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ORIGINAL RESEARCH ARTICLE

Validation of non-invasive ramp testing for HeartMate 3

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Abstract

Aims Ramp testing in the postoperative period can be used to optimize left ventricular assist device (LVAD) speed for optimal left ventricular (LV) unloading. We tested the hypothesis that a non-invasive echocardiographic ramp test post-HeartMate 3 implantation improves LV unloading immediately after and 1–3 months after as compared with before the test. We also tested a secondary hypothesis that speed adjustments during echocardiography-guided ramp testing do not worsen right ventricular (RV) function immediately after and 1–3 months after.

Methods and results We retrospectively reviewed data from patients who underwent an echocardiographic ramp test. A total of 14 out of 19 patients were clinically stable and were enrolled. Adequate LV unloading was defined as no more than mild mitral regurgitation, and intermittent aortic valve (AV) opening or closed AV, and reduction of left ventricular end-diastolic diameter (LVEDD); and for the follow-up measurement, decreased NT-proBNP. Median (interquartile range) time from implantation to ramp test was 27 (16; 56) days, and median time from ramp test to follow-up echocardiography was 55 (47; 102) days. Median LVAD speed achieved during ramp testing was 5550 (5375; 6025) revolutions per minute (rpm), and median final LVAD speed was 5200 (5000; 5425) rpm. Ramp testing resulted in final LVAD speed increase in 11 (79%) patients and a median net change of 200 (200; 300) rpm. Speed adjustments after ramp testing resulted in improved LVAD unloading that was achieved in additional 3 (21%) patients who were not originally optimized. RV function did not worsen significantly during ramp testing or at final LVAD speed.

Conclusions The echocardiographic ramp test allowed LVAD speed adjustment and optimization and improved LV unloading during ramp testing and at final speed with no evidence of worsening of RV function.

Keywords HM3; LVAD; Ramp test

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Introduction

The use of left ventricular assist devices (LVADs) in advanced heart failure (HF) has increased during the last decade both as bridge to transplantation and destination therapy.[1–3] LVADs improve survival, functional capacity, and quality of life in appropriately selected HF patients.[4–6] However, LVAD technology is still challenged by infection, right ventricular (RV) failure, and haemocompatibility-related adverse events (HRAEs) of thrombosis, stroke, and bleeding[7–9] despite the advances in bioengineering and the introduction of more haemocompatible devices; namely, HeartMate 3 (HM3) LVAD (Abbott, Lake Bluff, IL, USA).[10]

The current focus of research in the area of LVADs has shifted towards the identification of strategies to reduce HRAEs, improve quality of life, and to decrease cost of care.[11–13] A key element is to improve postoperative management and optimize pump speed in order to achieve optimal haemodynamics and adequate left ventricular (LV) unloading and thus increase the chance to reduce adverse events, improve exercise capacity, and potentially enhance recovery rate.[14,15]

In 2012, Uriel and colleagues developed a novel echocardiography-guided ramp test for speed optimization by assessing the impact of acute changes in LVAD speed on LV unloading and haemodynamics[16]; however, the current echocardiography guidelines do not recommend the echocardiography-guided ramp test as a standard protocol for postoperative follow-up because of lack of evidence of impact on clinical outcomes.[17] The European Association for Cardio-Thoracic Surgery guidelines mention ramp testing to assess recovery and potential pump thrombosis but not as a routine test.[2] The International Society of Heart and Lung Transplantation guidelines have only few specific recommendations regarding LVAD speed optimization, and there are still significant differences in assessment and management of LVADs between different hospitals.[18]

On the other hand, an invasive haemodynamic ramp test with right heart catheterization appears to increase the likelihood of achieving optimal haemodynamics and reduce readmission rates,[12] reduce HRAEs,[19] and improve functional capacity assessed by 6 min walk distance.[20] However, whether to routinely use the echocardiography-guided ramp test or invasive haemodynamic ramp test remains controversial, and there is an ongoing trial (The Ramp-it-Up study, Unique identifier: NCT03021239, https://www.clinicaltrials.gov) that is addressing this question by randomizing patients to speed optimization using either echocardiography or invasive haemodynamic catheterization. It is also unknown whether patients optimized with the ramp test remain optimized at the time of follow-up. Finally, the scant published data have not assessed the ramp test in patients operated with the increasingly used HM3.

