Published in final edited form as:

J Card Fail. 2018 September ; 24(9): 575–582. doi:10.1016/j.cardfail.2018.08.003.

Decoupling between Diastolic Pulmonary Artery Pressure and Pulmonary Artery Wedge Pressure at Incremental LVAD speeds is Associated with Worse Prognosis following LVAD Implantation

Teruhiko Imamura, MD, PhD¹, Gene Kim, MD¹, Jayant Raikhelkar, MD¹, Nitasha Sarswat, MD¹, Sara Kalantari, MD¹, Bryan Smith, MD¹, Daniel Rodgers, BA¹, Ben Chung, MD¹, Ann Nguyen, MD¹, Takeyoshi Ota, MD, PhD², Tae Song, MD², Colleen Juricek, RN², Valluvan Jeevanandam, MD², Daniel Burkhoff, MD, PhD³, Gabriel Sayer, MD¹, and Nir Uriel, MD, MSc¹

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

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

³Columbia University Medical Center, and Cardiovascular Research Foundation, New York, New York

Abstract

Background: Decoupling between diastolic pulmonary artery pressure (dPAP) and pulmonary artery wedge pressure (PAWP) is an index of pulmonary vasculature remodeling and provides prognostic information. Furthermore, decoupling may change during incremental left ventricular assist device (LVAD) speed changes.

Methods: In this prospective study, patients underwent an echocardiographic and hemodynamic ramp test following LVAD implantation and were followed for one year. The change in decoupling (dPAP – PAWP) between the lowest and highest LVAD speeds during the ramp test was calculated. Survival and heart failure admission rates were assessed using Kaplan-Meier analysis.

Results: 87 patients were enrolled in the study; 54 had a HeartMate II LVAD (60.8 ± 9.3 years old and 34 male) and 33 had an HVAD LVAD (58.6 ± 13.2 years old and 20 male). Patients who experienced greater changes in decoupling (decoupling >3 mmHg) had a persistently elevated dPAP at incremental LVAD speed and had worse 1-year heart failure readmission-free survival as compared to the group without significant changes in the degree of decoupling (41% vs. 75%, p = 0.001).

Address for correspondence: Nir Uriel, MD, MSc, Department of Medicine, University of Chicago Medical Center, 5841 S. Maryland Avenue Chicago, IL 60637, Phone: 1-773-702-9396, Fax: 1-773-834-1764, nuriel@medicine.bsd.uchicago.edu.

Disclosures:

Teruhiko Imamura receives financial support from Postdoctoral Fellowship for Research Abroad of Japan Society for the Promotion of Science; Nir Uriel receives grant support from Abbott and Medtronic; Valluvan Jeevanandam receives consultant fee from Abbott. Gabriel Sayer has received consulting fees from Medtronic; Daniel Burkhoff receives consultant fee from Medtronic, Corvia Medical, Sensible Medical, Impulse Dynamics, Cardiac Implants, and educational grant support from Abiomed.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conclusion: An increase in decoupling between dPAP and PAWP at incremental LVAD speed changes was associated with worse prognosis in LVAD patients.

Graphical Abstract

Keywords

ramp; hemodynamics; unloading; pulmonary hypertension

INTRODUCTION

Pulmonary hypertension (PH) is one of the critical comorbidities in advanced heart failure (HF).^{1, 2} Indices of PH such as mean pulmonary artery pressure (mPAP), pulmonary vascular resistance (PVR), and trans-pulmonary artery pressure gradient improve following left ventricular assist device (LVAD) implantation mainly due to left ventricular unloading.^{3, 4} Several investigators demonstrated in small cohorts that patients whose elevated PVRs were normalized following LVAD implantation had comparable post-heart transplant survival rates to those without PH.^{5, 6} In contrast, Tsukashita and colleagues recently showed in a moderately large cohort that in-hospital mortality following heart transplantation was higher in patients with a pre-LVAD PVR ≥ 5 Wood units compared to those with lower PVR, despite the fact that the elevated PVRs were normalized following LVAD implantation.⁷ They speculated that unknown indices of PH might still exist and affect post transplant outcome.

Lately, our group demonstrated that "decoupling", which is defined as an excessive separation between the diastolic pulmonary artery pressure (dPAP) and the pulmonary artery wedge pressure (PAWP)⁸ and represents combined pre-capillary and post-capillary PH, is a strong predictor of post-LVAD HF-free survival.⁹ The aim of this study was to assess if the degree of decoupling changes with incremental changes in LVAD speed during a hemodynamic ramp test,¹⁰ and whether changes in the degree of decoupling predict clinical outcomes.

