

Clinical Investigation

Echocardiographic Changes in Patients Implanted With a Fully Magnetically Levitated Left Ventricular Assist Device (Heartmate 3)

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ABSTRACT

Background: The Heartmate 3 (HM3) is a Conformité Européenne mark–approved left ventricular (LV) assist device (LVAD) with fully magnetically levitated rotor and features consisting of a wide range operational speeds, wide flow paths, and artificial pulse. We performed a hemodynamic-echocardiographic speed optimization evaluation in HM3-implanted patients to achieve optimal LV- and right ventricular (RV) shape.

Methods and Results: Sixteen HM3 patients underwent pump speed ramp tests with right heart catheterization. Three-dimensional echocardiographic (3DE) LV and RV datasets (Philips) were acquired, and volumetric (Tomtec) and shape (custom software) analyses were performed (LV: sphericity, conicity; RV: septal and free-wall curvatures). Data were recorded at up to 13 speed settings. Speed changes were in 100-rpm steps, starting at 4600 rpm and ramping up to 6200 rpm. 3DE was feasible in 50% of the patients. Mean original speed was 5306 ± 148 rpm. LV end-diastolic (ED) diameter (−0.15 ± 0.09 cm/100 rpm) and volumes (ED: 269 ± 109 mL to 175 ± 90 mL; end-systolic [ES]: 234 ± 111 mL to 146 ± 81 mL) progressively decreased as the shape became less spherical and more conical; RV volumes initially remained stable, but at higher speeds increased (ED: from 148 ± 64 mL to 181 ± 92 mL; ES: 113 ± 63 mL to 130 ± 69 mL). On average, the RV septum became less convex (bulging toward the LV) at the highest speeds.

Conclusions: LV and RV shape changes were noted in HM3-supported patients. Although a LV volumetric decrease and shape improvement was consistently noted, RV volumes grew in response to increase in speed above a certain point. A next concern would be whether understanding of morphologic and function changes in LV and RV during LVAD speed change assessed with the use of 3DE helps to optimize LVAD speed settings and improve clinical outcomes. (*J Cardiac Fail* 2019;25:36–43)

Key Words: HVAD, Heartmate 3, echocardiography, conicity, sphericity, ramp test.

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Continuous-flow left ventricular assist devices (LVADs) have become the mainstay of therapy^{1–4} in patients with advanced heart failure and are used as a bridge to transplantation and destination therapy (DT).⁵ Evidence is mounting on the survival benefit from these devices, and now attention is focused on improving pump performance by patient-specific adjustments.⁶ Furthermore, recent reports have demonstrated the occurrence of myocardial recovery during support, further evidencing the need for optimal device setting. An important goal in device optimization is to achieve maximal reverse remodeling of both left and right ventricles, which is strongly dependent on the complex interaction between the patient's pathophysiology and pump characteristics.^{7,8}

The Heartmate 3 (HM3) LVAD (Saint Jude Medical, Pleasanton, California) is a centrifugal device for

intrapericardial placement designed to improve hemocompatibility by incorporation of an optimized biomaterial interface and minimizing the effect of shear forces on blood components.⁹ The pump is a fully magnetically levitated pump that can produce a wide range of flow (2–10 L).

The first experience with HM3 was reported by Netuka et al, who summarized the short-term results of 50 patients in Europe, which led to the approval of HM3 in Europe.¹⁰ Recently, Mehra et al published the results of the short-term cohort of MOMENTUM 3, a randomized study comparing Heartmate II (HMII) and HM3, demonstrating the superiority of HM3 over HMII, mainly due to the elimination of device thrombosis in the former cohort.^{11,12} Our group reported excellent hemodynamic support achieved by the HM3 over a wide range of speeds,¹³ which appeared to be superior to the hemodynamics attained with the HMII and another centrifugal pump (HVAD).^{7,14,15}

The aim of the present study was to describe left (LV) and right (RV) ventricular echocardiographic changes across a wide spectrum of operating speeds in clinically stable HM3 patients. Accordingly, we used a standardized 3-dimensional echocardiographic (3DE) and hemodynamic ramp protocol in stable HM 3 patients to assess the effect of acute changes in LVAD speed on (1) 2-dimensional echocardiographic (2DE) parameters, (2) 3DE LV and RV size and function, and (3) 3DE-derived LV and RV shape.

Methods

In this prospective observational multicenter study, 16 consecutive clinically stable HM3 LVAD patients from the Institute for Clinical and Experimental Medicine (Prague, Czech Republic) and Hannover Medical School (Germany) were enrolled and evaluated with the use of a hemodynamic 2DE and 3DE ramp-testing protocol. These patients were supported with the HM3 as part of the Conformance Européenne (CE) mark–approved LVAD study. All ambulatory patients were electively admitted for right heart catheterization. Patients were classified as clinically stable based on the assessment of the treating cardiologist and deemed to be well supported by their device based on routine clinical assessment. All centers obtained Ethics Committee approval, and informed consents were obtained from all of the patients.

