Ramp-Test Echocardiography in Patients with Long-Term Continuous-Flow Ventricular Assist Device: Case Report and Systematic Review

Marco Stephan Lofrano-Alves,[1,2] Carolina Santana dos Reis Santos,[1] Ana Carolina Miguel,[1] Pedro Henrique Basto Miranda,[1] Marlon Almeida Guedes,[1] Silvia Moreira Ayub-Ferreira[1]

Instituto do Coração (InCor),[1] Faculdade de Medicina da Universidade de São Paulo, São Paulo, SP; Hospital das Clínicas, Universidade Federal do Paraná,[2] Curitiba, Paraná – Brazil

Introduction

Cardiac transplantation is considered the definitive treatment for refractory heart failure (HF), but insufficient donors limit this therapeutic option for a large proportion of patients.[1,2] Long-term continuous-flow ventricular assist devices (CF-LVAD) have become an effective therapeutic option for heart transplantation in refractory patients. Initially used as bridge for transplantation, these devices have been increasingly used as destination therapy in patients with contraindications to heart transplantation, and this indication accounts for half of the devices currently implanted.[3]

Compared with first-generation pulsatile-flow devices, CF-LVAD improved survival and quality of life due to their greater efficiency, durability, smaller size and portability (Figure 1). However, in spite of the advances on this technology, the complex interaction between device and patient still favors the thrombus formation within the pump and cannulae, which can lead to mechanical malfunction and thromboembolic events.[4] For this reason, the management of the device-patient interface is of paramount importance for longer survival, and continuous monitoring of thrombus formation is necessary for the institution of adequate treatment.[5,6]

The echocardiogram is a useful tool for individual setting of the device parameters and for diagnosis of device-related complications. After implantation, a comprehensive echocardiogram should include measurement of intracavitary dimensions, Doppler study of transvalvular fluxes and flow velocities in the cannulae, as well as the search for thrombus, vegetation, pericardial effusion and aorta abnormalities. Currently, the use of echocardiography in patients with CF-LVAD includes three main indications: 1) surveillance echocardiogram, with or without parameter adjustment protocol; 2) problem-focused echocardiography, with or without ramp protocol (speed-change velocity protocol); and 3) myocardial recovery diagnosis.[7]

Ramp protocols (ramp test), or speed-change protocols, are characterized by performing the echocardiographic study with recording of morphological and hemodynamic parameters at increasing support speeds, within a limit tolerated by the patient.[8-10] According to recommendations, the optimal velocity for a given patient would be the one with intermittent opening of the aortic valve, neutral position of the interventricular septum in relation to the ventricles, minimal mitral and aortic regurgitations, mean arterial pressure > 65 mmHg, pulmonary capillary pressure < 18 mmHg and central venous pressure < 12 mmHg.[7]

Although this is a current recommendation, the use of these parameters is based on studies with a small number of patients performed mostly in a single center, with great variability in patient and/or echo parameter selection. In addition, studies have shown that anatomic or hemodynamic response differs in the presence of significant aortic insufficiency, hypertension and in the different types of CF-LVAD (axial vs. centrifugal flow, for example), raising the question as to the use of additional evaluation parameters to currently recommended.[11,12]

Thus, a critical analysis of the protocols and parameters proposed in these studies is necessary for a better understanding on this new methodology and its correct use in clinical practice. We present an illustrative case of a ramp protocol in a patient undergoing CF-LVAD and a systematic review of the literature regarding this modality.

Case Report

A 53-year-old female patient with idiopathic dilated cardiomyopathy and significant left ventricular systolic dysfunction who had been followed since 2008. She had an ischemic stroke in November 2010 with no neurological sequelae, receiving oral anticoagulation since then. Two previous hospitalizations for decompensated HF with use of dobutamine in 2010 and 2011, underwent cardiac resynchronization therapy in 2013. She has shown progression on cardiac disease in the last year becoming refractory to medical treatment, but unfavorable to cardiac transplantation due to high reactivity against the immunological panel (C-I 85% and C-II 69%). Thus, a long-term CF-LVAD implantation was indicated as destination therapy in the last hospitalization in June 2016 when she was classified as INTERMACS 3.[13]

The pre-implantation echocardiogram showed left ventricle with diffuse hypokinesia, LVDD = 88 mm, LVSD = 80 mm, LVEF = 23%, LVMI = 175 g/m^2, E/e'ratio = 23. LAVI = 83 mL/m^2. Right ventricle with base diameter = 32 mm and mean cavity = 20 mm, sphericity index = 0.3, with preserved systolic function. Right ventricle quantitative functional parameters TAPSE = 20 mm, s' = 14 cm/s, FAC = 32% and right-ventricle free-wall longitudinal strain = 21%. Presence of pacemaker wire in right chambers. Important secondary mitral regurgitation, discrete tricuspid regurgitation. Pulmonary artery systolic pressure (PSAP) estimated at 50 mmHg. Absence of thrombi.

Keywords

Heart Failure/physiopathology; Heart Transplantation/trends; Exercise; Echocardiography/methods; Ramps; Velocity; Ventricular Dysfunction, Left/physiopathology; Hemodynamics/physiology.