METHODS

Patient selection:

We prospectively collected data on clinically stable outpatients with LVADs (HVAD or HeartMate II) who were evaluated with a hemodynamic ramp testing and followed at our institution. All patients received guideline-directed medical therapy during the study period.¹¹ Patients with suspicion for device malfunction were excluded. Written informed consent was obtained from all participants before ramp test. The study protocol was approved by the Institutional Review Board at the University of Chicago beforehand.

Ramp test protocol:

Patients underwent an echocardiographic and hemodynamic LVAD speed ramp study in the cardiac catheterization laboratory according to the previously detailed protocol.¹⁰ Cardiac output and cardiac index (CI) were calculated by the direct Fick method. 2D echocardiographic parameters including left ventricular dimension and valve features were measured as detailed previously.¹²

Pump speeds were lowered to 2,300 RPM in patients with HVAD and 8,000 RPM in patients with HeartMate II at the initiation of the study. After a five-minute stabilization period, echocardiographic and hemodynamic values were taken. Then, device speeds were increased 100 RPM increments for HVAD patients and 400 RPM increments for HeartMate II patients. After a two-minute stabilization period, the same parameters were recorded. This procedure was repeated until a maximum speed of 3,200 RPM for HVAD patients or 12,000 RPM for HeartMate II patients. Eventually, all echocardiographic and hemodynamic data at each LVAD speed setting (from the lowest to the highest) were completed.

At the conclusion of each test, the attending cardiologist reviewed the results and the device was set at the speed which yielded an optimal hemodynamic profile, as defined by central venous pressure (CVP) <12 mmHg, PAWP <18 mmHg, and CI >2.2 L/min/m²; secondary goals of speed optimization included intermittent aortic valve opening and minimal mitral regurgitation.¹³

Variables evaluated:

Patient preoperative background characteristics, including demographic, echocardiographic, and hemodynamic data, were obtained within the one-month period preceding LVAD implantation. During the ramp test, hemodynamic and echocardiographic data were obtained per protocol. All hemodynamic data were obtained at end-expiration and were manually reviewed by the attending cardiologist. Decoupling was defined as the difference between dPAP and PAWP.⁹ For example, when dPAP is 14 mmHg and PAWP is 9 mmHg, decoupling is calculated as 5 mmHg.

Echocardiographic and hemodynamic changes at incremental LVAD speeds from the lowest to highest speed setting, including that of decoupling, were calculated. For example, when decoupling is 2 mmHg at the lowest LVAD speed and 6 mmHg at the highest LVAD speed, the change in decoupling (decoupling) is calculated as 4 mmHg.

All patients were followed at our institution for one year at the set LVAD speed determined according to the results of the ramp test. HF readmission or all-cause death was recorded during the one-year observational period.

Statistical Analyses:

The primary endpoint of this study was the composite of all-cause mortality and HF readmission from the time of the ramp test (time zero) through one-year follow-up. Continuous variables were presented as mean and standard deviation unless otherwise described, and compared between groups using the unpaired t-test or Mann-Whitney U test, as appropriate. Continuous data between the lowest LVAD speed and the highest LVAD speed were compared by paired t-test. Categorical variables were compared between groups using the chi-square test or Fisher's exact test as appropriate.

A cutoff value of decoupling during ramp test was calculated by using receiver operating characteristic analysis with the endpoint of death or HF admission during one year as a point minimizing the distance from the curve to the top left corner of the graph, and patients were divided into two groups by this cutoff. Patient prognosis stratified by decoupling during ramp test was assessed by Kaplan-Meier analysis and Cox proportional hazards analysis, and compared by log-rank test.

Also in the multivariate Cox proportional hazards analysis, the prognostic impact of decoupling was adjusted by the other clinical variables that were significant in the univariate analyses with $p < 0.05$. Statistical analyses were performed using SPSS Statistics 22 (SPSS Inc, Chicago, IL, USA). A two-tailed p -value < 0.05 was considered significant.

RESULTS

Baseline Characteristics:

Eighty-seven LVAD patients (60.0 ± 10.9 years old, 54 male, 54 HeartMate II, and 33 HVAD) were enrolled (Table 1). The majority of patients were implanted as destination therapy (78%) and 37 (43%) had an ischemic etiology for their cardiomyopathy. Ramp tests were performed at a median of 307 days following LVAD implantation.

