A New Hemodynamic Index To Predict Late Right Failure In Patients Implanted With Last Generation Centrifugal Pump.

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Abstract

Background. Right ventricular failure (RVF) is a severe event that increases perioperative mortality after Left Ventricle Assist Device (LVAD) implantation. RV function is particularly affected by the LVAD speed by changing RV preload and afterload as well as the position of the interventricular septum. However, there are no studies focusing on the relationship between pump speed optimization and risk factors for development of lateRVF. Methods. Between 2015 and 2019,50 consecutive patients received LVAD implantation at San Camillo Hospital in Rome. Of these, 38 who underwent pump speed optimization were included. Post optimization hemodynamic data were collected. We assessed: a new Hemodynamic Index (HI), calculated as follows HI=MAP x PCWP/CVP x RPM set/RPM max; risk factors for late RVF, which was defined as the requirement for 7 days or more of inotropic support. Results 10 patients had late RVF after LVAD implantation. 5 patients required diuretic therapy and speed optimization. In 3 patients inotropic support with adrenaline 0.05 ?g/kg/min was started. 2 patients required prolonged continuous veno-venous hemofiltration and high dosage inotropic support. Multivariate analysis revealed that a low HI (odds ratio 11.5, 95 % confidence interval,1.85-65.5,p[.003] was an independent risk factor for late RVF after LVAD implantation. Conclusion A low HI, according to our study, is a significant risk factor for the development of RVF after LVAD implantation. We suggest adopting this index during the follow-up to stratify the different hemodynamic profiles and modify the therapeutic strategies according to the different HI levels obtained for every single patient.

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Short Title : New Index predicts late Right Failure

INTRODUCTION

Mechanical ventricular assistance systems are increasingly acquiring a pivotal role in the treatment of heart failure refractory to medical therapy [1]. The technological evolution has led to the development of remarkably reliable systems, also suitable for use as destination therapy in those who are not candidates for heart transplantation. Although these systems offer increasingly excellent safety profiles, lower risks of device failure, and improved blood compatibility, the prospect of left ventricular system supporting life long term is dependent on right ventricular (RV) function. Right ventricular failure (RVF) is a frequent and severe event that increases perioperative mortality after Left Ventricle Assist Device (LVAD) implantation. Previous reports revealed that the prevalence of RVF after LVAD implantation ranged from 10% to 40% [2-3-4]. To date, many studies have reported hemodynamic predictors of RVF including elevated central venous pressure (CVP), CVP/Pulmonary Capillary Wedge Pressure (PCWP) ratio, Right Ventricular Stroke Work Index (RVSWI), and Pulmonary Artery Pulsatility index (PAPi) [5-6-7]. Although these scores have possible utility in identifying preoperative features that increase the risk of right heart failure during left ventricle mechanical support, they are not appropriate to predict late right heart failure, because the hemodynamic conditions are completely modified. RV function is particularly affected by the LVAD speed by changing RV preload and afterload as well as the position of the interventricular septum. All these parameters are susceptible of echocardiographic or hemodynamic optimizations that are gaining interest in the setting of the so-called postoperative RAMP test. Despite a growing body of evidences and number of publications on this topic, no guidelines have drawn indications on how set-up correctly the speed and medical therapy during this test. There have been no studies focusing on the combined effect of right heart function, left ventricular preload, mean arterial blood pressure and pump speed on the incidence of late right ventricular failure.

In the present study, we proposed a new **HEMODYNAMIC INDEX** formulated using data obtained after from postoperative right-sided heart catheterization and integrates preload, afterload and pump speed. Finally, we determined its relationship with late RVF after LVAD implantation.