Mailing Address: Marco Stephan Lofrano-Alves •
Rua Mateus Leme 3945 apto 504B. Postal Code 82200-000, São Lourenço, Curitiba, PR – Brazil
Email: mslalves@hotmail.com/marco.alves@hc.ufpr.br
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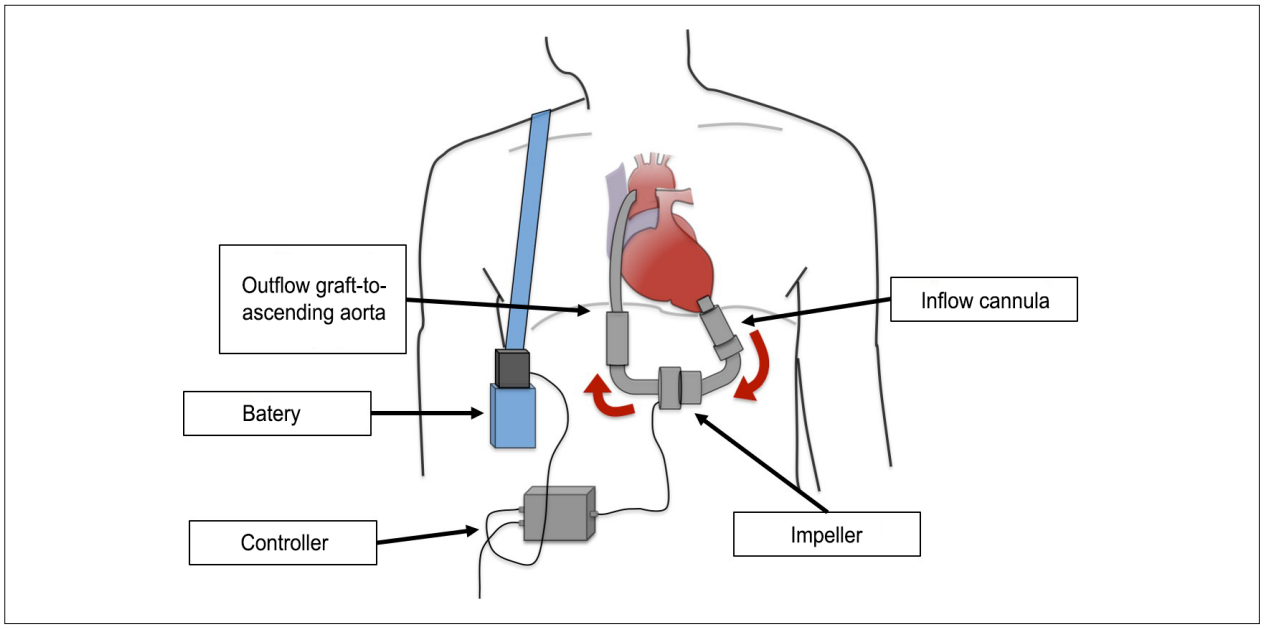

Figure 1 – *Continuous flow ventricular assist device. CF-LVAD is composed of 1) an inflow cannula connected to the LV apex (withdraws blood and directs to the impeller device; 2) impeller, flow generating mechanism; 3) outflow graft, which receives blood from the impeller and returns it to the target circulation (by anastomosis in the ascending aorta); 4) external controller and 5) external rechargeable battery.*

She underwent to an axial CF-LVAD implant (HeartMate-II, CentriMag, Thoratec, Pleasanton, CA), presenting transient right ventricular dysfunction after LVAD implantation, requiring mechanical right-side support with a short-stay device (CentriMag, Thoratec, Pleasanton, CA) for 7 days. An index study 28 day after the implantation demonstrated left ventricle with diffuse hypokinesia, interventricular septum in neutral position and with atypical movement, LVDD = 50 mm, LVEF = 30%, E/A ratio = 1.7, E-wave DT = 159 ms, inflow cannula well positioned at the LV apex without signs of dynamic obstruction with maximum systolic velocity = 1.6 m/s. Right ventricle with mild to moderate hypokinesia with s' = 8 cm/s. Minimal mitral regurgitation, mild aortic and tricuspid regurgitations. Maximum systolic velocity at the outflow cannula = 0.6 m/s. SPAP estimated at 40 mmHg. She was discharged after 30 days on oral anticoagulation with warfarin (INR = 2.5) and aspirine 100 mg daily. The device settings: 9600 rpm, 5.3 L/min, Power = 5.9 W, pulsatility index 5.3.

One hundred and five days after implantation, an echo surveillance study was requested with parameter-adjustment protocol. The protocol used was described by Uriel, et al.,[8] Before the protocol was performed, demographic information, medical and surgical history, medications in use, laboratory data including anticoagulation, platelet count, LDH and bilirubin were collected. Anticoagulation was measured, with INR in therapeutic range. The device safety speed has been set to 8000 rpm to allow the actual speed to decrease without triggering the low flow alarms, with a gradual decrease of the support speed performed according to patient tolerance. After 2 minutes of stabilization at 8000 rpm, the following parameters were obtained: LVDD, LVSD, aortic valve opening frequency (in 10 consecutive cycles), graduation of aortic/mitral/tricuspid regurgitations, SPAP calculation, systemic blood pressure and heart rate. In addition, the pulsatility index, power and flow rates provided by the device were recorded. The velocity was increased by 400 rpm every 2 minutes, within a range of 8000 - 11000 rpm, with acquisition of the echocardiographic and device parameters at each stage (Figures 2, 3 and 4). Interruption of the protocol was advised before 11000 rpm, in the occurrence of any suctioning event, or if LVDD < 3.0 cm. At the end of the protocol, the physician reviewed the parameters obtained and the optimum velocity was set at 9200 rpm, in which intermittent aortic opening, mean arterial pressure > 65 mmHg, and minimal mitral regurgitation were obtained. The data were plotted in relation to the studied velocities in a graph, using linear regression to obtain the equation for each continuous parameter for further comparisons (Figure 5).