Change in decoupling during LVAD speed change:

Among all patients, as speed was changed from the lowest to the highest setting, dPAP decreased from 20.8 ± 7.7 to 15.9 ± 5.8 mmHg, PAWP decreased from 17.4 ± 7.3 to 9.2 ± 5.3 mmHg, and decoupling increased from 3.4 ± 5.0 to 6.7 ± 4.4 mmHg ($p < 0.001$ for all).

decoupling (the change in decoupling from low to high speed) averaged 3.4 ± 0.6 mmHg, ranging between -7 mmHg and 18 mmHg. Forty-eight patients (55%) had decoupling > 3 mmHg, which means, for example, when decoupling at the lowest speed is 3 mmHg, decoupling at the highest speed is > 6 mmHg (Figure 1). This cutoff of decoupling 3 mmHg was derived from the receiver operating characteristic analysis with sensitivity of 0.757 and specificity of 0.600 .

Comparison between the decoupling >3 mmHg group and the decoupling 3 mmHg group:

A higher proportion of HeartMate II patients than HVAD patients had decoupling >3 mmHg. All other preoperative background characteristics including mPAP showed no significant differences between the decoupling >3 mmHg group and the decoupling 3 mmHg group (Table 1).

Following LVAD implantation, the decoupling >3 mmHg group had a larger left ventricular diastolic diameter and higher CVP compared with the decoupling 3 mmHg group (Table 2; $p < 0.05$ for both).

During the ramp test, patients with decoupling >3 mmHg had less reduction in dPAP (i.e., persistently elevated dPAP) and a greater reduction in PAWP compared with patients with decoupling <3 group (Table 3; $p < 0.05$ for both). As a result, decoupling increased significantly from 1.0 ± 4.6 to 8.2 ± 4.1 mmHg in the decoupling >3 mmHg group (Figure 2A; $p < 0.001$), whereas decoupling decreased significantly from 6.1 ± 4.2 to 4.9 ± 4.2 mmHg in the decoupling 3 mmHg group (Figure 2B; $p = 0.009$). PAWP at the lowest LVAD speed was higher in the decoupling >3 mmHg group ($p = 0.004$), whereas dPAP at the highest LVAD speed was higher in the decoupling >3 mmHg group ($p = 0.048$; Appendix Table 1).

At the set LVAD speed, the decoupling >3 mmHg group had a significantly larger left ventricular diastolic diameter (Table 4; $p = 0.007$) and a numerically higher CVP and PAWP compared to patients with decoupling <3 mmHg ($p = 0.07$ for both).

Prognostic impact of the change in decoupling during ramp test:

Among the group with decoupling >3 mmHg, 8 (17%) patients died and 21 (44%) had a HF admission following the ramp test. In the comparison group, 5 (13%) patients died and 7 (18%) had a HF admission.

Patients with decoupling >3 mmHg had a significantly worse HF readmission-free survival compared to those without during the 1-year study period (Figure 3; 41% vs. 75%, $p = 0.001$). In the multivariate Cox hazard regression analyses, decoupling >3 mmHg was a significant predictor of death or HF readmission with an unadjusted hazard ratio of 3.2 (95% confidence interval 1.5–6.9, $p = 0.002$) and 2.4 (95% confidence interval 1.1–5.3, $p = 0.032$) when adjusted by other variables significant in the univariate analyses (CVP, PAWP, and decoupling >5 mmHg at set LVAD speed; Table 5).

Similar results were found in the subgroup analysis of each device type. In patients with HeartMate II ($N = 54$), 1-year HF readmission-free survival was lower in decoupling >3 mmHg compared to others (42% vs. 72%, $p = 0.028$) with hazard ratio of 2.9 (95% confidence interval 1.1–7.6, $p = 0.035$). In patients with HVAD ($N = 33$), 1-year HF readmission-free survival was also lower in decoupling >3 mmHg compared to others (39% vs. 77%, $p = 0.028$) with hazard ratio of 3.7 (95% confidence interval 1.1–12.5, $p = 0.040$).

DISCUSSION

In this prospective study, we analyzed the prognostic implications of a change in the degree of decoupling between the lowest and highest LVAD speeds during a hemodynamic ramp study. Our main findings are: (1) decoupling >3 mmHg was common in clinically stable outpatients receiving LVAD support irrespective of the perioperative existence of PH. (2) The main mechanism of the increase in decoupling at incremental LVAD speeds was persistent elevation of dPAP despite decreases in PAWP. (3) decoupling >3 mmHg was a strong predictor of the composite endpoint of death or HF readmission demonstrated by multivariate analyses.