Ramp Test Protocol

All tests were performed in catheterization laboratories of the participating institutions. The overall methods used in this study for hemodynamic assessment have been detailed previously.^{16,17} The only change of the protocol included adjustments to the HM3 speed range. The lower speed limit was set at 4600 rpm and increased in 100-rpm increments up to 6200 rpm. Device parameters, including pulsatility index, pump power, and calculated pump flow, were recorded throughout each ramp test. Simultaneously, we assessed hemodynamics by means of right heart catheterization together with 2DE and 3DE parameters.^{16,18}

Speed increase was repeated until 1 of the following occurred: 1) reaching the maximum of 6200 rpm; 2) occurrence of suction events; or 3) LV end-diastolic diameter (LVEDD) decreased to <3.0 cm. 3D images were acquired at every other step when suitable acoustic windows were available.

At the conclusion of each test, the attending cardiologist reviewed the data and device speed was set at the speed wherein hemodynamic normalization was achieved, ie, pulmonary capillary wedge pressure <18 mm Hg and central venous pressure <12 mm Hg with the secondary goals of intermittent aortic valve opening and minimal mitral regurgitation (MR). To simplify pooling of the 3DE data by ramp speed, 3DE imaging steps were defined as in [Table 1](#).

3D Transthoracic Echocardiography

3D transthoracic echocardiography (TTE) LV and RV full-volume datasets were obtained at each stage of the ramp test with the use of electrocardiographic gating over 4–6 consecutive cardiac cycles during a single breath-hold (Philips iE33, transducer X5-1).¹⁹ To maximize images, both ventricles were assessed separately, including decrease of sector width and excluding the atria from the dataset to minimize depth. 3DE LV images were acquired from a standard apical 4-chamber view, and a modified apical focused RV 4-chamber view was used for RV imaging.

3D TTE datasets were analyzed with the use of commercial software (4D LV-Function and 4D RV-Function, version 2.0; Tomtec Imaging Systems, Unterschleissheim, Germany) to quantify end-diastolic (EDV) and end-systolic (ESV) volumes and ejection fraction (EF) of both ventricles. End-diastole was identified automatically by the software as the time point at which the ventricular cavity was at its largest. Analysis required manual initialization of the contours in both end-systolic and end-diastolic frames in the apical 4-, 2-, and 3-chamber views for the LV, and in the long-axis and basal, middle, and apical short-axis views for the RV. Endocardial boundaries were traced to include trabeculae and the papillary muscles in both ventricles and the moderator band in the RV cavity. 3D renderings of the LV and RV endocardial surfaces were then automatically generated and stored for input into custom software for shape analysis.

Table 1. Steps of Three-Dimensional Echocardiographic Imaging Used During Ramp Studies and the Corresponding LVAD Pump Speeds

Protocol Step	HM3 LVAD Pump Speed (rpm)
1	4600–4900
2	5000–5200
3	5300–5500
4	5600–5800
5	5900–6200

HM3, Heartmate 3; LVAD, left ventricular assist device.

Left Ventricular Shape Analysis

The 3D LV endocardial surfaces were exported as a series of unstructured meshes of connected points that were used as input to a custom software package for analysis of LV conicity and sphericity via an algorithm described in detail previously.^{20,21} Briefly, LV global shape indices were defined by measuring the degree of similarity between the signal obtained by sampling along a helical pattern on the 3D LV surface and a signal obtained by means of the same procedure from an idealized sphere or cone used as a reference. To ensure the independence of LV shape indices from LV dimensions, the reference shapes were constructed for each individual heart according to geometric properties of each individual LV (principal moments of inertia). Accordingly, the indices of sphericity and conicity assume values between 0 and 1, with higher values associated with a better similarity to the reference shape.

Right Ventricular Shape Analysis

3D RV endocardial surfaces were exported as a series of unstructured meshes of connected points that were used as input to a custom software package for analysis of regional RV curvature.²² To accomplish this, a quadratic polynomial function was fitted to the local neighborhood of each point belonging to the RV surface. This allowed computing for each point the values of curvature k_1 and k_2 , each corresponding to the inverse of the radius of the 2 circles in orthogonal planes best fitting the local surface. Then, the mean curvature, K , was obtained by averaging the above 2 curvature values for each point. Finally, to compensate for changes in RV curvature secondary to changes in RV volume, the local value of the 3D curvature K was normalized (K_n) by the value of the curvature of a sphere having the same instantaneous volume as the RV. Of note, 0 curvature indicates a flat surface and positive and negative values signify, respectively, more convexity and concavity of the surface from the perspective of a reference point located outside of the RV. Finally, the RV surface was divided into 2 distinct regions: septum and free wall. The regional 3D curvature K_n was obtained by averaging the values of all points within each region.