METHODS

A retrospective analysis was conducted. We examined 50 consecutive patients who underwent **Full MagLev, *HeartMate 3*** continuous-flow LVAD (cf-LVAD) implantation for end-stage heart failure at our department from November 2015 to December 2019. A written informed consent was obtained from all the patietns. LVAD pump speed was optimized perioperatively in the intensive care unit using Swan-Ganz catheter measurements and echocardiography aiming for neutral interventricular septum position and intermittent aortic valve opening with minimal aortic regurgitation. After LVAD implantation, all patients received optimal heart failure medication and anticoagulation. The inclusion were as follows: LVAD support for at least six months with a stable clinical and hemodynamic status in the ambulatory setting. Finally, 38 patients who underwent ramp test during right-sided heart catheterization after LVAD implantation were included in this study. Excluded from the study were: two patients with severe tricuspid regurgitation, who were candidates for temporary right ventricular support; one patient who was supported preoperatively with extracorporeal membrane oxygenation or extracorporeal left ventricular support; two patients who died as a consequence of significant events occurring post-LVAD implantation; and seven patients who did not undergo postoperative ramp testing. The study was approved by the Ethical committee at Rome San Camillo

Hospital and all the patients were enrolled with informed consent.

Surgical Procedures

All the patients received a HeartMate 3 continuous-flow LVAD. Patients underwent LVAD implantation through a median sternotomy with systemic cardiopulmonary bypass (CPB), during which the inflow cannula was inserted into the apex of the left ventricle, and the outflow graft was anastomosed to the ascending aorta. Three patients with at least mild aortic insufficiency received aortic valve replacement with a tissue valve. In four patients with mild or moderate tricuspid regurgitation a concomitant tricuspid valve repair was conducted by implanting 28 mm Contour 3D?Medtronic annuloplasty rings were implanted. There was no statistical difference between the two groups in terms of CPB time that resulted 75,6 ± 23,7 minutes for RVF + group and 85,0 ± 44,5 minutes for RVF – group (p=0,371). Early right ventricular failure occurred in three patients requiring temporary right ventricular support instituted through femoral-pulmonary cannulation. All three patients were successfully weaned from RV support after a mean time of 8,5 ± 2,7 days.

Ramp Test Protocol

All patients underwent a ramp test using hemodynamic monitoring with a Swan Ganz catheter after an average period of 6.4 ± 1.2 months after LVAD implantation. The ramp test consisted of three stages. First, clinical parameters were reviewed to ensure safety. Appropriate anticoagulation was defined as INR >1.8 or PTT >60. If inadequate anticoagulation was demonstrated, 60 u/kg of Heparin was administered intravenously before the test. Transthoracic echocardiography confirmed absence of an intraventricular or aortic root thrombus. If a thrombus was identified, the ramp study was not performed due to the possibility of thrombus dislodgement. After this initial safety pre-test screening, a pulmonary artery catheter was inserted via the right internal jugular vein. Baseline right heart catheterization and estimation of cf-LVAD flows were performed, followed by baseline echocardiographic images. The hemodynamic parameters included central venous pressure (CVP), systolic (SPAP), diastolic (DPAP) and mean pulmonary artery pressures (MPAP) and pulmonary capillary wedge pressure (PCWP). Blood samples were obtained from the pulmonary artery for measurement of mixed venous oxygen saturation. Cardiac output (CO) and cardiac index (CI) were calculated by thermodilution. Hemoglobin was measured from the venous blood gas and arterial oxygen saturation measured using pulse oximetry. Echocardiographic parameters included Left ventricular end-diastolic and end-systolic dimensions (LVEDD and LVESD), measured from the parasternal long-axis view. Percent aortic valve (AV) opening and qualitative estimation of the severity of aortic and mitral regurgitation (AR and MR, respectively) were noted. Preload and afterload were optimized. Mean blood pressure between 75 and 85 mmHg was maintained. If the patient experienced mean blood pressure greater than 100 mmHg, an infusion of nitroprusside was started and the test was deferred to a later time when blood pressure was under better control. A CVP between 8 and 10 mmHg was considered optimal to start the test. If the patient had a CVP less than 8 mmHg, an infusion of 250 ml/h physiological solution was administered. After completion of baseline measurements, HM3 patients' device speeds were lowered to 5200 Revolutions per Minute (RPM) or the lowest tolerated speed. After at least a 2-minute stabilization period, echocardiographic and hemodynamic parameters, and device flows were repeated. Device speeds were then increased by 200 RPM. Another two minutes were allowed for stabilization, and all parameters were again recorded. This procedure was repeated until one of the following occurred:

1) Reaching the maximum of 6400 RPM.