In this pilot study, we tested the hypothesis that an echocardiography-guided HM3 LVAD ramp test improves LV unloading immediately after and 1–3 months after a ramp test as compared with before the test. We also tested a secondary hypothesis that the echocardiography-guided ramp test optimize LVAD speed and LV unloading without worsening RV function immediately after and 1–3 months after.

Materials and methods

Study population

We retrospectively reviewed data from patients followed at the Karolinska University Hospital after HM3 implantation between December 2017 and April 2019, who underwent an echocardiographic ramp test before discharge or as outpatient in the early postoperative phase. The test was performed in clinically stable and ambulatory patients with no inotropic or vasopressor therapy, based on symptoms and clinical assessment of the treating cardiologist. Of 19 patients who received HM3, 14 were included in the analysis. Five patients were not examined with ramp test because of a suction event during speed optimization before ramp testing or clinical deterioration and death or the need for biventricular support with two HM3.

Echocardiographic examination

Echocardiographic examinations were performed according to a fixed protocol (described in the Appendix) using either ViVid 7 or E9 (GE Healthcare, Horten, Norway) or Philips (Medical Systems, Amsterdam, Netherlands) ultrasound machines. The 2D echocardiographic variables were collected before implantation, pre-RAMP test, during ramp testing, and at the time of follow-up echocardiography as detailed in the current guidelines.[17,21] In summary, LV diastolic and systolic dimensions, volumes, and function were assessed. LV end-diastolic diameter (LVEDD) and end-systolic diameter (LVESD) were measured perpendicular to the LV long axis at the level of the mitral valve leaflet tips in the parasternal long-axis view. RV dimensions and function were evaluated by: (i) RV end-diastolic diameter (RVEDD), (ii) tricuspid annular plane systolic excursion (TAPSE), and (iii) fractional area change measured as difference between diastolic and systolic RV area divided by diastolic RV area and expressed as percentage. Quantification of the degree of aortic, mitral, and tricuspid regurgitation (TR) was performed according to the current criteria for the evaluation of valvular regurgitation.[22,23]

RV systolic pressure (RVSP), calculated using the TR maximal jet velocity and an estimation of right atrial pressure based on inferior vena cava (IVC) diameter and collapsibility were reported when a TR Doppler velocity envelope was present. At pre-RAMP, during ramp testing, and at follow-up echocardiographic examinations, M-mode recording through aortic valve (AV) cusps was used to sample at least three beats in the parasternal long- and short-axes views to assess the frequency of AV opening. AV opening was described as closed all the time, open all the time, open intermittently, or not visualized. When the AV is not visualized, the patient is considered to have a negative outcome. Moreover, the HM3 inflow cannula and outflow graft were visualized and flow velocities were measured when possible. All echocardiographic examinations were performed by experienced in LVAD imaging echocardiographers (M. E. and E. M.). The echocardiographic measurements during the ramp test were performed online to make it possible for the cardiologist to optimize LVAD speed immediately after the test. For the purpose of this study one non-blinded cardiologist (E. N.) reviewed the measurements from all echocardiographic examinations and constructed a database.

Adequate LV unloading was defined as no more than mild mitral regurgitation (MR), *and* intermittent AV opening or closed AV, and reduction in LVEDD, and for the follow-up measurement, *also* decreased N-terminal pro brain natriuretic peptide (NT-proBNP). Worsening RV function was defined as an increase in RVEDD *or* increase in TR or reduction in TAPSE or an increase in central venous pressure (CVP) (judged by IVC size and collapsibility) and, for the follow-up assessment, an increase in diuretic dose.

Ramp test protocol

Patients underwent an echocardiography-guided ramp test performed by one of two experienced echocardiographers and in the presence of a cardiologist and LVAD-coordinator at the Department of Clinical Physiology. The protocol was similar to those previously reported for HM3,[8] however, the ramp test was considered completed once the upper limit speed decided by the attending cardiologist was reached even if the maximum speed limit of 6200 revolutions per minute (rpm) was not achieved. Criteria for stopping the ramp test were LVEDD being less than 30 mm, suction events, or occurrence of frequent ventricular ectopic beats. LVAD speed was increased by 100 rpm increments at 1 min intervals. Echocardiographic images were acquired; blood pressure was measured in a brachial artery by Doppler device. LVAD device parameters, including pump power, pulsatility index, and calculated pump flow were assessed at each step. Based on the results of the test, an optimal LVAD speed (goal speed) was set according to the current recommendations to adequately unload the LV while maintaining minimal/mild MR (Class of recommendation I, level of evidence C), intermittent AV opening to prevent development of aortic regurgitation (Class of recommendation IIB, level of evidence B),[18] and to avoid worsening of RV function. A direct and gradual rpm increase under a period of few weeks was the strategy we had to reach the final LVAD speed.