Data Analysis and Statistical Methods

Ramp-test parameter recordings at different speeds were entered into a spreadsheet (Excel 2010; Microsoft Corp, Redmond, Washington) and plotted with the use of either Excel or Origin (Originlab Corp, Northampton, Massachusetts) software. Slopes were calculated as previously described.²³ All statistical analyses were performed with the use of SPSS (IBM; version 22). Normally distributed continuous variables are reported as mean \pm SD, and skewed continuous data are reported as median and interquartile range. Categorical variables were summarized as frequency and percentage. The sample slopes of the ramp parameters were calculated with the use of linear regression.

Table 2. Patient Demographics (n = 16)

Age (y)	66.2 \pm 7.56
Male	11 (68.8%)
CHF ischemic etiology	5 (31.3%)
DT	11 (68.8%)
DM	5 (31.3%)
HTN	12 (75.0%)
PAD	4 (25.0%)
AFIB	6 (37.5%)
History of VT	1 (6.25%)
COPD	3 (18.8%)
BSA (m ²)	1.86 \pm 0.22
BMI (kg/m ²)	26.3 \pm 4.19
LVEDD (cm)	7.26 \pm 0.94
LVESD (cm)	6.43 \pm 1.2

CHF, congestive heart failure; DT, destination therapy; DM, diabetes mellitus; HTN, hypertension; PAD, peripheral artery disease; AFIB, atrial fibrillation; VT, ventricular tachycardia; COPD, chronic obstructive pulmonary disease; BSA, body surface area; BMI, body mass index; LVEDD, left ventricular end-diastolic dimension; LVESD, left ventricular end-systolic dimension.

Results

Baseline Characteristics

Patient characteristics are summarized in [Table 2](#). Patients were 66 ± 8 years old and mostly male (68.8%). The majority of patients were implanted for DT (68.8%). Results from the hemodynamics evaluation during the ramp test in these patients were reported previously.¹³

The average time from implantation to ramp test was 292.1 ± 100 days, with an average baseline speed of 5306 ± 148 rpm. The average maximum ramp speed achieved was 6088 ± 206 , with 15 patients (94%) reaching 6000 rpm and 11 (69%) reaching 6200 rpm.

Ramp Study Results

The mean results of the 2DE and 3DE parameters for each stage are summarized in [Tables 3–5](#). In 8 of the 16 patients (feasibility 50%), 3DE shape analysis could not be performed owing to low-quality images caused by pump-related echocardiographic artifacts, body habitus, and presence of arrhythmia, mainly atrial fibrillation. LV and RV shape analyses were performed in the remaining 8 patients. 2DE analysis was performed in the entire study group. We show a representative case of 3D endocardial surfaces of LV and RV obtained at the lowest and highest rpm ([Fig. 1](#)).

Table 3. Two-Dimensional Echocardiographic Analysis of Valvular Severity During 10 Different Speeds in Ramp Studies

Speed	AV Opening	AI	MR
Low speed	11 (69%)	0	0
High speed	2 (13%)	4 (25%)	0

AV, aortic valve; AI, aortic-valve insufficiency; MR, mitral-valve regurgitation.

Table 4. Two-Dimensional Echocardiographic Analysis of Left Ventricular Dimensions During 10 Different Speeds in Ramp Studies

Parameter	LVEDD	LVESV
Δ fastest – lowest	-1.51 ± 0.82	-1.35 ± 0.87
Δ by step at each 100 rpm	-0.17 ± 0.19	-0.15 ± 0.19
Slope	-0.14 ± 0.07	-0.12 ± 0.07

LVEDD, left ventricular end-diastolic diameter; LVESV, left ventricular end-systolic diameter.

Left Ventricle Analyses

2DE analysis depicted a decrease in LVEDD from the onset of the ramp test, with an LVEDD slope of -0.14 ± 0.07 . None of the patients had MR more than mild to moderate in severity at base speed and during the ramp test. The aortic valve (AV) was intermittently open in 11 patients at the lower speed and was completely closed in 14 patients at an average speed of 5533 rpm.