Methodology

This is a systematic review according to the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA).[14]

We conducted a search for articles in MEDLINE, EMBASE, OVID, SCOPUS, WEB OF SCIENCE and GOOGLE SCHOLAR databases in the period of January 2000 to October 2017, without language restriction, with a target population of adults over 18 years of age, with full texts, and with descriptors present in the title or abstract. The following English descriptors were used for the search: assist device OR ventricular assist device OR mechanical circulatory support OR echocardiography. These descriptors were combined with one of the following: ramp test OR speed-change OR pump speed OR pump speed optimization. We also searched the Cochrane Library for any previous or ongoing systematic

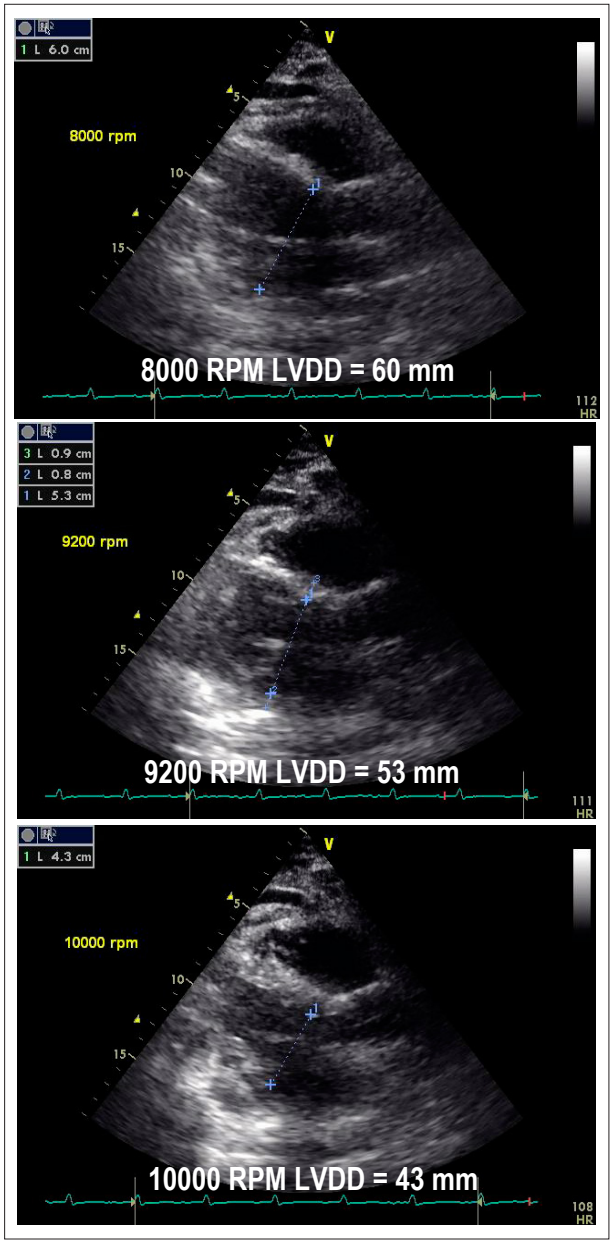

Figure 2 – *Measurement of the diastolic diameter of the left ventricle at different support speeds during the echocardiographic ramp test. Top panel 8000 rpm, middle panel 9200 rpm and bottom panel 10000 rpm. The diastolic dimension of the left ventricle gradually decreases with increasing support velocity, from 60 mm to 53 mm, and finally 43 mm. RPM, revolutions per minute; LVDD, left ventricle diastolic dimension.*

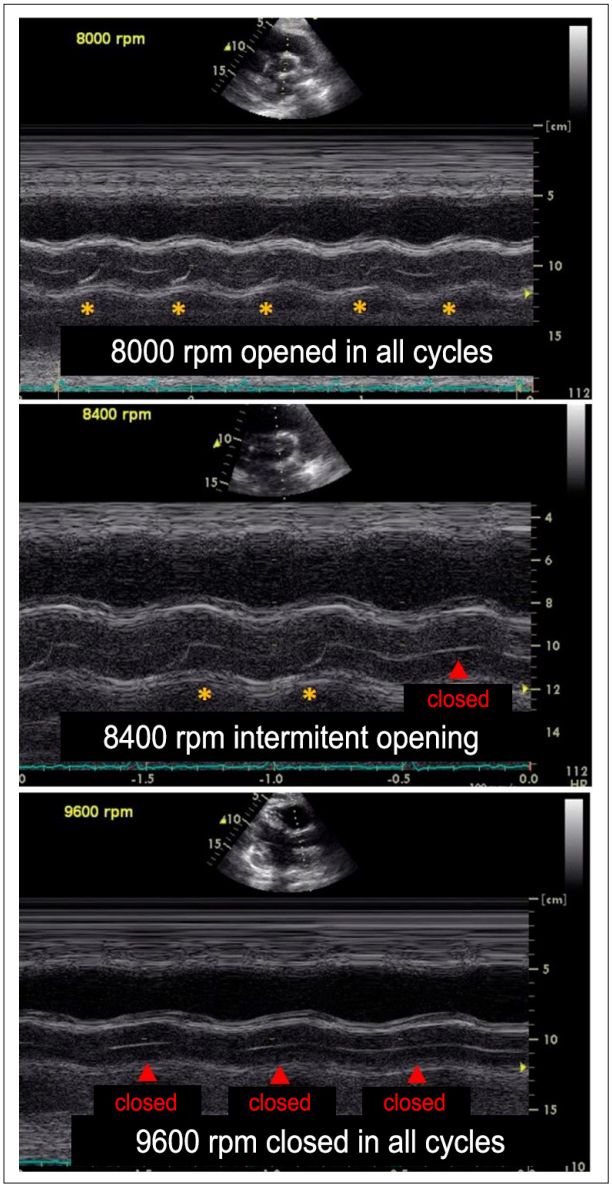

Figure 3 – *Observation of the aortic valve (AV) opening frequency by the M mode at different support speeds during the echocardiographic ramp test. Top panel 8000 rpm, middle panel 9200 rpm and bottom panel 10000 rpm. Initially on low support at 8000 rpm, AV has normal opening at all cycles. With intermediate support at 9200 rpm, intermittent opening of the valve is observed. With high support at 10000 rpm, we observe the AV closed in all cycles. RPM, revolutions per minute.*

review on the subject. The results from the various databases were combined and the repeated results were discarded. Two investigators (M.S.L.A. and C.S.R.S.) conducted the search independently and reached agreement on the eligibility of the studies. Initially we performed a first screening to identify those studies that considered adult patients with refractory HF undergoing CF-LVAD who were indicated for a ramp protocol. In a second step, we obtained the full text articles and assessed whether the data were relevant, as well as whether there was more than one article evaluating the same cohort of patients. A third step included reviewing the references of these selected articles to obtain other sources not revealed in the digital search. We classified the studies according to their design (case-control, randomized, retrospective cohort, prospective cohort, case report), as to the primary objective of the ramp protocol in the given study (adjustment protocol, diagnosis of thrombosis or both) and type of CF-LVAD used. For each study, we extracted the following information: first author; institution of the study; start and end date; year of publication; single or multicentric center; characteristics of the study population (mean age, gender distribution); NYHA functional class; INTERMACS; type of CF-LVAD (axial flow, centrifugal, other); study design.