2) Occurrence of suction events.

3) LVEDD decreased to less than 3.0 cm.

Doppler ultrasound blood pressure (BP) measurements were obtained using a calibrated sphygmomanometer. The doppler probe was placed over the brachial artery, and the examiner verified that the brachial pulse could be auscultated. Then the cuff, placed proximal to the doppler probe, was inflated until the doppler identified no signal. The cuff was then slowly deflated (2-3 mmHg/s), allowing the reestablishment of blood flow and a reading was taken when the pulse became audible again. Once an adequate balance between preload and

afterload and RPM was obtained, hemodynamic data were estimated and then a new hemodynamic index was calculated for all patients based on the following formula:

$$\text{HI}=\text{MAP} \times \frac{\text{PCWP}}{\text{CVP}} \times \frac{\text{RPM set}}{\text{RPM max}}$$

HI = Hemodynamic Index; MAP = Mean arterial pressure; PCWP= pulmonary capillary wedge pressure; CVP = central venous pressure; RPM = Revolutions per minute

This formula was developed with the primary intention to obtain an index that, integrating the afterload value represented by the mean arterial pressure (MAP), the ratio between the right (CVP) and left (PCWP) filling pressures and the ratio between the number of RPM set and the maximum RPM available for the HM3, could provide a parameter representing a specific hemodynamic profile.

Definition and Management of Right-Side Heart Failure

The primary outcome was late RVF after pump speed optimization during the follow-up period after LVAD implantation. Patients underwent standard treatment to prevent RVF after LVAD implantation.

These included:

1) maintaining optimal preload by preserving euvolemia;

2) optimizing pump speed to achieve maximum cardiac output, without the development of complications associated with excessive pump speeds. During the optimization test, echocardiographic images were obtained at incremental speed settings with steps of 100rpm. Optimal pump speed was defined as the highest speed that allowed intermittent aortic valve opening and neutral interventricular septum position without increased aortic or tricuspid regurgitation or RV dilatation;

3) maintaining mean arterial pressure in the range of 75- 85 mmHg.

Late right ventricular failure was defined when the following parameters were found:

1. Leftward shift of interventricular septum (SIV), MAP $<$ 65 mmHg; CVP $>$ 15 mmHg;
2. LVAD flow $<$ 3.5 L / m;
3. Moderate-severe Tricuspid Regurgitation (TR);
4. Frequent suction events.

When a moderate right function was diagnosed, intravenous diuretic therapy and aggressive fluid removal was started. Patients admitted with signs of severe right ventricular failure received inotropic support and high dosage diuretic therapy. When a severe right sided volume overload was found , fluid removal by continuous veno-venous hemofiltration (CVVH) was necessary.

Statistical Analysis

All statistical analyses were performed using SPSS 25 Categoric variables were summarized as frequencies and percentages and compared among groups using χ^2 or Fisher's exact test. Continuous variables were summarized as the mean $\pm$ standard deviation. Differences between groups were assessed using the Mann-Whitney test for unpaired samples and the Wilcoxon's test for paired samples. All P values for statistical analysis were two-tailed, and a P value less than .05 was considered to indicate a statistically significant difference. COX multiple regression analysis was used to identify risk factors for RVF after LVAD implantation. Hemodynamic data obtained during a ramp test for speed optimization were included as factors for this analysis. Initially, a univariate analysis was performed; factors with a P value less than 0.10 were then considered as candidates for a multiple regression model to identify the risk factors. We used the receiver-operating characteristic (ROC) curve with the area under the curve (AUC) analysis to calculate the best cutoff point for Hemodynamic Index association with RHF. The RVF rate after discharge was estimated using COX survival analysis.