3DE analysis showed the largest LV volumes at the lowest speed (LVEDV 269 ± 109 mL and LVESV 234 ± 111 mL) and decreasing by 24 mL per 100 rpm as the speed was increased throughout the ramp study. At the highest pump speeds, reductions were observed for both LVEDV (to 175 ± 90 mL) and LVESV (to 146 ± 81 mL), with changes, respectively, of -94 ± 19 mL and -88 ± 20 mL from baseline. (Fig. 2, top). Despite these changes in volumes, the 3D LVEF did not change considerably: $15\% \pm 7\%$ at the lowest speeds with a gradual increase to $18\% \pm 5\%$ at the highest speeds (Fig. 2, bottom).

LV shape analysis at the lowest speeds showed a conicity index of 0.73 ± 0.004 and sphericity index of $0.777\% \pm 0.009\%$. Both indices changed gradually as the speed of the pump was increased during the ramp study. At the highest speed, the conicity index increased to 0.76 ± 0.004 and the sphericity index decreased to 0.72 ± 0.009 (Fig. 3).

Combined 3DE volumetric, functional, and shape analyses demonstrated that as the LVAD speed increased throughout the ramp study, the LV volumes decreased and

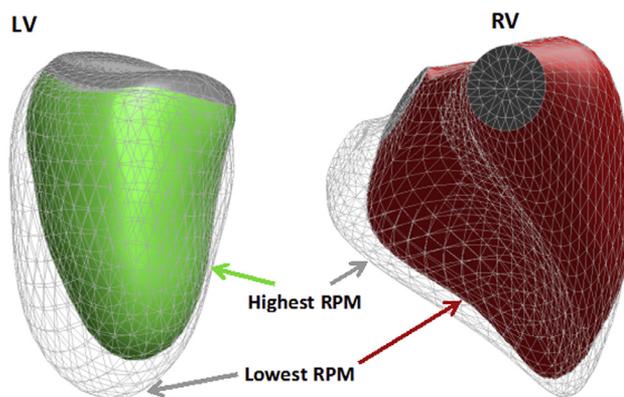


Fig. 1. 3D endocardial surfaces of the left (LV) and right (RV) ventricles obtained at the lowest and highest rpms in a representative patient with an HM3 device. Surfaces obtained at lowest rpm, shown by the gray frame for the LV and the red frame for the RV, and at the highest rpm, shown by the green frame for the LV and by the gray frame for the RV, are superimposed in each panel.

the LV shape became more conical. All of these volumetric and shape changes occurred with no obvious change in LV function.

Right Ventricle Analyses

RV volumes were mildly increased at the lowest speeds (RVEDV 148 ± 64 mL and RVESV 113 ± 63 mL) and gradually increased as the speed of the ramp test progressed: at the highest speeds the RVEDV increased to 181 ± 92 mL and the RVESV to 130 ± 69 mL (Fig. 2, top). Compared with baseline, the RVEDV change was 33 ± 21 mL and the RVESV change 17 ± 6 mL. Despite the changes in volumes, similarly to the left side, the RVEF did not change considerably: $26\% \pm 11\%$ at the lowest speeds and $30\% \pm 8\%$ at the highest speeds (Fig. 2, bottom).

At the lowest speeds the RV shape analysis showed a septal curvature index of 0.97 ± 0.059 and a free wall

Table 5. Three-Dimensional Echocardiographic Analysis During Ramp Studies

Measure	Ramp Speed Step				
	1	2	3	4	5
LVED volume (mL)	269 ± 109	249 ± 102	229 ± 89	205 ± 83	$175 \pm 89.7^*$
LVES volume (mL)	234 ± 111	215 ± 97	194 ± 92	171 ± 79	$146 \pm 81.4^*$
LVED length (mm)	9.2 ± 0.99	8.7 ± 0.82	8.5 ± 0.77	8.4 ± 0.82	8.1 ± 0.73
LVES length (mm)	8.4 ± 0.98	8.1 ± 0.89	7.9 ± 0.79	7.7 ± 0.68	7.5 ± 0.63
RVED volume (mL)	148 ± 64	143 ± 60	147 ± 55	157 ± 53	181 ± 92.2
RVES volume (mL)	113 ± 63	115 ± 59	115 ± 49	115 ± 40	130 ± 69.1
LV EF (%)	14.9 ± 7.0	15.1 ± 4.7	17 ± 7.8	18 ± 7.6	18.1 ± 5.1
RV EF (%)	25.7 ± 11.4	22.6 ± 10.6	22.7 ± 8.1	27.9 ± 6.6	30.0 ± 8.4
LV conicity	0.73 ± 0.004	0.73 ± 0.005	0.73 ± 0.006	0.75 ± 0.006	$0.76 \pm 0.004^*$
LV sphericity	0.77 ± 0.009	0.76 ± 0.010	0.77 ± 0.014	0.74 ± 0.012	$0.72 \pm 0.009^*$
RV free wall	1.21 ± 0.031	1.15 ± 0.018	1.20 ± 0.026	1.20 ± 0.019	1.25 ± 0.040
RV septal wall	0.97 ± 0.059	0.88 ± 0.036	0.87 ± 0.033	0.89 ± 0.035	0.88 ± 0.037

LV, left ventricular; RV, right ventricular; ED, end-diastolic; ES, end-systolic; EF, ejection fraction.