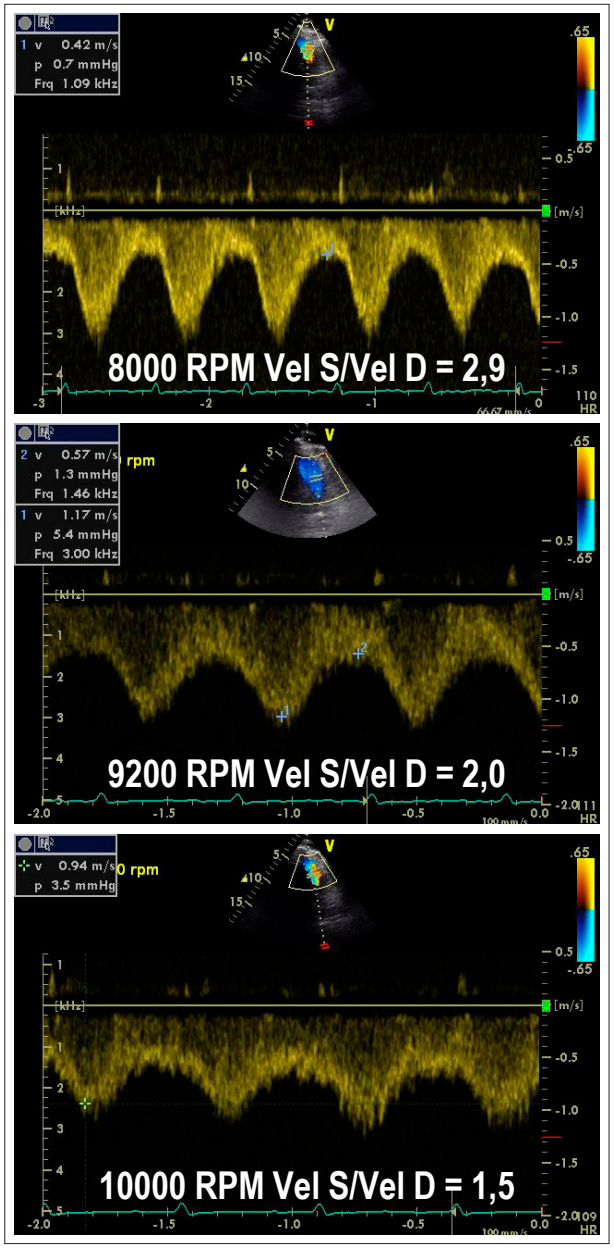

Figure 4 – *Observation of flow in anastomosis of the outflow cannula with ascending aorta by pulsed Doppler at different support speeds during the echocardiographic ramp test. Initially, low support at 8000 rpm (top panel) shows a relationship between the peak systolic velocity and the diastolic velocity of 2.9. With intermediate support at 9200 rpm (middle panel), this ratio decreases to 2. With high support at 10000 rpm, the lowest ratio equals 1.5 (bottom panel). RPM, revolutions per minute. Vel S, maximum velocity associated with ventricular systole; Vel D, basal or diastolic velocity.*

Results

We identified 789 references through the search in electronic databases, discarding 332 duplicates. Of the remaining 457 studies, we obtained 26 full-text articles for analysis after title and abstract screening. Three additional articles were included after manual search of the references (Figure 6). A total of 29 articles were included in the qualitative analysis of this review, being classified in three main categories: 1) studies using the echocardiographic ramp test to diagnose device thrombosis (N = 6, Table 2); 2) studies using the ramp test to evaluate physiological, hemodynamic and morphological effects (N = 18, Table 3); and 3) studies using the ramp test to assess the change in support speed in exercise capacity (N = 5, Table 3). All articles have been published in English. Twenty-eight articles were single center, with 19(65.5%) from the United States, 3 (10%) from the United Kingdom, 2 (7%) from Sweden, 2 (7%) from Netherlands, 1 (3.5%) from Italy and 1 (3.5%) from Belgium. A single article was developed in two centers (USA and Denmark). Twenty-three studies were prospective cohorts, 1 case-control, 1 retrospective cohort and 4 case reports. Altogether, 686 patients received CF-LVAD with a combined mean age in the studies of 54.2 ± 17.5 years, the majority being male (median 82.5%, 95%CI 71-86). The most frequent indication was as bridge for transplantation (median 70%, 95%CI 48-73). In 69% of the studies, only the axial CF-LVAD was used, in 10% of the studies, only the centrifugal CF-LVAD was used. Both types were used in 21%, with axial flow implants being more frequently in these studies (median 62%, IQR 60-67).

