laminar flow across the blood-washed inflow bearing of the pump is critical for heat transfer.²⁴ If not maintained, it can lead to thrombus formation and successive systemic thrombosis. The event rates of pump thrombosis did not reach statistical difference probably because of multifactorial causality.²⁵

Management of Deep y-Descent

Deep y-descent was associated with an increased risk in the development of HRAE. Clinically-defined RVF is associated with increased mortality, impaired exercise capacity, and reduced quality of life.⁵ We demonstrated for the first time that even subclinical RVF, which is defined by a deep y-descent among clinically stable outpatients, also had an impact on clinical outcomes. We may be able to reduce the risk of both bleeding and

thromboembolic events when surrogates of subclinical RVF, such as deep y-descent, are recognized earlier. Furthermore, deep y-descent was superior in predicting HRAE among other conventional RVF indicators including RAP and pulmonary artery pulsatility index.²⁶

A focus on the prevention of subclinical RVF would be the next step in improving outcomes in the LVAD population. Most post-LVAD implant deep y-descents occurred de novo in our study. We did not find significant pre-LVAD risk factors for the development of de novo deep y-descent.²⁶

Subclinical RVF may be managed by LVAD speed adjustment, anti-pulmonary hypertension agents, or aggressive diuretic therapy incorporating vasopressin type-2 antagonist.^{27,28} Changes in the y-descent at different loading conditions or any other interventions would be a next concern. Further studies are warranted to develop a better strategy to prevent de novo deep y-descent following LVAD implantation and assess for therapies that may attenuate progression of subclinical RVF to clinical RVF.

Limitation

This study has several limitations worth noting. This is a single-center, moderate size cohort, but with comprehensive data including hemodynamic, echocardiographic, and laboratory data. We measured the absolute values of height and depth of each waveform, but the percentage change, width, slope, or square of each waveform may also be useful to accurately assess the features of the waveform, though this presents many technical challenges. We did not routinely assess the Kussmaul's sign, which is an indicator of dilated RV that has difficulty in accommodating venous return. All hemodynamic data were obtained at end-expiratory setting as stated, and data can vary at different respiratory setting. We used pulmonary artery pulsatility index to assess RV dysfunction, but the utility of this index during LVAD support may need further investigation.

We assessed RHC waveforms before and 6 months after LVAD implantation. Longitudinal trend of RHC waveform, particularly the prevalence and magnitude of deep y-descent, remains uncertain. However, the invasive nature of serial RHC's may be unreasonable to implement. Implantable or noninvasive devices to continuously monitor RHC waveform may overcome this limitation and more strengthen the utility of our findings.

We focused on the implication of the y-descent in this study considering its significant impact on HRAE, whereas other parameters may also have significant implications on other clinical outcomes such as exercise capacity. De novo deep y-descent was associated with worse outcome, but we have not yet demonstrated its causality, which should be clarified in the prospective randomized control trial. We enrolled also those with atrial fibrillation, but the applicability of our findings to those with severe bradycardia and tachycardia remains unknown. The prevalence of deep y-descent was statistically not different between HeartMate II and HVAD (43% vs 38%, $P = .38$), but the prevalence in other devices is unknown.

Clinicians may sometimes confuse when patients had borderline y-descent depth around the cutoff 3 mmHg. Although the cutoff was statistically calculated, we can change the cutoff

for any purposes. For example, we can find specific cases with a giant y-descent. For example, all 4 patients with y-descent >5 mmHg experienced HRAEs. Or clinicians can refer hazard ratio 1.55 per 1 mmHg increase in the depth of y-descent.