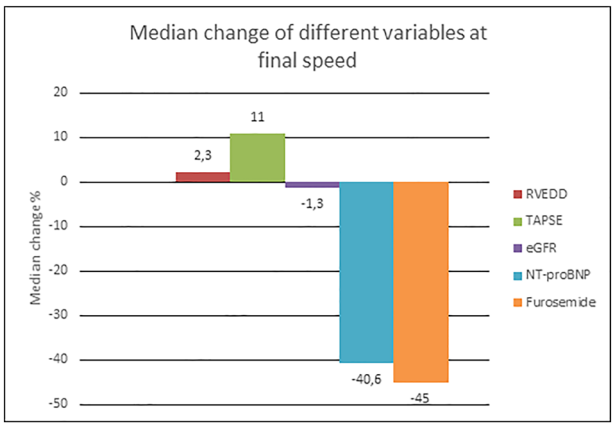
Ethics

This retrospective study complies with the Declaration of Helsinki and was approved by the regional ethical review board (Dnr2016/2576-32). Individual patient consent was not required or obtained because the study was a retrospective analysis of available data from patients with LVADs.

Statistical analysis

Statistical analysis was performed using SPSS version 23.0 (SPSS Inc., Chicago, IL, USA). Continuous variables are shown as median and interquartile range and categorical variables are shown as number (*n*) and percentages. The Wilcoxon's paired test was used to compare median values before and after ramp test. A two-sided *P*-value of <0.05 was considered statistically significant.

Figure 1 Median change of RVEDD, TAPSE, eGFR, NT-proBNP, and, and furosemide dosage at final follow-up LVAD compared with pre-RAMP pump speed.



Results

Baseline characteristics at implantation

Baseline characteristics at the time of LVAD implantation are shown in *Table 1*. Out of 19 patients implanted with an HM3, 14 patients were included in the study; the remaining 5 patients did not have an ramp test performed or were not discharged alive. 93% were men; median (interquartile range) age was 49 (41; 59) years; median LVEF was 16 (14; 20) %; median LVEDD was 67 (61; 77) mm; median TAPSE was 13 (13; 20) mm, median estimated glomerular filtration rate (eGFR) was 56 (38; 78) mL/min/1.73 m^2, and median NT-proBNP 4325 (2650; 6408) ng/L. Eight patients (57%) had moderate to severe MR. Dilated cardiomyopathy was the main underlying cause of HF and accounted for 57% of all causes and 64% had INTERMACS III. The indications for LVAD were destination therapy (7%), bridge to transplantation (43%), and bridge to decision (50 %).

Pre-RAMP characteristics

Intraoperatively, the patients were titrated to median LVAD speed of 4800 (4500; 4850) rpm that post-operatively was gradually increased during the time preceding the ramp test to 4950 (4875; 5225) rpm as depicted in *Tables 2* and *3*. Median time from implantation to the ramp test was 27 (16;

Table 1 Pre-implant baseline clinical characteristics; median (interquartile range) and n (%).

Demographics (*n* = 14)	
Age (years)	49 [41;59]
Gender (male)	13 (93)
Medical history	
Diabetes mellitus	3 (21)
Hypertension	2 (14)
Atrial fibrillation/flutter	8 (57)
Hyperlipidemia	4 (29)
Functional status at implantation	
NYHA III	10 (71)
NYHA IV	4 (29)
INTERMACS 2	5 (36)
INTERMACS 3	9 (64)
Heart failure aetiology	
Ischemic cardiomyopathy	2 (14)
Dilated cardiomyopathy	8 (57)
Other causes	4 (29)
LVAD indication	
DT	1 (7)
BTT	6 (43)
BTD	7 (50)
Echocardiographic measurements	
LVEF (%)	16 [14;20]
LVEDD (mm)	67 [61;77]
RVEDD (mm)	48 [45;52]
TAPSE (mm)	13 [10;20]
RVSP (mmHg)	45 [33;56]
Treatment	
ARB/ACE-I/ARNI	11 (79)
Beta blocker	13 (93)
MRA	8 (57)
Loop diuretic	14 (100)
Calcium channel blockers	0 (0)
ICD/CRT-D	11 (79)
Laboratory	
Haemoglobin (g/L)	141 [137;153]
NTproBNP (ng/L)	4325 [2650;6408]
eGFR (mL/min/1.73m^2)	35 [30;54]