RESULTS

Baseline Characteristics and Right Ventricular Failure

Table 1 shows the comparison of patients' characteristics, preoperative echocardiographic and hemodynamic variables, and operative details in 10 patients that developed late right ventricular failure (RVF +) and 28 patients without late RVF (RVF -) after LVAD implantation. The mean age was 56,1 ± 6,9 years in the first group and 56 ± 9 years in the second one (p=0,973). Six patients in the second group (21%) were female. Idiopathic dilated cardiomyopathy was seen in 8 RVF + patients (80%) and in 12 RVF - patients (42%), p=0,053. Ischemic cardiomyopathy was diagnosed in 2 patients (20%) of the RVF + group and in 16 (57%) of the RVF - group, p=0,048. Most of these patients, 80% RVF + and 67 % RVF -, had received inotropic therapy before LVAD implantation, and a large part was in INTERMACS class 3. All of the patients belonging to the RVF + group received LVAD therapy as Bridge to Transplant (BTT). We compared preoperative echocardiographic variables, data obtained with right heart catheterization, and preoperative laboratory variables of the two groups. There were no statistical differences in terms of preoperative echocardiographic measurements, including the grade of mitral, tricuspid and aortic regurgitation, left ventricular end-diastolic dimension, left ventricular ejection fraction, and tricuspid annular systolic excursion (TAPSE). Preoperative laboratory data, including hemoglobin, blood urea nitrogen, AST, ALT, total bilirubin, white blood cells count, creatinine, albumin, INR, and brain natriuretic peptide level, also revealed no significant difference between the groups. The preoperative right catheterization findings, including cardiac index, pulmonary vascular resistance, CVP, PCWP were also similar between the groups; however, RV stroke work index was significantly lower among patients with RVF after LVAD implantation. Of the 10 patients in the RVF + group, 8 had frequent suction events. 5 patients were readmitted for concomitant frequent low flow events with PF <3L / m. 2 patient arrived in hospital suffering from recurrent episodes of ventricular fibrillation (FV). For all patients the echocardiographic control confirmed the leftward shift of SIV and moderate-severe right ventricle disfunction. In 4 patients a LVEDD < 3 cm was found. Moderate IT and an estimated CVP > 15 mm Hg were present in 6 patients. In 2 patients, IT was judged to be severe with CVP value> 25 mmHg. 5 patients required diuretic therapy and speed optimization. in 3 patients inotropic support with adrenaline 0.05 μg / kg / min was started and progressively reduced until recovery obtained, then the medical treatment was optimized. 2 patients with severe right ventricular failure required prolonged continuous veno-venous hemofiltration and high dosage inotropic support.

Predictive value of the new Hemodynamic Index

During the ramp test, the final step at 6400 RPM was obtained in 3 (10%) patients in the RVF - group. No patient in the second group tolerated a pump speed over 6100 RPM. In 30 patients (78%) the test was stopped because frequent suction events occurred. In the other 8 patients the test was interrupted when a significant leftward shift of the SIV were diagnosed and an LVEDD less than 3 cm was echocardiographically assessed. Once speed optimization was obtained, the final increase in PS resulted significant for both groups (Table 2). Only 2 patients in the RVF + group and 5 patients in the RVF group – showed residual pulsatility. Given the small number of subjects, the level of pulsatility was not considered in our inferential analysis.

Hemodynamic variables, before and after a ramp test for patients with and patients without RVF after LVAD implantation were compared (Table 2). As shown in the table, a significant increase in pump flow (PF) and pump speed (PS) was observed in both the RVF+ group and the RVF- group. A significant reduction in the PCWP was also detected. In the RVF – group, we observed an increase in the cardiac output (CO) and a significant reduction in CVP. There were no statistical differences for the two groups between values estimated before and after the ramp test in terms of PI, MAP, SPAP, DPAP, MPAP, PVRI, SVRI, RVSWI.

Using the parameters obtained from catheterization, the hemodynamic index was calculated, as already mentioned above, before and after ramp tests with the following results:

Group RVF-: The Hemodynamic Index calculated before and after the ramp resulted respectively 96,10 ± 26,24 and 80,10 ± 13,45 (p=0,010).