* $P < .01$ between highest and lowest speed.

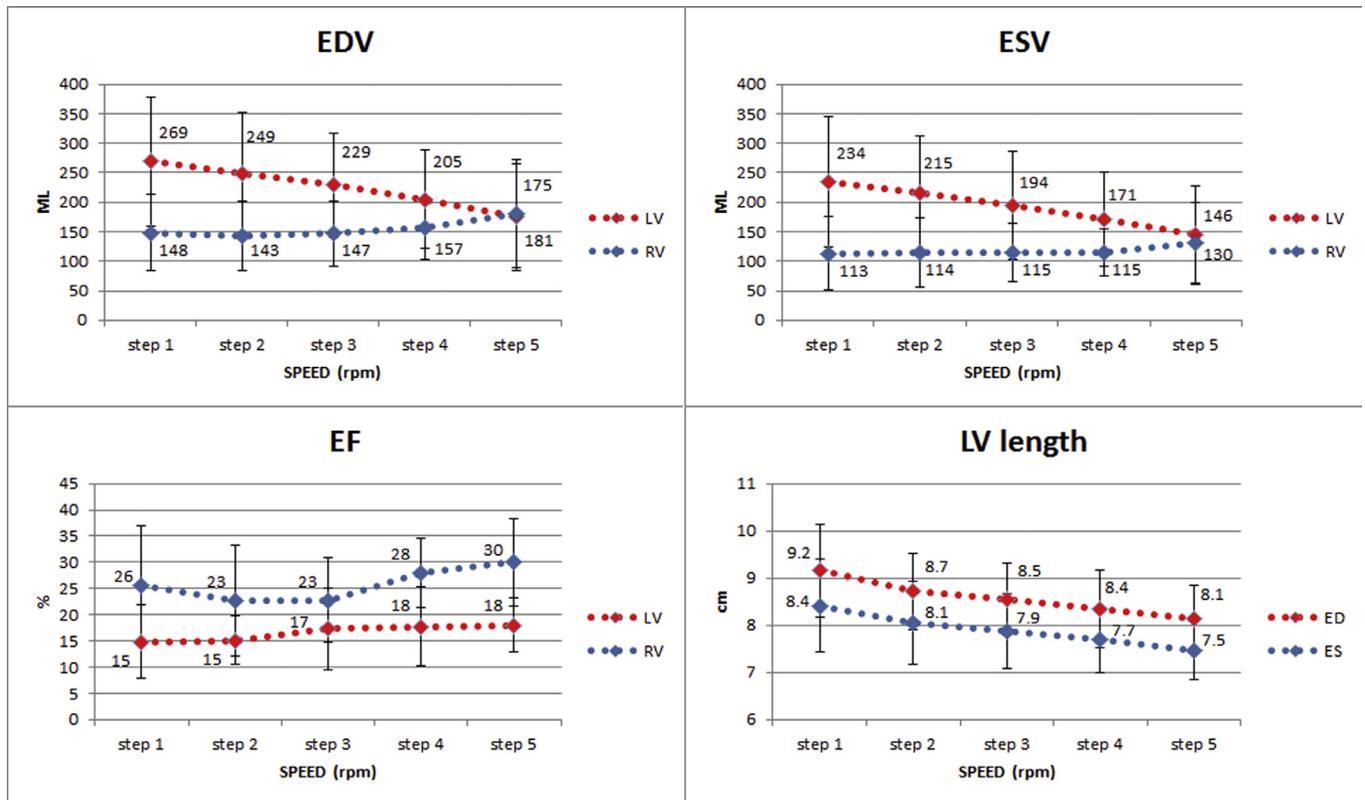


Fig. 2. 3D left ventricular (LV) volumes decreased progressively as speed increased (top, red line). Average RV volumes did not change significantly until step 4, when volumes increased significantly (top, blue line). EDV, end-diastolic volume; ESV, end-systolic volume. LV and right ventricular (RV) ejection fraction (EF) did not change significantly (bottom left). LV length decreased progressively as speed increased (bottom right).