Conclusion

A post-LVAD deep y-descent in RA waveform during LVAD support was associated with impaired right heart function and HRAEs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Kormos RL, Cowger J, Pagani FD, Teuteberg JJ, Goldstein DJ, Jacobs JP, et al. The Society of Thoracic Surgeons Intermacs database annual report: evolving indications, outcomes, and scientific partnerships. *J Heart Lung Transplant* 2019;38:114–26. [PubMed: 30691593]
2. Mehra MR. The burden of haemocompatibility with left ventricular assist systems: a complex weave. *Eur Heart J* 2019;40:673–7. [PubMed: 28329374]
3. Mehra MR, Goldstein DJ, Uriel N, Cleveland JC Jr., Yuzefpolskaya M, Salerno C, et al. Two-year outcomes with a magnetically levitated cardiac pump in heart failure. *N Engl J Med* 2018;378:1386–95. [PubMed: 29526139]
4. Imamura T, Nguyen A, Kim G, Raikhelkar J, Sarswat N, Kalantari S, et al. Optimal haemodynamics during left ventricular assist device support are associated with reduced haemocompatibility-related adverse events. *Eur J Heart Fail* 2018;21:655–62. [PubMed: 30592363]
5. Rich JD. Right ventricular failure in patients with left ventricular assist devices. *Cardiol Clin* 2012;30:291–302. [PubMed: 22548819]
6. Kormos RL, Teuteberg JJ, Pagani FD, Russell SD, John R, Miller LW, et al. Right ventricular failure in patients with the HeartMate II continuous-flow left ventricular assist device: incidence, risk factors, and effect on outcomes. *J Thorac Cardiovasc Surg* 2010;139:1316–24. [PubMed: 20132950]
7. Matthews JC, Koelling TM, Pagani FD, Aaronson KD. The right ventricular failure risk score a pre-operative tool for assessing the risk of right ventricular failure in left ventricular assist device candidates. *J Am Coll Cardiol* 2008;51:2163–72. [PubMed: 18510965]
8. MacGowan GA, Schueler S. Right heart failure after left ventricular assist device implantation: early and late. *Curr Opin Cardiol* 2012;27:296–300. [PubMed: 22327288]
9. Kapelios CJ, Charitos C, Kaldara E, Malliaras K, Nana E, Pantsios C, et al. Late-onset right ventricular dysfunction after mechanical support by a continuous-flow left ventricular assist device. *J Heart Lung Transplant* 2015;34:1604–10. [PubMed: 26163154]
10. Takeda K, Takayama H, Colombo PC, Jorde UP, Yuzefpolskaya M, Fukuhara S, et al. Late right heart failure during support with continuous-flow left ventricular assist devices adversely affects post-transplant outcome. *J Heart Lung Transplant* 2015;34:667–74. [PubMed: 25577566]
11. American College of Cardiology Foundation Appropriate Use Criteria Task F, American Society of Echocardiography, American Heart Association, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society. ACCF/AHA/ASNC/HFSA/HRS/SCAI/SCCM/SCCT/sCMR 2011 Appropriate Use Criteria for Echocardiography: a report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Society of Echocardiography, American Heart Association, American Society of Nuclear

- Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Critical Care Medicine, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance American College of Chest Physicians. *J Am Soc Echocardiogr*. 2011;24:229–67. [PubMed: 21338862]
12. INTERMACS Adverse Event Definitions: adult and pediatric patients. Available at www.INTERMACS.org. 2013.
 13. Swan HJ, Ganz W, Forrester J, Marcus H, Diamond G, Chonette D. Catheterization of the heart in man with use of a flow-directed balloon-tipped catheter. *N Engl J Med*. 1970;283: 447–51. [PubMed: 5434111]
 14. Sharkey SW. Beyond the wedge: clinical physiology and the Swan-Ganz catheter. *Am J Med* 1987;83:111–22. [PubMed: 3300319]
 15. Vaitkus PT, Cooper KA, Shuman WP, Hardin NJ. Images in cardiovascular medicine. Constrictive pericarditis. *Circulation* 1996;93:834–5. [PubMed: 8641014]
 16. Addetia K, Uriel N, Maffessanti F, Sayer G, Adatya S, Kim GH, et al. 3D morphological changes in LV and RV during LVAD ramp studies. *JACC Cardiovasc Imaging* 2018;11: 159–69. [PubMed: 28412431]
 17. Beck DR, Foley L, Rowe JR, Moss AFD, Weitzel NS, Reece TB, et al. Right ventricular longitudinal strain in left ventricular assist device surgery: a retrospective cohort study. *J Cardiothorac Vasc Anesth* 2017;31:2096–102. [PubMed: 29103855]
 18. Chumnanvej S, Wood MJ, MacGillivray TE, Melo MF. Perioperative echocardiographic examination for ventricular assist device implantation. *Anesth Analg* 2007;105:583–601. [PubMed: 17717209]
 19. Uriel N, Pak SW, Jorde UP, Jude B, Susen S, Vincentelli A, et al. Acquired von Willebrand syndrome after continuous-flow mechanical device support contributes to a high prevalence of bleeding during long-term support and at the time of transplantation. *J Am Coll Cardiol* 2010;56: 1207–13. [PubMed: 20598466]
 20. Tabit CE, Coplan MJ, Chen P, Jeevanandam V, Uriel N, Liao JK. Tumor necrosis factor- α levels and non-surgical bleeding in continuous-flow left ventricular assist devices. *J Heart Lung Transplant* 2018;37:107–15. [PubMed: 28651907]
 21. Tomizawa Y, Tanaka A, Kitahara H, Sakuraba A, Uriel N, Jeevanandam V, et al. Preoperative right-sided cardiac congestion is associated with gastrointestinal bleeding in patients with continuous-flow left ventricular assist devices. *Dig Dis Sci* 2018;63:1518–24. [PubMed: 29417325]
 22. Sparrow CT, Nassif ME, Raymer DS, Novak E, LaRue SJ, Schilling JD. Pre-operative right ventricular dysfunction is associated with gastrointestinal bleeding in patients supported with continuous-flow left ventricular assist devices. *JACC Heart Fail* 2015;3:956–64. [PubMed: 26577618]
 23. Boley SJ, Sammartano R, Adams A, DiBiase A, Kleinhaus S, Sprayregen S. On the nature and etiology of vascular ectasias of the colon: degenerative lesions of aging. *Gastroenterology* 1977;72:650–60. [PubMed: 300063]
 24. Kirklin JK, Naftel DC, Pagani FD, Kormos RL, Myers S, Acker MA, et al. Pump thrombosis in the Thoratec HeartMate II device: an update analysis of the INTERMACS registry. *J Heart Lung Transplant* 2015;34:1515–26. [PubMed: 26681121]
 25. Maltais S, Kilic A, Nathan S, Keebler M, Emani S, Ransom J, et al. Prevention of HeartMate II pump thrombosis through clinical management: the PREVENT multi-center study. *J Heart Lung Transplant* 2017;36:1–12. [PubMed: 27865732]
 26. Kang G, Ha R, Banerjee D. Pulmonary artery pulsatility index predicts right ventricular failure after left ventricular assist device implantation. *J Heart Lung Transplant* 2016;35:67–73. [PubMed: 26212656]
 27. Uriel N, Sayer G, Addetia K, Fedson S, Kim GH, Rodgers D, et al. Hemodynamic ramp tests in patients with left ventricular assist devices. *JACC Heart Fail* 2016;4:208–17. [PubMed: 26746378]
 28. Imamura T, Kinugawa K. Update of acute and long-term tolcaptan therapy. *J Cardiol* 2019;73:102–7. [PubMed: 30420105]

Fig. 1. Definition of waveform variables in right atrial pressure (A) and right ventricular pressure (B). Wave height and descent depth were measured from the level of mean right atrial pressure. RVP, right ventricular pressure; RVEDP, right ventricular end-diastolic pressure.

Fig. 2. Representatives of composite waveform (A–D). Composite waveforms were created using each waveform variable. RVP, right ventricular pressure.

Fig. 3.

One-year survival free from HRAEs (**A**) and event rates of individual HRAEs (**B**) stratified by the existence of deep y-descent. $*P < .05$ by log rank test. $^\dagger P < .05$ by Mann-Whitney U test.