Group RVF+: HI calculated pre ramp test (Fig 1) resulted 87,9 ± 19,5. In this group, the HI decreased significantly (p=<0,001) to 51,8 ± 5,3 after speed optimization.

The values of the different hemodynamic variables obtained after the ramp test, including the HI, were then analyzed in univariate analysis to evaluate the predictive effect on the right failure. Factors with a statistically significant difference between patients with and patients without RVF in the univariate analysis were considered for multivariate analysis. Multivariate analysis revealed that a low value of HI was independent risk factors for late RVF after LVAD implantation (Table 3). Other factors failed to show significant discriminatory capacity. In the resulting ROC curves, an HI of 55 provided a sensitivity of 83,2% and a specificity of 85% (Fig 2) for predicting late RVF. To examine the association between the Hemodynamic Index and outcomes, we divided patients into tertiles of the Hemodynamic Index (lowest tertile = HI < 50, middle tertile = HI between 50-80, highest tertile = HI > 80). The patients in the first group showed a worse outcome in terms of freedom from right ventricular failure when compared to the other two groups (Fig 3).

DISCUSSION

The relevant results of the present study were:

(1) The relevance of the ramp test during follow up for the hemodynamic optimization in patients implanted with Left ventricular support.

(2) Right ventricle function remains a limiting factor in patients with LVAD.

(3) The current parameters usually adopted for setting the RPM are not exhaustive to make the patient's hemodynamic profile optimal.

(4) This newly designed tool for hemodynamic optimization that we called hemodynamic index, can support clinicians to easily identify the hemodynamic profile of individual patients and to optimize medical treatment aiming to prevent events of right failure and related rehospitalizations. Based on this model, we recommend maintaining an HI above 60, during pump speed optimization, to preserve good right ventricle function while ensuring optimal left ventricle unloading. HI could provide a useful guide during ramp test, avoiding an excessive increase in rpm.

Ramp testing during right heart catheterization to optimize the RPM is recommended in the guidelines of the Society of Heart and Lung Transplantation to optimize the rpm of the device during the postoperative course. The current guidelines encourage the use of the echocardiography as an integral part in determining that adequate unloading of the left ventricle is obtained while maintaining central positioning of the septum and minimal mitral regurgitation (class I recommendation)[8]. Setting the RPM to ensure intermittent opening of the aortic valve is currently a class IIb recommendation, to prevent the development of aortic regurgitation or aortic leaflets fusion. These recommendations are somewhat vague and not standardized, and the application of right heart catheterization in conditions of clinical stability is not well defined. Right heart catheterization is currently recommended (class I) to cope with specific situations, such as when symptoms of heart failure occur, for evaluation of pulmonary hypertension in patients eligible for heart transplantation and in the event of right ventricular failure. When the explant of LVAD is planned, the hemodynamic evaluation is also recommended (class IIa) to obtain more data confirming myocardial recovery. Diagnosis of LVAD outflow obstruction or suspected device thrombosis is another indication for performing the ramp test during right heart catheterization [9]. Uriel et al. observed that an LV end-diastolic dimension slope less than an absolute value of 0,16 during a ramp test is a strong predictor of thrombosis in HeartMate II patients, and evidence not confirmed in patients implanted with HVAD [10-11]. There is no broad consensus on the routine use of right heart catheterization, and it is currently not recommended in the guidelines. Uriel et al. highlighted in their study that many patients have abnormal hemodynamic profiles at the set RPM level, despite no signs or symptoms of heart failure were identified [12]. Suwa et al. have recently demonstrated that 57% of clinically stable patients had a significant increase in CVP and PCWP at baseline LVAD speed [13]. These findings were also confirmed by our study, which estimated a PCWP value greater than 12 mmHg in 30 % of patients. In both groups, we achieved a significant reduction in PCWP after speed optimization. As highlighted by Table 2, the pre- and post- speed optimization PCWP values were respectively 17.15 $\pm$ 4.93 mmHg and 12.55 $\pm$ 2.21 mmHg ($p < 0.001$) respectively for the RVF- group. The PCWP values pre and post speed optimization in RVF + patients were 14.75 +- 3.46 mmHg and 10.16 +- 2.51 mmHg ($p < 0.001$) respectively.