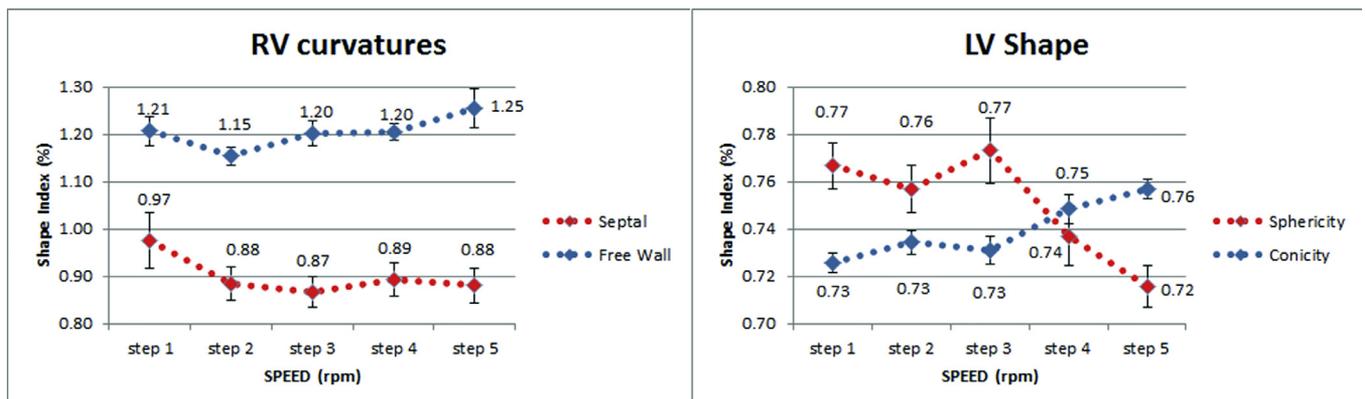


Fig. 3. 3D left ventricular (LV) shape analysis showed a progressive decrease in the sphericity index (right, red line) and an increase in conicity index (right, blue line). The interventricular septum (left, red line), became more flat, bulging into the LV when comparing the lowest with the highest speed settings. The right ventricular (RV) free wall became more curved at increased speeds.

curvature of 1.21 ± 0.031 . Both indices gradually changed as the speed increased during the ramp study. At the highest speeds, the septal curvature index decreased to 0.88 ± 0.037 and the free wall curvature index increased to 1.25 ± 0.040 (Fig. 3).

During the ramp study, the RV volumes increased. These changes were associated with an augmentation of RV free wall and a reduction of septal curvatures. All of these geometric RV changes happened with no obvious change in

RV function. In contrast to the LV, where changes in shape predominantly occurred at higher speeds, RV changes occurred progressively throughout the ramp study.

Discussion

HM 3 is a novel intrapericardial fully magnetic levitated centrifugal device approved for use in Europe¹⁰ and currently being evaluated in the United States by the

MOMENTUM 3 study.¹¹ In the present study, we explored the impact of increasing LVAD speeds during echocardiographic-hemodynamic ramp studies on the RV and LV with the use of 3DE-based volume and shape analysis. Specifically, the aim of this study was to examine the effect of speed changes on cardiac morphology and function in patients supported with the HM3.

The main findings of the study are: (1) LVEDD and LVEDV considerably decrease in response to increases in pump speed; (2) although the AV was intermittently open in 69% of the patients at baseline speeds, it was closed in 87% at the highest ramp speed; (3) no MR was seen, even at the lowest speeds; (4) the LV becomes more conical with an increase in speed, (5) RV volumes increased following LVAD speed augmentation; and (6) septal curvature became less convex and RV free wall curvature increased with increase in LVAD speed.

In this study, we demonstrated that with the use of the HM3, different LV and RV morphologic changes occur in patients. LV volumes decrease and the cavity becomes less spherical and more conical as LV unloading augments with higher pump speeds. However, with speed increases beyond 5600 rpm, morphologic cardiac changes were affected by increases in RV volumes, with the RV septum becoming less convex as it bulges into the LV, while at the same time the RV free wall became more curved. Although no direct comparisons with previously published analysis can be performed, similar general findings were found when observing changes that occur during ramp studies in patients with older LVAD pumps.²⁴

Although the present study includes the same population as in our previous publication,¹³ that previous article focused on invasive hemodynamic evaluation. The present manuscript describes the 2DE and 3DE analyses which were not included in our previous publication and are new data that were never reported. This novel echocardiographic analysis is unique owing to the volumetric and shape measurements, and it provides further understanding of the hemodynamics effects of the HM3 pump, for both the LV and the RV.