Change in the degree of decoupling with incremental LVAD speed changes:

We previously demonstrated that decoupling between dPAP and PAWP indicates remodeling to the pulmonary vasculature and is associated with a worse prognosis in LVAD patients.⁹ In this study, we focused on the change in the degree of decoupling between the lowest and highest LVAD speeds, which may represent a patient-specific index of decoupling that is independent of the LVAD speed setting.

This technique assesses how dynamic the pulmonary vasculature is, measuring its ability to adapt to decreases in post-capillary (i.e. LV) pressure. In the group of patients whose degree of decoupling increased during the ramp study, the primary hemodynamic finding was a minimal decrease in dPAP despite incremental decreases in PAWP with speed changes. These patients exhibited evidence of pulmonary vascular remodeling that is not responsive to acute decreases in post-capillary pressure through LV unloading.

Importantly, there was no difference in mPAP, PVR, or pulmonary artery compliance among patients with increases in the degree of decoupling and those without. Therefore, decoupling represents an independent marker of pulmonary vascular disease. By evaluating the response of the pulmonary vasculature to acute decreases in LV pressure, decoupling provides an assessment of whether pulmonary vascular abnormalities are “fixed” or “reversible”. Measurement of decoupling during ramp testing may be used to identify pulmonary vascular disease in all LVAD patients, even patients without evidence of PH using conventional markers. Further studies that incorporate pathological findings or pulmonary function assessments may provide further insight into the difference between decoupling abnormalities measured at a fixed LVAD speed or during dynamic LVAD speed changes.

Interestingly, the group with increased decoupling had a larger LV and higher CVP following LVAD implantation. The larger LV may reflect a greater degree of LV remodeling in these patients, possibly indicating a longer duration of HF, which may have promoted a greater degree of vascular remodeling. The elevation in CVP reflects the effect of pulmonary vascular remodeling on the right ventricle. Pulmonary vascular disease creates an increase in right ventricular afterload, impairing right ventricular contractile function. It is possible that decreased forward flow from the right ventricle at higher LVAD speeds may have also contributed to the sharper drop in PAWP among the group with increased decoupling.

Prognostic impact of decoupling:

decoupling was a significant predictor of the composite of mortality and HF readmission, even when it was adjusted by clinical variables including the absolute degree of decoupling at set LVAD speed and analyzed separately in each device group. This effect was primarily driven by an increase in HF admissions, reflecting the decremental effect of pulmonary vascular disease on right ventricular function, which was suggested by the higher CVP in the group with increased decoupling during the ramp study. The group with increased

decoupling had worse outcomes even though the absolute degree of decoupling at their set speed was similar to the other group, highlighting the value of a dynamic assessment of the pulmonary vasculature.¹⁴

Future directions and study limitations:

It is uncertain whether decoupling may change during long-term LVAD support. Repeated ramp tests may answer this question.¹⁵ We believe that decoupling is a patient-specific index of fixed PH, but whether optimization of LVAD speed or introduction of pulmonary vasodilators improves decoupling needs further study. The ongoing SOPRANO study will provide further information about the efficacy of pulmonary vasodilator therapy in the LVAD population ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT02554903) Identifier NCT02554903).

Several potential limitations of this study should be considered. First, this is a single center study with a moderate-sized patient cohort. Second, we did not specify any medication adjustments during the study period; patient management was dependent on the clinical decisions of multiple attending physicians. The physicians were blinded to the data on decoupling, and it seems unlikely to have changed management. Third, we did not show longitudinal data showing how decoupling and other clinical parameters vary during long-term LVAD support. Fourth, LVAD duration prior to the ramp testing varied widely. This wide variation may set up a time bias because it relates to subsequent outcome events. However, all participants were clinically stable outpatients until the time of ramp test and such bias may therefore be minimized. Consistently, 1-year HF readmission-free survivals were comparable irrespective of ramp test timing ($p = 0.65$; 58% in the <1 year group and 53% in the ≥1 year group). Fifth, we included HeartMate II and HVAD patients, and our results may not simply be adopted in patients with other devices such as HeartMate 3. More HeartMate II patients experienced decoupling >3 mmHg compared with the HVAD group. The association between device type and decoupling needs further evaluation. Sixth, we cannot exclude the possibility of regression to the mean, in which we would expect the group with the high PAWP at low speed (the decoupling >3 mmHg group) to have a greater change in PAWP during ramp testing as the value returns towards the mean. Seventh, decoupling was negative in several patients. We do not have appropriate physiological explanation of such phenomenon and cannot completely exclude the effects of catheter whip artifacts. Finally, we used a cutoff of decoupling >3 mmHg derived from our own dataset, and this value has not undergone external validation, which may lead to exaggeration of the true differences between the two groups. A next step would be to confirm the validity of this value in another dataset.