Although PF and CO increases were achieved in both patient groups by improving the LVAD speed, the CO increased significantly only in the RVF - group. This finding suggests that current approaches for setting the optimal LVAD speed are insufficient and that a hemodynamic evaluation provides important additional information about the clinical condition of the patient [14]. The hemodynamic profile obtained with ramp tests during right catheterization might be used to better tailor drug therapy so that a better hemodynamic profile and a better quality of life can be achieved. Although further studies are needed, Jung et al. have highlighted how changes in hemodynamic parameters during RPM changes can have important clinical implications. Jung pointed out that a reduction in PCWP during ramp tests in patients implanted with HM II correlated with a lower NYHA class and that an increase in CO was related to a better quality of life [15]. In addiction, data are emerging concerning the effect of pump speed optimization on long-term outcomes. Sarswat et al. conducted a two-year prospective observational study of 62 LVAD patients after performing hemodynamic optimization by invasive ramp test. The rate of hospital readmission was lower in patients with an optimized hemodynamic profile when compared with patients in whom the hemodynamic condition had not been optimized. Couperus also highlighted the effectiveness of speed optimization on the function of the right ventricle [16]. Our results showed the ramp test assists in the unloading of the left ventricle but was not so effective in improving the right heart function. A significant reduction of CVP was observed only in RVF- (Tab 2). If we consider that only in RVF - patients there was a significant increase in CO, we can conclude that despite optimal unloading of the left ventricle, hemodynamic optimization is substantially conditioned by the residual intrinsic function of the right ventricle. Despite the results obtained by Couperus and Coll, the correlation between hemodynamic optimization and a reduced incidence of right ventricular failure and better survival remains to be validated. An important aspect to highlight is that many studies focus on the incidence of early right failure with minimal focus on late right failure, which however represents an important complication during support with LVAD. As described by Burke et al., late RVF could be mostly related to intrinsic myocardial function, or it could be secondary to various etiologies such as ventricular arrhythmia, the progression of tricuspid insufficiency and pulmonary hypertension [17]. Identifying these risk factors for development of late RVF is clinically very relevant since planning biventricular support can result in a better outcome, especially for high-risk BTT patients [18]. Takeda et al. found that comparing the non-RHF and RHF group, similar hemodynamic values were found, including CVP and CVP / PCWP ratio [19]. These variables are commonly representative markers of intrinsic right ventricular dysfunction. Similarly Kormos et al. reported CVP and CVP/PCWP ratio values similar in those patients who did not develop RHF when compared to patients who developed late RHF. on the other hand, patients developing early RHF showed significantly higher CVP and CVP/PCWP ratio values when compared with data from the non-RHF population [20]. From these results, it emerges that the preoperative hemodynamic evaluation is not sensitive enough to identify patients at risk of late RVF after LVAD implantation. Once the right ventricle adapts to the new physiological state guaranteed by the continuous flow pump support, other factors like the intrinsic right ventricular dysfunction can result in right hear failure. Hence the purpose of our study was to develop a new hemodynamic index calculated on hemodynamic parameters obtained after speed optimization at follow-up. Since the normal parameters such as CVP and CVP / wedge, as previously anticipated, are not adequate to identify patients at risk of RVF, we developed a parameter that integrates the filling pressures of the right and left sections, the afterload represented by the MAP, and the ratio between the optimized RPM and the maximum RPM available. The latter parameter was intended as a correction factor and expressed the support level of the device. The main purpose of this hemodynamic index is to identify a reference parameter to guide the RPM setting during ramp tests in order to optimally balance all the variables involved, thus reducing the risk of right failure. Suboptimal unloading of the left ventricle and right dysfunction are the major determinants of long-term mortality in patients with LVAD [21-22]. The LVAD pump speed can influence both factors. A high LVAD speed increases the unloading of the left ventricle and increases the cardiac output and exercise capacity [23]. However, elevated speed has been associated with aortic valve dysfunction. In particular, a reduction in the opening of the valve due to the increased pump speed results in the fusion of the valve leaflets, thrombus formation and valve insufficiency which reduces survival in patients with long-term LVAD support [24-25]. LVAD speed also has an important effect on the function of the right ventricle, the degree of unloading of the VS, pulmonary arterial pressures,