Table 1.

Preoperative Baseline Characteristics

	All (N = 89)	Post-LVAD Deep y-Descent (N = 36)	Post-LVAD Normal y-Descent (N = 53)	P Value
Demographics				
Age, y	59 (48, 67)	60 (54, 67)	59 (47, 67)	.37
Gender, male	65 (73%)	22 (61%)	43 (81%)	.033*
Body mass index	29.2 (25.5, 36.3)	31.3 (25.7, 37.5)	28.8 (25.2, 35.6)	.31
Ischemic etiology	26 (29%)	13 (36%)	13 (25%)	.17
Destination therapy	63 (71%)	26 (72%)	37 (70%)	.50
Heartmate II LVAD	44 (49%)	19 (53%)	25 (47%)	.38
HVAD LVAD	45 (51%)	17 (47%)	28 (53%)	.38
Diabetes mellitus	31 (35%)	15 (42%)	16 (30%)	.19
History of stroke	16 (18%)	8 (22%)	8 (15%)	.28
Atrial fibrillation	39 (44%)	19 (53%)	20 (38%)	.12
History of ventricular tachyarrhythmia	36 (40%)	13 (36%)	23 (43%)	.32
Chronic kidney disease	41 (46%)	19 (53%)	25 (47%)	.38
Pre-LVAD hemodynamics				
Mean right atrial pressure, mmHg	11.1 ± 5.9	11.7 ± 6.6	10.7 ± 5.4	.47
Pulmonary capillary wedge pressure, mmHg	24.2 ± 8.4	25.2 ± 9.2	23.4 ± 7.8	.34
Cardiac index, L/min/m ²	1.91 ± 0.56	1.98 ± 0.51	1.87 ± 0.59	.42
Mean arterial pressure, mmHg	82.2 ± 12.1	84.0 ± 13.7	81.0 ± 10.9	.26
Pre-LVAD waveform variables				
Deep y-descent (>3 mm)	10 (11%)	4 (11%)	6 (11%)	.98
a-wave height, mmHg	2.4 ± 1.9	2.4 ± 1.5	2.5 ± 2.2	.85
v-wave height, mmHg	2.8 ± 1.8	2.6 ± 1.5	2.9 ± 1.9	.44
x-descent depth, mmHg	1.0 ± 1.5	0.9 ± 1.7	1.1 ± 1.3	.58
RV systolic pressure, mmHg	50.4 ± 13.2	51.2 ± 13.1	49.9 ± 13.3	.64
RV end-diastolic pressure, mmHg	12.9 ± 5.7	13.3 ± 6.2	12.6 ± 5.3	.61
RV dP/dt, mmHg/s	466.4 ± 138.0	465.1 ± 123.4	467.2 ± 138.2	.95

* $P < .05$. Variables were compared using unpaired t test, Mann-Whitney U test, or Fischer's exact test as appropriate.

Table 2.

Changes in Waveform Parameters Before and After LVAD Implantation

	Pre-LVAD	Post-LVAD	P Value
Mean right atrial pressure, mmHg	11.1 ± 5.9	9.9 ± 5.9	.16
a-wave height, mmHg	2.4 ± 2.0	1.6 ± 1.5	<.001 [*]
v-wave height, mmHg	2.8 ± 1.8	2.3 ± 1.8	.12
x-descent depth, mmHg	−1.0 ± 1.5	−0.9 ± 1.3	.52
y-descent depth, mmHg	−1.5 ± 2.1	−3.2 ± 1.8	<.001 [*]
Systolic right ventricular pressure, mmHg	50.4 ± 35.5	35.5 ± 12.3	<.001 [*]
Right ventricular end-diastolic pressure, mmHg	12.9 ± 5.7	10.4 ± 6.1	.006 [*]
Right ventricular dP/dt, mmHg/s	466.4 ± 138.0	315.1 ± 121.2	<.001 [*]

^{*}
^{*} $P < .05$ by paired t test.

Table 3.