Discussion

In recent years, studies have been performed in order to validate echocardiographic ramp protocols for support adjustment or diagnosis of device thrombosis. In these protocols, echocardiographic measurements are acquired at low support speeds and after each stage of rate increase within a predetermined range. The variables studied were those related to morphological and hemodynamic changes that reflect the incremental velocity change and/or left ventricular residual function. For example, the position of the interventricular septum, frequency and duration of aortic valve opening, degree of mitral/tricuspid regurgitation, LVDD maximum variation, slope of the LVDD variation, E wave DT change, flow velocities in the inflow and outflow cannulae, relationship between the systolic (S) and diastolic (D) peak velocity in the cannulae[8,9]

Current recommendations indicate the use of these protocols only in the case of adequate anticoagulation within the therapeutic target.[7] The main risk is the detachment of an undiagnosed thrombus from the aortic root, upon return to pulsatile flow and aortic valve re-opening on lower support velocities. Therefore, it is contraindicated to perform these protocols when detecting an intracardiac or aortic root thrombus, since a thromboembolic event associated with a speed-change protocol may be catastrophic for the patient.[15]

It is advisable the exam be supervised by a physician with expertise in mechanical circulatory assistance. It is necessary that the person responsible for the examination indicates which speed range will be tested and which parameters will be used to adjust the velocity for the patient in question. The reasons for interrupting the test should also be pre-determined, including: 1) end of protocol, 2) new symptoms related to hypotension or hypoperfusion (palpitations, dizziness, dyspnea, angina, headache), 3) elevation of mean arterial pressure, 4) suction events in high

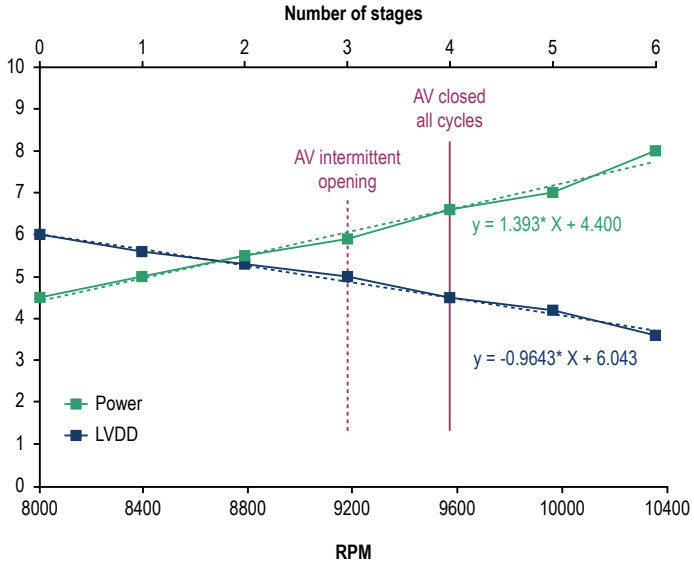

Figure 5 – *Values of left ventricular diastolic dimension and energetic consumption of the device as a function of the velocity. The values were obtained in anrange between 8000 rpm and 11400 rpm with increment of 400 rpm every 2 minutes. The equations of the lines formed by the points, in the form Y = aX + b, were obtained through linear regression. The slope is used as a measure of normal or abnormal response in patients with HeartMate-II. Power, energy consumption provided by the device; LVDD, left ventricle diastolic dimension.*

Table 1 – Evolutive parameters

	Preimplant	Ramp test 105 days after implant		195 days after implant
Device				
Rotations per minute RPM	-	9600	8000	9200
Flow (L/min)	-	5.6	4.5	5.3
Power (W)	-	6.0	4.4	5.9
Pulsatility index	-	5.5	4.3	5.5
Laboratory				
DHL	-	556		443
INR	-	2.7		2.6
Ecocardiography				
LVDD (mm)	88	53	60	53
IVS position	To right	Neutral	To Right	Neutral
Aortic valve opening	Normal	Intermittent	Opened all cycles	Intermittent
LVEF %	23	30	20	30
E/A ratio	1.7	0.8	1.7	0.8
E wave DT (ms)	98	159	81	144
MR	Important	minimum	discrete	minimum
AR	Normal	discrete	discrete	discrete
TR	discrete	discrete	discrete	discrete
Vel-S (outflow cannula) (m/s)	-	0.6	0.8	0.8
Vel-S/Vel-D (outflow cannula)	-	2.0	2.9	2.0
SPAP (mmHg)	50	23	23	27
S´- RV (cm/s)	14	8		8