ACE-I, angiotensin converter enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor; BTD, bridge to decision; BTT, bridge to transplantation; CRT, cardiac resynchronization therapy; DT, destination therapy; eGFR, estimated glomerular filtration rate; ICD, implantable cardioverter defibrillator; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; MRA; mineralocorticoid receptor antagonist; NT-proBNP, N-terminal pro brain natriuretic peptide; NYHA, New York Heart Association; RVEDD, basal end-diastolic right ventricular diameter; RVSP, right ventricular systolic pressure; TAPSE, tricuspid annular plane systolic excursion.

56) days. Median pre-RAMP LVEDD was 58 (55; 70) mm; median RVEDD 42 (40; 48) mm, and median TAPSE 8 (6.5; 9.5) mm. Adequate LV unloading was present in only 6 (43%) patients out of 14 patients at pre-RAMP when all the three criteria for LV unloading were applied (*Table 4*).

LV unloading and RV function during ramp testing

The median upper LVAD speed achieved during ramp testing (RAMP-High) was 5550 (5375; 6025) rpm, which was significantly higher than pre-RAMP LVAD speed ($P < 0.001$) (*Tables 2* and *3*). Increases in LVAD speed were associated with a significant reduction of LVEDD to 53 (46; 63) mm ($P < 0.001$) in 13 (93%) patients (one patient remained unchanged), despite the fact that maximum speed limit was not achieved. *Table 4* demonstrates the impact of acute changes in LVAD speed on LV unloading where 10 (71%) patients had adequate LV unloading at the highest LVAD speed (RAMP-High) when all the three criteria for LV unloading were applied. (out of 14 patients, 1 patient no reduction of LVEDD, 1 patient with moderate MR, 1 patient with open AV all the time, and 1 patient AV not visualized).

RV function did not worsen significantly, and no significant changes in RVEDD, TAPSE, CVP, and RVSP were observed at RAMP-High. However, seven (50%) patients had increased TR severity at RAMP-High (only one out of seven increased to severe TR). *Tables 3* and *4* and *Figure3* illustrate the acute impact of rpm changes on LV unloading and RV function. Ramp testing resulted in direct LVAD speed increase in 13 (93%) patients with a median speed change of 100 (100–200) rpm.

LV unloading and RV function at final LVAD speed (speed at follow-up)

Among patients who underwent the ramp test, one patient had a transplant before doing follow-up echocardiographic examination, and this patient was excluded from echocardiographic analysis at final LVAD speed. Median time from ramp test to follow-up echocardiography was 55 (47; 102) days. The median LVAD speed at the time of follow-up echocardiography was 5200 (5000; 5425) rpm, which was significantly higher than pre-RAMP LVAD speed ($P = 0.001$) but lower than goal rpm which was 5375 (5100; 5700) rpm. Ramp testing resulted in final follow-up LVAD speed increase in 11 (79%) patients and a median net change at the time of follow-up echocardiography of 200 (200–300) rpm. *Figure1* illustrates the median change of different study variables at final follow-up LVAD speed compared to pre-RAMP pump speed.

Increases in LVAD speed were associated with a reduction of LVEDD to 57 (49–62) mm, but the reduction was not significant ($P = 0.125$) compared with pre-RAMP, despite a significantly higher final follow-up LVAD speed (*Figure2*).

Adequate LV unloading was achieved in six (46%) patients (five out of six patients had increased speed between 100–300 rpm at final LVAD speed compared with pre-RAMP speed, one patient had no speed change), when the three echocardiographic criteria for LV unloading were applied at the time of follow-up, and in four (31%) patients when all four criteria (including N-terminal pro BNP) were applied [all of them had increased rpm 100–300 at final speed compared with pre-RAMP (*Table 4* and *Figure 3*)]. In summary, three patients who were adequately unloaded at pre-RAMP LVAD speed

Table 2 Direction of LVAD speed adjustment after ramp testing; median (interquartile range) and n (%).