Comparison of Postoperative Echocardiographic Variables of Right Heart

	Post-LVAD Deep γ -Descent (N = 36)	Post-LVAD Normal γ -Descent (N = 53)	P Value
TAPSE, cm	0.7 (0.5, 1.0)	1.0 (0.8, 1.2)	.001 *
TV S', cm/s	5.5 (4.9, 7.0)	7.5 (6.3, 9.1)	.002 *
TR grade	0.5 (0.5, 2.0)	0.5 (0.5, 1.0)	.069
RA area, cm ²	16.9 (14.3, 19.9)	13.8 (10.1, 17.3)	.006 *
RVEDA, cm ²	28.9 (20.6, 33.5)	22.0 (18.4, 27.3)	.023 *
RVFAC, %	15.5 (9.6, 28.0)	21.1 (15.3, 28.7)	.10

TAPSE, tricuspid annular plane systolic excursion; TV S', tricuspid annular systolic motion velocity; TR, tricuspid regurgitation; RA, right atrium; EDA, end-diastolic area; FAC, fractional area change.

Postoperative echocardiography was performed at 6 months following LVAD implantation (time zero). TR was graded as 0 none; 1 trace; 2 mild; 3 mild to moderate; 4 moderate; 5 moderate to severe; 6 severe.

* $P < .05$. Variables were compared using Mann-Whitney U test.

Table 4.

Impact of Post-LVAD Deep y-Descent and Other Variables on HRAEs

	Univariate Analyses		Multivariate Analyses	
	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
Demographics				
Age, y	1.00 (0.97–1.04)	.80		
Gender, male	0.60 (0.27–1.31)	.20		
Ischemic etiology	1.05 (0.47–2.37)	.90		
Destination therapy	1.83 (0.63–5.34)	.27		
HeartMate II LVAD	1.76 (0.80–3.88)	.16		
History of stroke	1.94 (0.81–4.61)	.14		
Atrial fibrillation	1.03 (0.47–2.24)	.95		
Chronic kidney disease	1.03 (0.46–2.32)	.94		
Medications at 6 mo				
No aspirin use	2.39 (1.04–5.56)	.040*	2.62 (1.13–6.06)	.024*
INR <1.5	2.44 (0.84–7.11)	.10		
Post-LVAD hemodynamic variables				
Mean right atrial pressure, mmHg	1.01 (0.95–1.07)	.80		
Pulmonary capillary wedge pressure, mmHg	1.02 (0.97–1.07)	.49		
Cardiac index, L/min/m ²	1.01 (0.56–1.82)	.98		
No optimal hemodynamics	2.27 (1.02–5.00)	.043*	2.54 (1.08–5.84)	.14
Mean arterial pressure, mmHg	1.03 (0.99–1.07)	.069		
Mean right atrial/pulmonary capillary wedge pressure	1.12 (0.40–3.14)	.84		
Pulmonary artery pulsatility index	0.96 (0.82–1.12)	.58		
Post-LVAD waveform variables				
Deep y-descent (>3 mmHg)	4.85 (2.04–11.6)	<.001*	4.94 (2.12–10.4)	<.001*
a-wave height, mmHg	0.80 (0.62–1.04)	.090		
v-wave height, mmHg	1.23 (1.04–1.46)	.018*	1.84 (1.12–1.84)	.23
x-descent depth, mmHg	0.98 (0.72–1.33)	.88		
RV systolic pressure, mmHg	1.01 (0.98–1.04)	.66		
RV end-diastolic pressure, mmHg	1.02 (0.96–1.08)	.59		

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	Univariate Analyses		Multivariate Analyses	
	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
RV dP/dt, mmHg/s	0.99 (0.99–1.00)	.35		

INR, international normalized ratio. Optimal hemodynamics is defined as right atrial pressure <12 mmHg, pulmonary capillary wedge pressure <18 mmHg, and cardiac index >2.2 L/min/m².
* *P* < .05. Variables with *P* < .05 in the univariate analyses were enrolled in the multivariate analyses with simultaneous forced entry method.