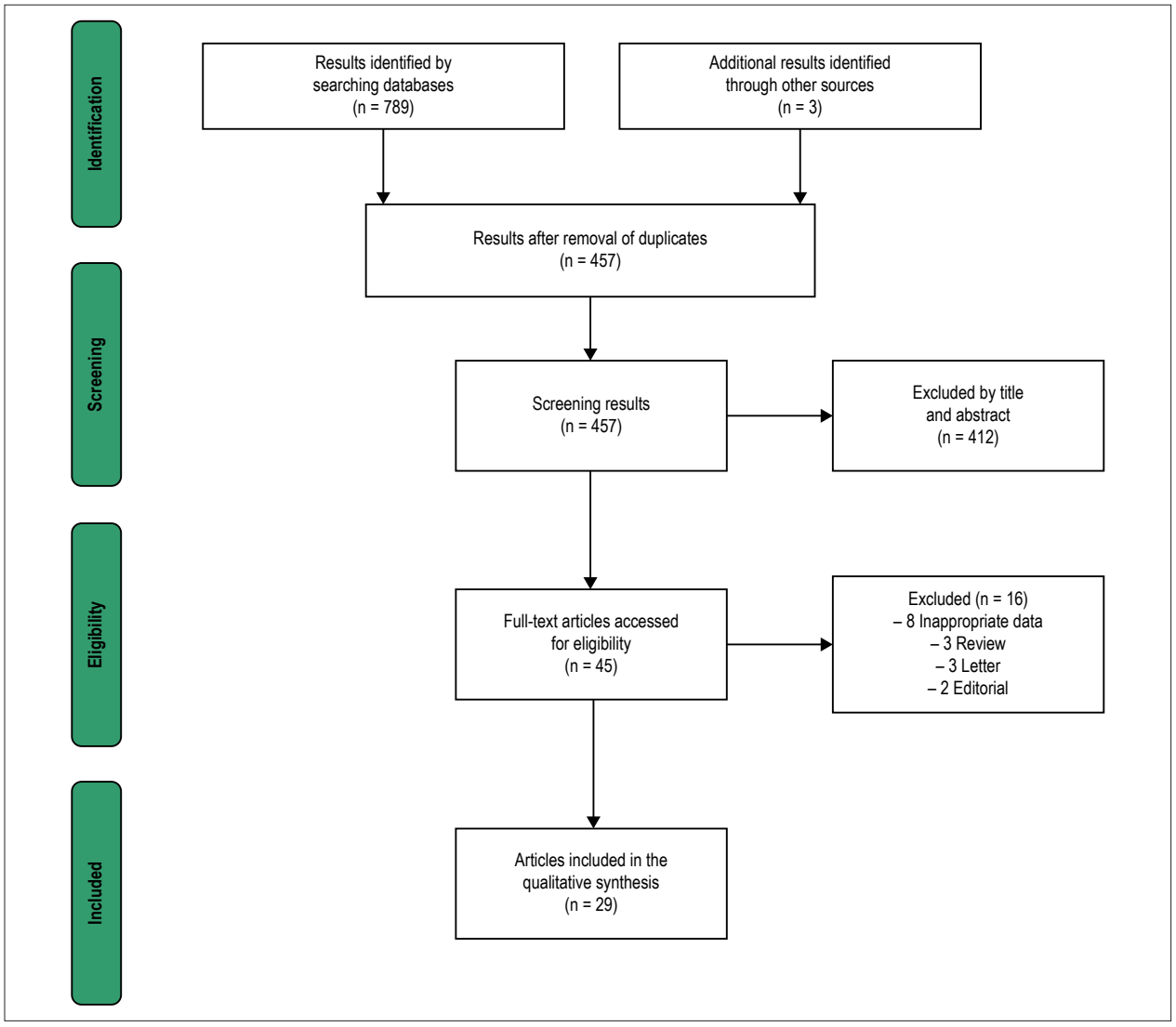

Figure 6 – *Flowchart of search and studies selection on echocardiographic ramp test in patients using CF-LVAD.*

Table 2 – Studies using ramp test for diagnosis of thrombosis

Author and year of publication	Country	Design	CF-LVAD	N. of patients	N. of RT	Study aim
Adatya et al., 2015[11]	USA	Prospective cohort	HeartMate-II	55	78	Evaluate the influence of AR and MAP on the ramp test result
Butera et al., 2017[15]	USA	Case report	HeartMate-II	1	1	Report case of multiembolic brain event related to the ramp test
Estep et al., 2014[9]	USA	Case-control	HeartMate-II	48	48	Elaboration of protocol with echocardiographic ramp test for diagnosis of thrombosis
Iacovoni et al., 2017[10]	Italy	Prospective cohort	HVAD	17	18	Ramp protocol for diagnosis of thrombosis in centrifugal flow LVAD
Kato et al., 2014[33]	USA	Case report	HeartMate-II	1	3	Serial ramp test for thrombus diagnosis
Uriel et al. 2012[8]	USA	Prospective cohort	HeartMate-II	39	52	Elaboration of protocol with echocardiographic ramp test for diagnosis of thrombosis

Table 3 – Ramp test for speed-adjustment or evaluation of physiological, hemodynamic or morphologic effects

Author and year of publication	Country	Design	CF-LVAD	N. of patients	N. of RT	Study aim
Addetia et al., 2017[18]	USA	Prospective cohort	HeartMate-II (19) HVAD (12)	31	31	To evaluate the impact of the two types of LVAD on the LV/RV morphology by 3D echo.
Banerjee et al., 2017[34]	USA	Case report	ReliantHeart HeartAssist 5	1	1	Optimization of parameters with right catheterization and simultaneous echo.
Cornwell et. al., 2015[25]	USA	Prospective cohort	HeartMate-II	13	13	To evaluate whether the restoration of the pulsatile pattern through the change of velocity reduces the sympathetic activity
Couperus et al., 2017[24]	Netherlands	Prospective cohort	HeartMate-II	17	17	Evolution of right ventricular function after optimization of parameters with ramp test in stable patients
George et al., 2010[16]	UK	Prospective cohort	HeartMate-II	15	46	Improved speed to access LV residual function and speed reduction safety
Hubbert et al., 2017[23]	Sweden	Prospective cohort	HeartMate-II	4	3	Monitoring of the LA pressure with wireless micro-electromechanical pressure sensor during the ramp test
Imamura et. al., 2017[17]	USA	Prospective cohort	HeartMate-II (8) HVAD (8)	16	32	Repeated evaluation of the ramp test in stable patients
Jung et al., 2016[32]	USA	Prospective cohort	HeartMate-II	44	80	Prognostic value of the echocardiographic ramp test in functional capacity, quality of life and survival
Jung et al., 2015[21]	USA	Prospective cohort	HeartMate-II	10	10	To evaluate the correlation between PCP and LVDD during the ramp test
Lund et al., 2012[35]	Sweden	Prospective cohort	HeartMate-II	5	20	To evaluate the reproducibility and variability of the energy consumption, PI and flow in the echocardiographic ramp test
Martina et al., 2014[20]	Netherlands	Prospective cohort	HeartMate-II (28) HVAD (1)	29	29	Evaluation of non-invasive BP during the ramp test
Sayer et al., 2017[36]	USA	Case report	HeartAssist5	1	1	Morphological and hemodynamic evaluation in a new axial flow LVAD model
Sayer et al., 2017[26]	USA	Prospective cohort	HeartMate-II (35) HVAD (20)	55	55	Comparison between patients with and without AR in the ramp test
Shah et al., 2017[22]	USA	Prospective cohort	HeartMate-II (71) HVAD (34)	105	38	Evaluation of routine right catheterization in patients with LVAD in the ramp test
Stainback et al. 2005[37]	USA	Prospective cohort	Jarvic 2000	11	11	Morphological and hemodynamic evaluation of an axial flow LVAD with ramp test
Uriel et al. 2017[19]	USA	Prospective cohort	HeartMate-3	16	16	Morphological and hemodynamic evaluation of an intrapericardial centrifugal flow LVAD with ramp test
Uriel et al. 2015[12]	USA	Prospective cohort	HVAD	26	26	Evaluation of the utility of the ramp test in LVAD of centrifugal flow
Uriel et al. 2016[38]	USA	Prospective cohort	HeartMate-II (21) HVAD (14)	35	35	Combination of ramp test and invasive hemodynamic evaluation for optimization of management