Pre-RAMP LVAD duration (days)	27 [16;56]
Days between ramp and follow-up echocardiography	55 [47;102]
Intraoperative pump speed (rpm)	4800 [4500;4850]
Pre-RAMP pump speed (rpm)	4950 [4875;5225]
Highest pump speed at ramp (rpm)	5550 [5375;6025]
Achieved pump speed at follow-up echocardiography (rpm)	5200 [5000;5425]
Goal pump speed according to ramp (rpm)	5375 [5100;5700]
Direct LVAD speed change after ramp (rpm)	100 [100;200]
Net LVAD speed change at follow-up echocardiography (rpm)	200 [200;300]
Direct changes in LVAD speed after ramp test	
Increased	13 (93)
Unchanged	1 (7)
Decreased	0 (0)
Net changes in LVAD speed between ramp test and follow-up echocardiography	
Increased	11 (79)
Unchanged	3 (21)
Decreased	0 (0)

LVAD, left ventricular assist device; rpm, revolutions per minute.
Ramp test data and direction of LVAD speed changes in the short- and long-term settings.

Table 3 Characteristics before ramp, during ramp testing, and at final follow-up LVAD speed; median (interquartile range).

				P-value	
	Pre-RAMP	RAMP-High	Final speed at follow-up	RAMP-High vs. Pre-RAMP	Final Speed vs. Pre-RAMP
Pump speed (rpm)	4950 (4875;5225)	5550 (5375;6025)	5200 (5000;5425)	<0.001	0.001
LVEDD (mm)	58 (55;70)	53 (46;63)	57 (49;62)	<0.001	0.125
RVEDD (mm)	42 (40;48)	46 (42;50)	46 (40;47)	0.391	0.625
TAPSE (mm)	8 (6.5;9.5)	8 (6.5;10.5)	8 (7.5;10)	0.425	0.200
CVP (mmHg)	5 (4;10)	5 (5;11)	5 (5;10)	0.437	1.000
RVSP (mmHg)	24 (20;31)	23 (21;30)	26 (23;30)	0.344	0.180
Furosemide (mg)	120 (80;260)		80 (20;220)		0.072
eGFR (mL/min/1.73m^2)	45 (31;71)		52 (32;66)		0.855
NTproBNP (ng/L)	2320 (1845;3593)		1310 (812;2653)		0.002

CVP, central venous pressure; eGFR, Estimated glomerular filtration rate; LVEDD, left ventricular end-diastolic diameter; rpm, Revolutions per minute; RVEDD, basal end-diastolic RV diameter; RVSP; right ventciular systolic pressure, TAPSE, Tricuspid annular plane systolic excursion.

Table 4 LV unloading pre-RAMP, RAMP-High, and final follow-up LVAD speed

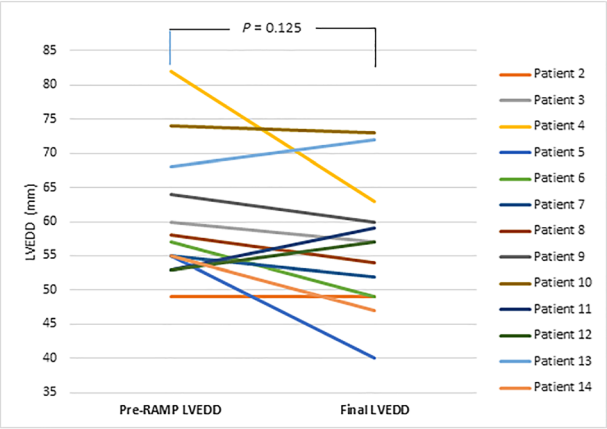
LVAD speed	Number of patients	Reduced LVEDD	≤ mild MR	Closed or intermittently opened AV	All three criteria	Reduced NTproBNP	All four criteria
Pre-RAMP vs. pre-implant	14	13 (93%)	13 (93%)	8 (57%)	6 (43%)	11 (79%)	5 (36%)
RAMP-High vs. pre-RAMP	14	13 (93%)	13 (93%)	12 (86%)	10 (71%)		
Final vs. pre-RAMP	13	9 (69%)	13 (100%)	7 (54%)	6 (46%)	12 (86%)	4 (31%)

AV, aortic valve; LVAD, left ventricular assist device; LVEDD, left ventricular end-diastolic diameter; MR, mitral regurgitation, NT-proBNP, N-terminal pro brain natriuretic peptide.
LV unloading at pre-RAMP, RAMP-High, and final LVAD speed, *n* (%). Reduced NT-proBNP was calculated in 14 patients.

remained unloaded at follow-up, and another three patients become adequately unloaded using the echocardiographic LV unloading criteria.