Conclusion:

An increase in decoupling between dPAP and PAWP during incremental LVAD speed changes may be a sign for pulmonary vascular remodeling and is associated with worse prognosis in LVAD patients.

Acknowledgment:

None.

Sources of Funding:

None.

Appendix

Table A1.

Comparison in PAWP and dPAP at the lowest LVAD speed and at the highest LVAD speed.

	decoupling >3 (N = 48)	decoupling 3 (N = 39)	p value
Lowest LVAD speed			
PAWP, mmHg	19.5 ± 7.0	15.0 ± 6.9	0.004 [*]
dPAP, mmHg	20.5 ± 6.8	21.2 ± 8.8	0.69
Highest LVAD speed			
PAWP, mmHg	8.8 ± 4.8	9.9 ± 5.8	0.35
dPAP, mmHg	17.0 ± 5.7	14.8 ± 5.7	0.048 [*]

Abbreviations as in Table 1

^{*} p < 0.05 by unpaired t-test or Mann-Whitney U test as appropriate.

REFERENCES

- Galie N, Humbert M, Vachiery JL, Gibbs S, Lang I, Torbicki A, Simonneau G, Peacock A, Vonk Noordegraaf A, Beghetti M, Ghofrani A, Gomez Sanchez MA, Hansmann G, Klepetko W, Lancellotti P, Matucci M, McDonagh T, Pierard LA, Trindade PT, Zompatori M, Hoeper M, Aboyans V, Vaz Carneiro A, Achenbach S, Agewall S, Allanore Y, Asteggiano R, Paolo Badano L, Albert Barbera J, Bouvaist H, Bueno H, Byrne RA, Carerj S, Castro G, Erol C, Falk V, Funck-Brentano C, Gorenflo M, Granton J, Jung B, Kiely DG, Kirchhof P, Kjellstrom B, Landmesser U, Lekakis J, Lionis C, Lip GY, Orfanos SE, Park MH, Piepoli MF, Ponikowski P, Revel MP, Rigau D, Rosenkranz S, Voller H, Luis Zamorano J. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). *Eur Heart J*. 2016;37(1):67–119. [PubMed: 26320113]
- Aronson D, Eitan A, Dragu R, Burger AJ. Relationship between reactive pulmonary hypertension and mortality in patients with acute decompensated heart failure. *Circ Heart Fail*. 2011;4(5):644–650. [PubMed: 21606213]
- Pauwaa S, Bhat G, Tatoes AJ, Aggarwal A, Martin M, Kumar A, Modi H, Pappas PS. How effective are continuous flow left ventricular assist devices in lowering high pulmonary artery pressures in heart transplant candidates? *Cardiol J*. 2012;19(2):153–158. [PubMed: 22461048]
- Kutty RS, Parameshwar J, Lewis C, Catarino PA, Sudarshan CD, Jenkins DP, Dunning JJ, Tsui SS. Use of centrifugal left ventricular assist device as a bridge to candidacy in severe heart failure with secondary pulmonary hypertension. *Eur J Cardiothorac Surg*. 2013;43(6):1237–1242. [PubMed: 23345184]
- Zimpfer D, Zrunek P, Sandner S, Schima H, Grimm M, Zuckermann A, Wolner E, Wieselthaler G. Post-transplant survival after lowering fixed pulmonary hypertension using left ventricular assist devices. *Eur J Cardiothorac Surg*. 2007;31(4):698–702. [PubMed: 17289396]
- Alba AC, Rao V, Ross HJ, Jensen AS, Sander K, Gustafsson F, Delgado DH. Impact of fixed pulmonary hypertension on post-heart transplant outcomes in bridge-to-transplant patients. *J Heart Lung Transplant*. 2010;29(11):1253–1258. [PubMed: 20620083]
- Tsukashita M, Takayama H, Takeda K, Han J, Colombo PC, Yuzefpolskaya M, Topkara VK, Garan AR, Mancini DM, Kurlansky PA, Naka Y. Effect of pulmonary vascular resistance before left ventricular assist device implantation on short- and long-term post-transplant survival. *J Thorac Cardiovasc Surg*. 2015;150(5):1352–1360, 1361 e1351–1352. [PubMed: 26253875]
- Gerges C, Gerges M, Lang MB, Zhang Y, Jakowitsch J, Probst P, Maurer G, Lang IM. Diastolic pulmonary vascular pressure gradient: a predictor of prognosis in "out-of-proportion" pulmonary hypertension. *Chest*. 2013;143(3):758–766. [PubMed: 23580984]
- Imamura T, Chung B, Nguyen A, Rodgers D, Sayer G, Adatya S, Sarswat N, Kim G, Raikhelkar J, Ota T, Song T, Juricek C, Kagan V, Jeevanandam V, Mehra M, Burkhoff D, Uriel N. Decoupling Between Diastolic Pulmonary Artery Pressure and Pulmonary Capillary Wedge Pressure as a Prognostic Factor After Continuous Flow Ventricular Assist Device Implantation. *Circ Heart Fail*. 2017;10(9).
- Uriel N, Sayer G, Addetia K, Fedson S, Kim GH, Rodgers D, Kruse E, Collins K, Adatya S, Sarswat N, Jorde UP, Juricek C, Ota T, Jeevanandam V, Burkhoff D, Lang RM. Hemodynamic Ramp Tests in Patients With Left Ventricular Assist Devices. *JACC Heart Fail*. 2016;4(3):208–217. [PubMed: 26746378]
- Hunt SA, American College of C, American Heart Association Task Force on Practice G. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). *J Am Coll Cardiol*. 2005;46(6):e1–82. [PubMed: 16168273]
- Uriel N, Morrison KA, Garan AR, Kato TS, Yuzefpolskaya M, Latif F, Restaino SW, Mancini DM, Flannery M, Takayama H, John R, Colombo PC, Naka Y, Jorde UP. 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*. 2012;60(18):1764–1775. [PubMed: 23040584]