support and 5) reverse flow in the cannulae in low support. It is recommended to record the information given by the device at each measured speed, such as flow, pulsatility index and energy consumption. The use of model tables for recording of echocardiographic parameters at the corresponding velocities is useful in the standardization and reproducibility of the test. During the examination, continuous monitoring of the heart rate with electrocardiogram and blood pressure is recommended. The evaluation of flow velocities in the infusion cannula by spectral Doppler is a useful parameter of control during the ramp test. The inflow cannula should be questioned at each stage for: 1) expected progressive decrease in the ratio of maximum (S) and diastolic (D) systolic velocities (Figure 4); 2) presence of reverse flow during low speeds and 3) suctioning events and dynamic obstruction of the inflow cannula during high support speeds. The assessment of flow

Table 4 – Studies using speed-change protocol in the exercise capacity

Author and year of publication	Country	Design	CF-LVAD	N. of patients	N. of TR	Study aim
Fresiello et al., 2016[27]	Belgium	Prospective cohort	HeartMate-II	14	14	To investigate whether the change of velocity alters exercise capacity in cycloergometer
Jakovljevic et al., 2010[28]	UK	Prospective cohort	HeartMate-II	12	12	Evaluate heart and exercise performance at optimal and reduced speed
Jung et al., 2014[29]	USA	Prospective cohort	HeartMate-II	12	12	To assess the effect of peak velocity on exercise capacity measured by peak VO2
Jung et al., 2017[30]	USA Denmark	Prospective cohort	HeartMate-II	19	19	To determine the effect of the change in velocity on the submaximal exercise capacity
Noor et al., 2012[31]	UK	Prospective cohort	HeartMate-II	30	30	Effect of residual left ventricular function on VO2 peak at different support speeds

velocities should be obtained in the anastomosis of the outflow cannula with the ascending aorta when the device in question is intrapericardial (HVAD centrifugal CF-LVAD, for example) due to the artifact caused by the proximity of the apparatus to the cardiac apex, which hinders the Doppler study in the inflow cannula.[10]

In low-speed support, especially in the case of hypertension, reverse flow can occur in the cannulae. George et al. prospectively studied 15 male patients using axial-CF-LVAD (HeartMate-II). In this study, anterograde and reverse flow velocities were studied using Doppler echocardiography at baseline and after reduction to 6000, 5000 and 4000 rpm. The authors observed a significant reduction in anterograde velocity and cardiac output with reduction to 6000 rpm, but no significant effect on left ventricular preload. There was no further change with reduction greater than 5000 or 4000 rpm. No adverse side effects have been reported. The authors concluded that the reduction to 6000 rpm is safe, being the ideal velocity for evaluation of left ventricular residual function.[16]

Imamura et al.,[17] studied the reproducibility of the ramp test in 8 patients using HeartMateII and 8 patients with HVAD submitted concomitantly to the right chamber catheterization. All patients repeated the test after 278 (126-560) days. All hemodynamic variables remained statistically stable between the first and second tests. The authors concluded that stable patients have a similar hemodynamic profile over the years, including the response to the ramp test. The authors suggest that the hemodynamic response to the ramp test may be considered a "fingerprint" and that deviations from the initial study may serve as suspected clinical deterioration or malfunction of the device.[17]

In 2012, Uriel et al.,[8] published a study with 39 patients using HeartMateII for the elaboration of a ramp protocol for the purpose of speed adjustment before discharge after implantation of the device, or for the diagnosis of suspected thrombosis. In this study, blood pressure, LVDD, aortic valve opening frequency and gradient of valve regurgitations were recorded at every 400 rpm of speed increase within a range of 8000 to 12000 rpm. The linear angular coefficients for LVDD, pulsatility index and energy consumption were calculated by linear regression. There was a change in baseline velocity in 61% of the cases, with an average change of 424 ± 211 rpm. In 17 patients who underwent the protocol for suspected thrombosis, 10 had a change in the ramp test. Of these 10 patients, 8 had confirmation of thrombus after device explant. A cutoff point for the LVDD slope of ≥ -0.16 was established for the diagnosis of thrombosis.[8]

Estep et al.,[9] evaluated 11 patients using HeartMateII with suspected thrombosis determined by clinical, laboratory, device parameters or confirmation after device explant. These patients were compared with 36 randomized patients without suspected thrombosis. In their study, echocardiographic variables were collected at each stage of 1000 rpm increase over a range of 8000-11000 rpm. The variables with higher AUC were the variations in the LVDD (> 0.6 cm), the aortic valve opening time (< 80 ms) and the mitral E wave DT. The presence of one parameter had 100% sensitivity and 80% specificity for thrombosis, and the presence of two positive parameters had 100% sensitivity and 95% specificity.[9]

Ramp testing has since been used in patients with axial CF-LVAD (mainly HeartMate-II). Recently, there was an increase in the number of patients using centrifugal CF-LVAD (HVAD). In a prospective study, the utility of the ramp test was evaluated in the left ventricular decompression in patients using HVAD, using the LVDD coefficient, the aortic opening frequency and the degree of valvular insufficiency. The protocol included stages with increasing speed at 100 rpm in a range of 2300 to 3200 rpm. The authors performed 19 tests for speed adjustment and 7 tests for the diagnosis of thrombosis. The reduction of LVDD was significantly different when the aortic valve was opened (- 0.09 cm/stage) compared to the closed aortic valve (- 0.15 cm/stage, p = 0.013). The angular coefficient for energy consumption also did not change after aortic valve closure. The authors concluded that the slope coefficient for LVDD cannot be applied to ramp tests in patients using HVAD.[12]