Different Behavior Between HM3 and HMII Pumps

Both HM3 and HMII pumps are continuous-flow devices. The HM3 pump is a centrifugal device, where blood flow is directed perpendicularly to the rotation axis. In contrast, the HMII pump is an axial-flow device, where blood outflow is directed parallel to the axis of the rotor. Previous studies based on 2DE measurements have shown that HMII results in more LV diameter reduction with increasing LVAD speed compared with HM3.^{25,26} However, our recent publication demonstrated that HM3-supported patients have excellent hemodynamic support at the average speed compared with what was previously observed in ramp studies with HMII.¹⁴

A possible explanation for the different changes in LV and RV shape seen in this study during unloading is the

different pump location. The HM3 pump is inserted at the LV apex in the pericardial space, thereby resulting in less deformation at the base of the heart due to the limited pericardial space. In contrast, the HMII pump is located subdiaphragmatically, likely resulting in inferior displacement of the LV apex because the inflow cannula acts as a lever.

Different Behavior Between HM3 and HVAD Pumps

Similarly to the HM3, the HVAD is a centrifugal device implanted in the intrapericardial space. However, the HM3 design allows higher LV inlet suction, meaning that at higher speeds, it can unload the LV more forcefully. This probably contributes to the changes in LV and RV volumes and leftward shift of the interventricular septum at higher speeds.

Right Ventricular Changes at Higher LVAD Speeds

RV failure remains a key adverse effect in patients supported with LVADs, affecting both survival and quality of life.^{11,27} The ability to measure RV and LV volumes and shape during incremental ramp-test speeds may enable appreciation of the counterbalancing effects of LVAD speed on RV geometry. Increasing LVAD speed leads to decreased pulmonary capillary wedge pressure,¹³ thereby reducing RV afterload and facilitating RV function.

However, speed augmentation can also result in septal shift toward the LV, which results in unfavorable RV geometry. Moreover, at higher LVAD speeds, the RV seems to start failing, as evidenced by increased RV volumes and less favorable RV geometry. Nevertheless, at low-to-moderate LVAD speeds, these effects counterbalance each other, without negative effects on RV size and function.

Study Limitations

This was a multicenter nonrandomized study with a small number of patients. Because of small sample size, we could not perform statistical comparisons, including generalized estimating equation analyses, with sufficient statistical power. In addition, 3DE analysis was feasible in only 50% of the patients undergoing LVAD ramp studies. We considered changes in LV and RV geometry only in response to acute changes in LVAD speed. Chronic geometric responses to such changes may be different, and the long-term clinical consequences of observed changes remain unknown. Furthermore, we did not provide any associating clinical outcomes, and the prognostic implication of this modality remains uncertain. Nevertheless, we think that this study is a proof of concept, and a next concern would be whether 3DE assessment helps to optimize LVAD speed settings and improve clinical outcomes in HM3 patients, which should be investigated in larger-scale randomized control trials.

Conclusion

Although the use of 3DE analysis for patients undergoing echocardiography-guided ramp studies for LVAD speed optimization is technically challenging and time consuming, the present study provides valuable insight on the impact of HM3 speed settings on the volumes and shape of both ventricles. A next concern would be whether understanding of morphologic and function changes in LV and RV during LVAD speed change, assessed with the use of 3DE, helps to optimize LVAD speed settings and improve clinical outcomes.

Clinical Perspectives

Competency in Medical Knowledge

Most of the patients supported with HM3 had normal hemodynamics in a speed range of 5200–5600 rpm with significant improvement in LV size and shape however with increase in RV size and change in geometry.

Disclosures

Dr Uriel is a consultant for Saint Jude Medical and Medtronic and serves as the national principal investigator for the MOMENTUM 3 study with no financial benefits. Dr Maly is a consultant for Saint Jude Medical. Dr Poornima Sood and Gerald Heatley are employed by Saint Jude Medical. Dr Schmitto is a consultant for Heartware and Saint Jude Medical and serves as the national principal investigator for the CE HM3 study with no financial benefits. Dr Netuka is a consultant for Saint Jude Medical and serves as the national principal investigator for the CE HM3 study with no financial benefits. Dr Lang is a member of the Philips Healthcare speaker bureau and has received research equipment grants from Philips. The other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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References