13. Feldman D, Pamboukian SV, Teuteberg JJ, Birks E, Lietz K, Moore SA, Morgan JA, Arabia F, Bauman ME, Buchholz HW, Deng M, Dickstein ML, El-Banayosy A, Elliot T, Goldstein DJ, Grady KL, Jones K, Hryniewicz K, John R, Kaan A, Kusne S, Loebe M, Massicotte MP, Moazami N, Mohacsi P, Mooney M, Nelson T, Pagani F, Perry W, Potapov EV, Eduardo Rame J, Russell SD, Sorensen EN, Sun B, Strueber M, Mangi AA, Petty MG, Rogers J. The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support: executive summary. *J Heart Lung Transplant*. 2013;32(2):157–187. [PubMed: 23352391]
14. Bohm M, Moll M, Schmid B, Paul M, Ganten D, Castellano M, Erdmann E. Beta-adrenergic neuroeffector mechanisms in cardiac hypertrophy of renin transgenic rats. *Hypertension*. 1994;24(6):653–662. [PubMed: 7995621]
15. Imamura T, Burkhoff D, Rodgers D, Adatya S, Sarswat N, Kim G, Raikhelkar J, Ota T, Song T, Juricek C, Jeevanandam V, Sayer G, Uriel N. Repeated Ramp Tests on Stable LVAD Patients Reveal Patient-Specific Hemodynamic Fingerprint. *ASAIO J*. 2017;doi: 10.1097/MAT.0000000000000705.

Highlights

Diastolic PAP remained elevated despite significant decrease in PCWP at incremental LVAD speed during ramp test in some patients

Such increase in decoupling between diastolic PAP and PCWP may indicate fixed pulmonary vasculature damage

Increase in decoupling was associated with higher HF readmission

Figure 1.
Distribution of the changes in decoupling between minimum and maximal LVAD speed

Figure 2.

Changes in dPAP, PAWP, and decoupling between minimum and maximal LVAD speed in decoupling >3 mmHg group (A) and decoupling ≤ 3 mmHg group (B) DC, decoupling $p < 0.05^*$ by paired t-test

Figure 3.

HF admission-free survival rate in decoupling >3 mmHg group and decoupling ≤3 mmHg group following ramp test

p < 0.05* by the log-rank test

Table 1.

Comparison of baseline preoperative characteristics.