Thus, Addetia et al.,[18] questioned whether changes in left ventricular volume and shape assessed by 3D echocardiography could better describe the impact of the two types of axial and centrifugal CF-LVAD during the ramp test. Ramp test with 3D echocardiography and right chamber catheterization was performed in 19 patients with HeartMateII and 12 HVAD. In both devices, pulmonary

capillary pressure decreased while cardiac output increased. There was a progressive decrease in left ventricular volume and right ventricular enlargement, being more pronounced in HeartMateII. There was displacement of the interventricular septum to the left in the HeartMateII at high speed, but not in the HVAD. The authors concluded that hearts respond differently to changes in velocity with the two types of CF-LVAD. The authors suggest that adding right ventricular morphological assessment by 3D echocardiography may be useful in optimizing velocity.[18]

Iacovoni et al.,[10] developed a ramp protocol for patients using HVAD. The authors demonstrated that the S/D ratio obtained by the evaluation of flow velocities with pulsed Doppler in the outflow cannula decreases progressively with the increase of the support speed in patients using HVAD, being a promising parameter for the ramp test with this device.[10]

In another study, the heart hemodynamic response of 16 patients using a new centrifugal CF-LVAD (HeartMate-3) was studied in a concomitant echocardiographic ramp test with right heart catheterization. The authors demonstrated that in this device, LVDD decreased at a rate of -0.15 ± 0.09 cm per 100 rpm increase in speed, concomitantly with reduction in capillary pressure and increase in cardiac output. The velocity adjustment using the ramp test with hemodynamic normalization was possible in 81.3% of the patients.[19]

Recently, Adatya et al.,[8] questioned the effects of load conditions on ramp test results. In an elegant study with 55 patients using HeartMateII, the authors prospectively evaluated whether the presence of continuous aortic insufficiency or elevated mean arterial pressure were associated with false positive results in ramp tests. The criterion used to consider the positive ramp test (suggestive of thrombosis) was that described by Uriel et al. being the angular coefficient for LVDD ≥ -0.16.[8] Confirmation of thrombosis was obtained after device explant. The angular coefficient obtained was -0.14 ± 0.17 in patients with aortic insufficiency and -0.25 ± 0.11 in patients without aortic insufficiency ($p < 0.001$). In patients with MAP > 85 mmHg, the angular coefficient was -0.18 ± 0.07 and in those with MAP < 85 mmHg -0.23 ± 0.14 (p = NS). However, 50% of patients with aortic insufficiency had false positive results. The AUC of the ramp test increased from 0.76 to 0.88 after removal of patients with aortic insufficiency. The authors concluded that the presence of altered loading conditions such as aortic insufficiency and elevated MAP may result in false positive results in the echocardiographic ramp test. The authors also demonstrated that the combination of the LVDD coefficient and the serum lactate dehydrogenase concentration increased the AUC from 0.88 to 0.96 in patients using HeartMateII.[11]

In addition to the clinical applicability discussed above, several studies have used the echocardiographic ramp test to evaluate the effects of changing the supportive speed in physiology. Among these studies, the associations between the ramp test in the blood pressure,[20] pulmonary capillary pressure,[21, 22] left atrial pressure,[23] evolution of right ventricular function after CF-LVAD implantation,[24] evaluation of the residual left ventricular function,[16] sympathetic activity,[25] and presence of aortic insufficiency.[26]

Other studies have evaluated the effects of supportive speed change on exercise capacity.[27-31]Fresiello et al.,[27] evaluated 14 patients with HeartMateII undergoing two maximal cardiopulmonary exercise tests on a cycle ergometer on the same day. In the first, the support velocity was kept constant and in the second test the speed was increased by 200 rpm every 2 minutes. There were no significant differences in heart rate, blood pressure, peak VO_2, peak minute ventilation, or ventilation efficiency despite an additional increase of 1.6 L/min in cardiac output. [27]

However, in another study, patients using HeartMateII were also submitted to the cardiopulmonary test in cycle ergometer twice in the same day, being one with fixed speed and another with progressive increment of the speed. The sequence of the tests was randomized between the patients. In this study, the peak VO_2 was significantly higher in the test performed with increasing speed. The authors suggest that an automatic rate increase control could improve functional capacity.[29] Additionally, the authors demonstrated in another study that hemodynamic changes during the ramp test correlate with functional capacity and quality of life but not with survival in patients with CF-LVAD.[3]

In the present case, the comparison of the echocardiographic parameters in the pre-implantation echocardiogram and after device implantation demonstrates adequate left ventricle decompression (Table 1), with a neutral position of the interventricular septum, marked reduction in LVDD and mitral insufficiency, and an increase in E wave DT. The ramp test demonstrated adequate angular response to LVDD and energy consumption (Figure 5), consistent with the normal pattern in patients using axial CF-LVAD (HeartMateII). Based on the current recommendations, it was possible to adjust the speed from 9600 rpm to 9200 rpm, which was the best speed that maintained the previous findings with intermittent aortic valve opening.

We emphasize the importance of an in-depth knowledge of the echocardiographer on the subject for the safe and correct performance of the echocardiographic ramp test, as well as for the interpretation of the multiple relevant findings of this test. The correct interpretation of the findings can lead to a fundamental diagnosis for patient evolution in mechanical circulatory support, with therapeutic consequences and even the explant of the device. The need for an institutional protocol for the proper use of the test in clinical practice is also highlighted.

Authors' contributions

Research creation and design: Lofrano-Alves MS; Data acquisition: Lofrano-Alves MS, Santos CSR, Miguel AC, Miranda PHB, Guedes MFA; Data analysis and interpretation: Lofrano-Alves MS, Santos CSR; Statistical analysis: Lofrano-Alves MS; Manuscript writing: Lofrano-Alves MS, Santos CSR, Miguel AC, Miranda PHB, Guedes MFA; Critical

revision of the manuscript as for important intellectual content: Lofrano-Alves MS, Ayub-Ferreira SM.

Potential Conflicts of Interest

There are no relevant conflicts of interest.

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