RV function did not worsen significantly, and only one (8%) patient had increased TR severity at the time of follow-up echocardiography (*Table 3* and *Figure 3*). No significant

Figure 2 Individual LVEDD at pre-RAMP and final follow-up LVAD speed.



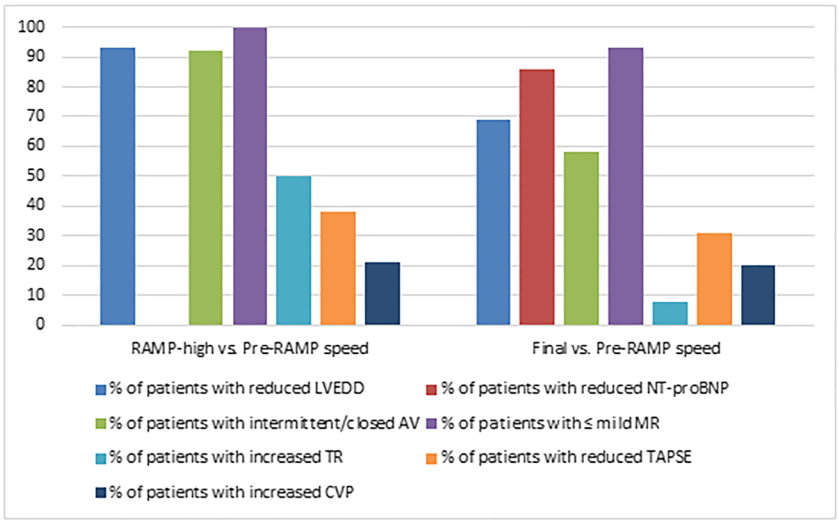
changes in RVEDD, TAPSE, CVP, and RVSP were seen at the time of follow-up as depicted in *Table 3*. Notably, there were changes in HF therapy in four patients during the time between ramp test and follow-up echocardiography. One patient was medically optimized by adding an angiotensin receptor blocker, another patient by adding a mineralocorticoid receptor antagonist, and a third patient by adding both. The mineralocorticoid receptor antagonist was stopped in the fourth patient because of renal function; however, his furosemide dose was reduced by 50%. Additionally, there was a reduction in daily furosemide dose of the whole cohort from 120 (80–260) mg to 80 (20–220) mg, but the decrease was not statistically significant (P = 0.070).

Discussion

We studied the impact of non-invasive ramp test guided optimization of LVAD speed on LV unloading and RV function in patients with a HM3 LVAD. The main findings of this study are (i) in clinically stable patients, baseline pre-RAMP LVAD speeds based on clinical assessment alone were inappropriately low, and there was a significant speed increase during ramp testing and at final speed that resulted in higher final speed in 79% of patients; (ii) there was a positive impact of echocardiographic ramp testing on LV unloading with improved LV unloading from 43 to 71% of patients in response to acute changes of LVAD speed despite submaximal speeds at ramp testing, and there was a sustainable positive effect at follow-up; (iii) speed adjustments after ramp testing resulted in optimized final follow-up LVAD speed, manifested as improved LVAD unloading that was achieved in an additional 21% of patients who were not originally optimized at pre-RAMP (all of them had an increase of LVAD speed at the time of follow-up echocardiography); and (iv) RV function did not worsen during ramp testing or at final LVAD speed, and only one patient developed severe TR at RAMP-High.

An important finding from this study is that clinical stability does not necessarily mean optimal LVAD speed and adequate unloading. This is consistent with previous studies by Uriel et al, where only 63% of HM3 patients had optimal

Figure 3 Left ventricular unloading and right ventricular function at final follow-up LVAD speed vs. pre-RAMP pump speed, and at RAMP-high vs. pre-RAMP pump speed. AV, aortic valve; CVP, central venous pressure; LVEDD, left ventricular end-diastolic diameter; MR, mitral regurgitation; NTproBNP, N-terminal pro BNP; TAPSE, tricuspid annular plane systolic excursion; TI, tricuspid insufficiency



haemodynamics (compared with 43% of our patients who were adequately unloaded) at baseline LVAD speed of 5307 ± 149 rpm, which was considerably higher than our pre-RAMP speed.[24]