	Total (N = 87)	decoupling >3 mmHg (N = 48)	decoupling 3 mmHg (N = 39)	p value
Demographics				
Age, years	60.0 ± 10.9	60.3 ± 9.2	59.6 ± 12.8	0.77
Gender (Male)	54 (62%)	30 (63%)	24 (62%)	0.55
Race (Caucasian)	51 (59%)	26 (54%)	25 (64%)	0.37
Body mass index	29.8 ± 7.2	31.1 ± 8.2	28.1 ± 5.5	0.087
Ischemic etiology	37 (43%)	18 (38%)	19 (49%)	0.20
Destination therapy	68 (78%)	38 (79%)	30 (77%)	0.50
LVAD duration before ramp test, days	494.5 ± 533.1	510.8 ± 563.6	474.5 ± 499.7	0.75
HeartMate II	54 (62%)	36 (75%)	18 (46%)	0.006*
HVAD	33 (38%)	12 (25%)	21 (54%)	-
Comorbidity				
Hypertension	48 (55%)	27 (56%)	21 (54%)	0.50
Diabetes mellitus	33 (38%)	21 (44%)	12 (31%)	0.15
Atrial fibrillation	33 (38%)	16 (33%)	17 (44%)	0.22
History of ventricular arrhythmia	18 (21%)	9 (19%)	9 (23%)	0.41
Chronic obstructive pulmonary disease	16 (18%)	10 (21%)	6 (15%)	0.36
Obstructive sleep apnea	15 (17%)	11 (23%)	4 (10%)	0.10
Echocardiography				
LVDD, cm	7.35 ± 1.14	7.51 ± 1.22	7.15 ± 1.01	0.16
Hemodynamics				
CVP, mmHg	11.4 ± 7.0	12.8 ± 7.7	9.8 ± 5.8	0.063
mPAP, mmHg	36.1 ± 11.2	37.4 ± 10.9	34.5 ± 11.4	0.25
dPAP, mmHg	27.0 ± 10.1	28.6 ± 9.6	25.1 ± 10.5	0.13
PAWP, mmHg	23.5 ± 9.1	24.4 ± 8.5	22.4 ± 9.8	0.34
CI, L/min/m ²	1.95 ± 0.67	1.85 ± 0.70	2.07 ± 0.62	0.16
PVR, WU	3.79 ± 2.94	3.91 ± 2.64	3.64 ± 3.30	0.70
PAC, mL/mmHg	1.84 ± 0.89	1.88 ± 0.89	1.79 ± 0.90	0.64
Decoupling, mmHg	3.5 ± 6.5	4.2 ± 5.3	2.7 ± 7.7	0.31

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

LVAD, left ventricular assist device; LVDd, left ventricular diastolic diameter; CVP, central venous pressure; mPAP, mean pulmonary artery pressure; PAWP, pulmonary artery wedge pressure; CI, cardiac index; PVR, pulmonary vascular resistance; PAC, pulmonary artery compliance.

* p <0.05 by chi-square test.

Table 2.

Comparison of post-LVAD clinical parameters.

	Total (N = 87)	decoupling >3 mmHg (N = 48)	decoupling 3 mmHg (N = 39)	p value
LVAD speed, rpm				
HeartMate II (N = 54)	9179.4 ± 389.1	9175.3 ± 432.1	9187.8 ± 295.6	0.91
HVAD (N = 33)	2679.4 ± 146.2	2670.0 ± 155.7	2684.8 ± 144.1	0.79
LYDD, cm	6.00 ± 1.16	6.54 ± 1.17	5.94 ± 1.00	0.002 *
CVP, mmHg	8.6 ± 5.0	10.7 ± 6.5	8.1 ± 4.7	0.041 *
mPAP, mmHg	24.5 ± 7.5	27.6 ± 7.8	26.8 ± 9.2	0.59
dPAP, mmHg	18.4 ± 6.7	20.4 ± 6.8	21.2 ± 8.8	0.93
PAWP, mmHg	13.7 ± 5.9	14.6 ± 5.7	12.5 ± 6.1	0.098
CI, L/min/m ²	2.68 ± 0.63	2.64 ± 0.68	2.73 ± 0.56	0.50
PVR, WU	2.19 ± 1.29	2.03 ± 1.19	2.39 ± 1.39	0.21
PAC, mL/mmHg	3.99 ± 1.69	3.88 ± 1.83	4.14 ± 1.49	0.49
Decoupling, mmHg	4.7 ± 4.7	3.8 ± 4.7	5.8 ± 4.4	0.10

Abbreviations as in Table 1

* p < 0.05 by unpaired t-test or Mann-Whitney U test as appropriate.

Table 3.

Comparison of changes in each clinical variable between the lowest and highest LVAD speed.