1. Aaronson KD, Slaughter MS, Miller LW, et al. Use of an intrapericardial, continuous-flow, centrifugal pump in patients awaiting heart transplantation. *Circulation* 2012;125:3191–200.
2. Kirklin JK, Naftel DC, Pagani FD, et al. Sixth INTERMACS annual report: a 10,000-patient database. *J Heart Lung Transplant* 2014;33:555–64.
3. Slaughter MS, Bartoli CR, Sobieski MA, et al. Intraoperative evaluation of the Heartmate II flow estimator. *J Heart Lung Transplant* 2009;28:39–43.
4. Slaughter MS, Rogers JG, Milano CA, et al. Advanced heart failure treated with continuous-flow left ventricular assist device. *N Engl J Med* 2009;361:2241–51.
5. Feldman D, Pamboukian SV, Teuteberg JJ, et al. The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support: executive summary. *J Heart Lung Transplant* 2013;32:157–87.
6. Hasin T, Marmor Y, Kremers W, et al. Readmissions after implantation of axial flow left ventricular assist device. *J Am Coll Cardiol* 2013;61:153–63.
7. Uriel N, Sayer G, Addetia K, et al. Hemodynamic ramp tests in patients with left ventricular assist devices. *JACC Heart Fail* 2016;4:208–17.
8. Burkhoff D, Sayer G, Doshi D, Uriel N. Hemodynamics of mechanical circulatory support. *J Am Coll Cardiol* 2015;66:2663–74.
9. Netuka I, Kvasnicka T, Kvasnicka J, et al. Evaluation of von Willebrand factor with a fully magnetically levitated centrifugal continuous-flow left ventricular assist device in advanced heart failure. *J Heart Lung Transplant* 2016;35:860–7.
10. Netuka I, Sood P, Pya Y, et al. Fully magnetically levitated left ventricular assist system for treating advanced HF: a multicenter study. *J Am Coll Cardiol* 2015;66:2579–89.
11. Mehra MR, Naka Y, Uriel N, et al. A fully magnetically levitated circulatory pump for advanced heart failure. *N Engl J Med* 2016.
12. Heatley G, Sood P, Goldstein D, et al. Clinical trial design and rationale of the Multicenter Study of Maglev Technology in Patients Undergoing Mechanical Circulatory Support Therapy With Heartmate 3 (MOMENTUM 3) investigational device exemption clinical study protocol. *J Heart Lung Transplant* 2016;35:528–36.
13. Uriel N, Adatya S, Maly J, et al. Clinical hemodynamic evaluation of patients implanted with a fully magnetically levitated left ventricular assist device (Heartmate 3). *J Heart Lung Transplant* 2017;36:28–35.
14. Lalonde SD, Alba AC, Rigobon A, et al. Clinical differences between continuous flow ventricular assist devices: a comparison between Heartmate II and Heartware HVAD. *J Card Surg* 2013;28:604–10.
15. Giridharan GA, Koenig SC, Soucy KG, et al. Left ventricular volume unloading with axial and centrifugal rotary blood pumps. *ASAIO J* 2015;61:292–300.
16. 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* 2012;60:1764–75.
17. Kato TS, Colombo PC, Nahumi N, et al. Value of serial echo-guided ramp studies in a patient with suspicion of device thrombosis after left ventricular assist device implantation. *Echocardiography* 2014;31:E5–9.
18. 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* 2015;21:785–91.
19. Lang RM, Badano LP, Tsang W, et al. EAE/ASE recommendations for image acquisition and display using three-dimensional echocardiography. *J Am Soc Echocardiogr* 2012;25:3–46.
20. Maffessanti F, Caiani EG, Tamborini G, et al. Serial changes in left ventricular shape following early mitral valve repair. *Am J Cardiol* 2010;106:836–42.
21. Maffessanti F, Lang RM, Corsi C, Mor-Avi V, Caiani EG. Feasibility of left ventricular shape analysis from transthoracic real-time 3-D echocardiographic images. *Ultrasound Med Biol* 2009;35:1953–62.
22. Addetia K, Maffessanti F, Yamat M, et al. Three-dimensional echocardiography-based analysis of right ventricular shape in pulmonary arterial hypertension. *Eur Heart J Cardiovasc Imaging* 2016;17:564–75.
23. Nahumi N, Jorde U, Uriel N. Slope calculation for the LVAD ramp test. *J Am Coll Cardiol* 2013;62:2149–50.

24. Addetia K, Uriel N, Maffessanti F, et al. 3-dimensional morphological changes in left and right ventricles during left ventricular assist device ramp studies. *JACC Cardiovasc Imaging* 2016. In press.
25. Morgan JA, Paone G, Nemei HW, et al. Impact of continuous-flow left ventricular assist device support on right ventricular function. *J Heart Lung Transplant* 2013;32:398–403.
26. Sauer AJ, Meehan K, Gordon R, et al. Echocardiographic markers of left ventricular unloading using a centrifugal-flow rotary pump. *J Heart Lung Transplant* 2014;33:449–50.
27. Rich JD, Gosev I, Patel CB, et al. The incidence, risk factors, and outcomes associated with late right-sided heart failure in patients supported with an axial-flow left ventricular assist device. *J Heart Lung Transplant* 2017;36:50–8.