Furthermore, our study shows that echocardiography-guided ramp tests can facilitate optimal speed changes, which in turn result in improved LV unloading. Better LV unloading reduces LV filling pressures and reduces maladaptive neurohormonal activation, which enhances beneficial structural, and molecular reverse remodelling and can potentially increase the likelihood of LV recovery. Our findings are similar to previous studies using echocardiographic ramp tests for optimization of LVAD speed in HM3[25] and even in other models of LVADs.[16]

The positive impact of the ramp test on LV unloading found in our study did not worsen the RV function despite the increase of LVAD speed with concerns over increased venous return to RV and leftward septal shift resulting in unfavourable RV geometry. These findings are in agreement with previous long-term echocardiographic evaluations after LVAD implantation that showed that RV size and TAPSE did not consistently change within 6 months after implantation.[26,27] LVAD implantation and speed augmentation lead to decreased RV afterload and improved RV function[28,29]; however, higher LVAD speeds beyond 5600 rpm in HM3 may affect the RV negatively as evidenced by increased RV volumes and less favourable RV geometry previously demonstrated in older LVAD pumps[30] and by Uriel *et al*. in HM3 who used three-dimensional echocardiography during ramp testing.[25] This may explain our findings of absent worsening RV function because the achieved final speeds were lower than 5600 rpm.

The echocardiographic parameter that most frequently did not meet criteria for successful unloading was LVEDD. Studies about another intrathoracically LVAD model (HVAD®; HeartWare® Inc., Framingham, MA, USA) inserted at the LV apex have shown lower degree of a reduction in LV chamber diameter during ramp testing that can possibly be explained by less deformation at the base of the heart because of the limited space in the chest.[30] Moreover, it has been shown in previous studies that changes in pulmonary capillary wedge pressure (which is the key parameter to describe LV unloading), as a function of rpm, was only weakly correlated with changes in LVEDD.[31] This indicates that other criteria should also be considered to define optimized speed using echocardiographic ramp tests as we did in this study using MR and AV opening.

Limitations

This study was a single-centre study with a small cohort and a limited power. The results of this study need a validation series to clarify the accuracy, cost-effectiveness, and the ultimate advantages of echocardiographic ramp test. In this pilot study, there was no validation against the invasive ramp test. The duration of LVAD support before the ramp test and the time to follow-up echocardiographic examinations varied, which may have caused a time bias. Even though the exams were evaluated and interpreted by one cardiologist (E. N.), the evaluation was not blinded. Different cardiologists attended the ramp tests, which may have caused variations in the decision concerning goal LVAD speed; however, this reflects real life clinical practice, and the same criteria for ramp test and LVAD unloading were applied in all patients. The upper speed limit of 6200 rpm was not reached; however, there was a significant increase of LVAD speed during ramp testing. Finally, we did not provide any associating powerful clinical outcomes like readmission rates, functional capacity, and HRAEs.

Conclusions

Echocardiography-guided ramp tests improved LV unloading during ramp testing and at final speed with no evidence of worsening of RV function. They allowed LVAD speed adjustment and optimization. This study adds to the evidence of echocardiographic ramp tests as an established, safe, and non-invasive technique for speed optimization in HM3 patients and, therefore, should be done routinely in HM3 recipients.

Conflict of interest

E. N. received speaker's honoraria from Novartis. L. H. L has no disclosures directly related to the present work. Unrelated disclosures are research grants from Astra Zeneca and Boston Scientific and consulting or speaker's honoraria from Novartis, Astra Zeneca, Bayer, St. Jude, Medtronic, and Vifor Pharma. The other authors have no relationships that could be construed as a conflict of interest.

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Permissions

All material is original to this submission.

Appendix

RAMP-test protocol

Speed (rpm)	Flow (LPM)	Power (Watt)	BP (mmHg)	HR (Beat/min)	LVEDD (mm)	LVESD (mm)	AV-opening	Septum (mm)	AR	MR	TR	TAPSE (mm)	RVSP (mmHg)	IVC (mm)

AR, aortic regurgitation; AV opening, aortic valve opening; BP, blood pressure; HR, heart rate; IVC, inferior vena cava; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; MR, mitral regurgitation; RVSP, right ventricular systolic pressure; TR, tricuspid regurgitation; TAPSE, tricuspid annular plane systolic excursion.

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