	Total (N = 87)	decoupling >3 mmHg (N = 48)	decoupling 3 mmHg (N = 39)	p value
LVDD, cm	-1.22 ± 1.32	-1.29 ± 1.60	-1.11 ± 0.86	0.60
CVP, mmHg	-1.22 ± 2.74	-1.4 ± 2.9	-1.0 ± 2.5	0.51
mPAP, mmHg	-5.5 ± 7.0	-4.8 ± 7.5	-6.3 ± 6.5	0.34
dPAP, mmHg	-4.6 ± 5.5	-3.3 ± 5.1	-6.4 ± 5.8	0.008*
PAWP, mmHg	-8.0 ± 6.6	-10.2 ± 6.5	-5.2 ± 5.5	<0.001*
CI, L/min/m ²	0.70 ± 0.83	0.81 ± 0.97	0.55 ± 0.60	0.14
Decoupling, mmHg	3.4 ± 5.3	7.2 ± 3.5	-1.2 ± 2.8	<0.001*

Abbreviations as in Table 1

* p < 0.05 by unpaired t-test or Mann-Whitney test as appropriate

Table 4.

Comparison of clinical parameters at set LVAD speed.

	Total (N = 87)	decoupling >3 mmHg (N = 48)	decoupling 3 mmHg (N = 39)	p value
LVAD speed, rpm				
HeartMate II (N = 54)	10933.3 ± 699.3	11011.1 ± 761.9	10777.8 ± 539.7	0.25
HVAD (N = 33)	3090.9 ± 158.8	3108.3 ± 173.0	3081.0 ± 153.7	0.64
LVDD, cm	5.96 ± 1.20	6.27 ± 1.30	5.59 ± 0.95	0.007*
CVP, mmHg	8.7 ± 5.0	9.8 ± 5.6	7.3 ± 3.8	0.068
mPAP, mmHg	24.8 ± 7.4	25.9 ± 7.9	23.4 ± 6.5	0.11
dPAP, mmHg	18.4 ± 6.5	19.2 ± 6.7	17.5 ± 6.1	0.21
PAWP, mmHg	13.0 ± 5.5	13.9 ± 5.5	11.8 ± 5.4	0.074
CI, L/min/m²	2.68 ± 0.60	2.72 ± 0.70	2.63 ± 0.46	0.51
PVR, WU	1.15 ± 0.93	1.07 ± 1.05	1.24 ± 0.77	0.39
PAC, mL/mmHg	3.87 ± 1.59	3.77 ± 1.54	3.99 ± 1.66	0.53
Decoupling, mmHg	5.5 ± 4.3	5.3 ± 4.5	5.7 ± 3.9	0.69

Abbreviations as in Table 1

* p < 0.05 by unpaired t-test or Mann-Whitney test as appropriate

Table 5.

Cox proportional hazards regression analyses for death or heart failure readmission.

	Univariate analyses Hazards ratio (95% CI)	p value	Multivariate analyses Hazards ratio (95% CI)	p value
Age, years	1.0 (1.0-1.0)	0.92		
Gender (Male)	1.3 (0.7-2.5)	0.45		
Race (Caucasian)	1.4 (0.9-2.0)	0.11		
Body mass index	1.0 (1.0-1.0)	0.71		
Ischemic etiology	0.7 (0.4-1.4)	0.37		
Destination therapy	1.7 (0.7-4.0)	0.26		
LVAD duration before ramp test, days	1.0 (1.0-1.0)	0.59		
HeartMate II vs. HVAD	1.5 (0.7-3.0)	0.26		
Δ decoupling >3 mmHg	3.2 (1.5-6.9)	0.002 *	2.4 (1.1-5.3)	0.032 *
LVDd at set LVAD speed, cm	1.2 (0.9-1.6)	0.18		
CVP at set LVAD speed, mmHg	1.1 (1.0-1.1)	0.024 *	1.0 (0.9-1.1)	0.72
PAWP at set LVAD speed, mmHg	1.1 (1.0-1.2)	0.008 *	1.1 (1.0-1.2)	0.11
CI at set LVAD speed, L/min/m ²	1.0 (0.6-1.8)	0.97		
PVR at set LVAD speed, WU	0.7 (0.4-1.2)	0.25		
PAC at set LVAD speed, mL/mmHg	1.0 (0.8-1.2)	0.86		
Decoupling >5 mmHg at set LVAD speed	2.9 (1.4-6.2)	0.005 *	2.2 (1.0-4.8)	0.059

Abbreviations as in Table 1

* p < 0.05 by Cox proportional hazards regression analyses