and the right ventricle afterload. A higher level of pump speed might improve right function by reducing the afterload on the right ventricle. However, excessive LVAD speed can also compromise right ventricular function because of increased preload, the leftward shift of the interventricular septum, and modification of the right ventricle's geometry. Therefore, the optimal hemodynamic balance during support with LVAD is the result of several variables that interact with each other. When considered individually, these variables fail to precisely identify a patient's hemodynamic profile and showed poor correlation with the incidence of right ventricular failure. The hemodynamic balance of patients with continuous-flow LVAD support is much more complex, and more than a single variable should be considered. The HI attempts to summarize the effects of the different variables by combining them into a single parameter that could represent a reference for the hemodynamic optimization of LVAD patients. By retrospectively evaluating our 38 patients, a HI of 51,66 +- 5,28 was found in those who required re-hospitalization with the diagnosis of late RVF and resulted significantly lower when compared with the group of patients who had not experienced a right failure episode, HI 80,10 +- 13,45 ($p<0,001$). In the RVF + group, the lower HI, according to our formula, was the result of a lower PCWP / CVP ratio, a reduced MAP, and a lower ratio between the RPM set/ RPM max. The reduced ratio between PCWP / CVP at a reduced RPM / RPM max ratio is due to a poor function of the right ventricle, illustrating a clear relationship between this hemodynamic feature and high risk of right failure. When a low hemodynamic index was found in conjunction with a low MAP, then the right dysfunction could have been explained by excessive unloading of the left ventricle and significant leftward shift of the septum and modified geometry of the right ventricle. In this case, attention should be paid to reduce antihypertensive therapy to restore normal afterload. According to our results, a ROC analysis identified a cut off level for HI of 55, a level significantly predictive of late right failure.

Our study shows that this new hemodynamic index can be used for various purposes:

1) Hemodynamic and pump speed optimization by aiming for a minimum HI of at least 55.

2) Identification of different hemodynamic profiles with stratification of patients according to the risk of late RVF. In these patients, a different strategy should be adopted by anticipating the inclusion in the transplant list or proceed with an emergency transplant.

3) Medical therapy optimization in patients with a very high HI. A very high HI is an expression of high PAM, a high value of the PCWP / CVP ratio, and high RPM set/max RPM ratio, indicative of poor left ventricular unloading. In such patients, an increase in antihypertensive therapy to reduce the afterload of the ventricle is certainly recommended (see algorithm Fig 4).

STUDY LIMITATION

Although only patients implanted with HM3 have been considered and examined, to avoid bias associated with the type of device implanted, our study has several limitations. First, this is a retrospective study conducted in a single center with a limited number of patients. Second, it was not possible, given the small number of patients, to investigate the effect of the associated repair of the tricuspid valve on the outcome and the incidence of late RVF. Third, the intervals between the patient's discharge and ramp test are variable because of different patient's eligibility to ramp test. Finally, since the limited numbers of patients, we didn't include in the analysis variables related to aortic valve opening and pulsatility that should be considered for further investigation.

CONCLUSIONS

A low HI, according to our study, is a significant risk factor for the development of RVF after LVAD implantation. This paper suggests that this index can be used during the follow-up to stratify the different hemodynamic profiles and modify the therapeutic strategies according to the different HI levels obtained for every single patient.

DATA AVAILABILITY STATEMENT

THE DATA THAT SUPPORT THE FINDINGS OF THIS STUDY ARE AVAILABLE FROM THE CORRESPONDING AUTHOR UPON REASONABLE REQUEST.

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