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RESEARCH

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Preoperative hemodynamics as predictors of right heart failure post-left ventricular assist device

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Abstract

Background: Mechanical circulatory support has garnered significant popularity as both a bridge to transplant as well as a destination therapy for patients with end-stage heart failure. Right heart failure (RHF) is a devastating complication after LVAD placement and is very unpredictable. Assisted circulation of the left ventricle (LV) with an LVAD device could unmask an underlying RHF. However, otherwise healthy right ventricles (RVs) can develop RHF after LVAD placement as well due to poor adaptation to new filling pressures and altered hemodynamics. It has been proposed that preoperative volumetric measurements in the pulmonary and systemic vasculature may serve as indicators for a risk of RHF after LVAD implantation. The aim of this study is to examine a potential relationship of preoperative hemodynamic values such as pulmonary artery pulsatility index (PAPi) and the ratio of central venous pressure to pulmonary wedge pressure (CVP/PWP) as preoperative predictors for RHF post LVAD placement.

Methods: We retrospectively reviewed patients undergoing initially planned isolated LVAD implantation with or without concomitant procedures in our institution from January 1, 2017 to June 12, 2020. Data were gathered from hemodynamic records, echocardiographic interpretations, and clinical notes. Patients who had RHF after LVAD implantation but without hemodynamic data available within 14 days from the operation were excluded. Univariable analysis was performed.

Results: Of the 114 patients who received planned isolated LVAD surgery, 70 (61.4%) experienced RHF within the first 7 days postoperatively. PAPi did not correlate significantly with RHF vs non-RHF among LVAD recipients (3.1 ± 2.1 vs. 3.8 ± 3.4 $P = 0.21$). Pre-op CVP/PWP did not differ significantly between RHF and non-RHF patients (0.4 ± 0.2 vs. 0.5 ± 0.8 $P = 0.28$). There was a nonsignificant correlation between elevated pre-op PWP and those with RHF vs those without, $OR = 1.05$ (95% CI: 1.00, 1.10). Pre-op systolic pulmonary artery pressure (SysPAP) was elevated in patients with post-LVAD RHF compared to those without (51.3 ± 12.3 vs. 47.2 ± 13.0, $P = 0.09$).

Conclusion: Preoperative hemodynamic variables such as PAPi or CVP/PWP did not show a significant correlation predicting RHF post LVAD implantation. Acute RHF post LVAD implantation remains a complex medical entity. Several studies have devised multivariable risk scores; however, their performance has been limited. Despite the widespread use of preoperative hemodynamics measurements as risk scores, our study suggests these scores are not as accurate as their use would suggest, particularly among especially morbid patient populations. More prospective studies are

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needed to accurately demonstrate how preoperative hemodynamics could predict and help prevent this catastrophic complication.

Keywords: LVAD, Right heart failure, Heart failure, Hemodynamics pulmonary artery pulsatility index

Background

Left ventricular assist device (LVAD) implantation is a mainstay in the treatment of end-stage heart failure. Unfortunately, up to 20 to 40% of device implantations are complicated by right heart failure (RHF), which results in significant morbidity and mortality [1–3]. It is a norm to require the use of pharmacologic support to wean off CPB and onto LVA—for instance, our institution starts nitric oxide and triple inotropic support before starting the CPB weaning, generally epinephrine .04–.06 mcg/kg/min, norepinephrine .04 mcg/kg/min, and vasopressin .04 U/min. However, the need for inotropic support secondary to right heart failure long after transition to LVAD is an unfortunate and common complication after LVAD implantation. To date, several studies have examined various predictors of RHF after LVAD implantation, including serum, echocardiographic, and invasive hemodynamic markers [4–10].

More recently, new methods of stratification have been developed: from selective and complex echocardiographic parameters such as RV global longitudinal strain (GLS) and free wall strain (FWS) [10], evaluation of right-sided pressure gradient (ΔpRV-RA), and RV load adaptation index (LAIRV) [11] to the compilation of various preoperative risk scores such as the Michigan risk score, PAPi, and RV-GLS [2, 6]. Newer scores have become available in recent years, like the EUROMACS-RHF score and the modified postoperative EUROMACS-RHF score, the Utah Right Ventricular Failure (RVF) risk score, and the modified Utah Right Ventricular Failure (RVF) risk score [4, 5]. The abundance of potential predictive measures and calculations is suggestive of both the universal agreement on the gravity of RHF as a postoperative complication as well as, inversely, the universal *dis*agreement on what predictive method may be best. Given the lack of consensus among these studies, accurately predicting the RV response to LVAD remains a challenge.

An important component of this challenge is the evolving definition of RHF post-LVAD, which is one of the causes of the lack of homogeneous results and criteria in the literature. The pulmonary artery pulsatility index (PAPi), defined as [(systolic pulmonary artery pressure — diastolic pulmonary artery pressure)/central venous pressure], is a hemodynamic index that predicts severe RHF in the setting of acute inferior wall myocardial infarction [12].

Previous studies have identified correlations between indices such as PAPi and CVP/PCWP with RHF after continuous-flow left ventricular assist device (CF-LVAD) surgery [3, 13]. Though the certainty of this correlation remains contested, these indices are commonly used in practice. If truly accurate, these indices would help identify which patients are at the highest risk of developing RHF after LVAD surgery and improve clinical outcomes by allowing for earlier treatment aimed at RV protection or optimization of patient selection. However, if not, providers may be giving undue significance to a predictive index that is potentially unhelpful or misguiding. The aim of the present study was to determine whether PAPi or the CVP/PCWP index predict RHF after LVAD implantation among the patient population at our institution, a tertiary care center with especially sick patients.

Methods

Patients undergoing initially planned isolated LVAD implantation with or without concomitant procedures at our institution from January 1, 2017, to June 12, 2020, were retrospectively reviewed. Data were gathered from hemodynamic records, echocardiographic interpretations, and clinical notes at our institution. Inclusion criteria for the study were patients who received an isolated LVAD at our institution in a non-emergent setting as bridge to transplant, destination therapy, or bridge to recovery within the aforementioned timeframe. Patients were excluded if there was insufficient hemodynamic data within 2 weeks of LVAD implantation, if the LVAD implantation was not planned, or if the operation occurred outside of our defined timeframe. Patients who had RHF after LVAD implantation but without sufficient hemodynamic data available were excluded. RHF was defined as either need for inotropic and/or nitric oxide support on day 7 post LVAD implantation and for 14 days postoperatively or need for right-sided circulatory support with a percutaneous or surgical RVAD. Supplementary and demographic data were collected from the Society of Thoracic Surgery National Database.

Statistics

Descriptive statistics were developed to describe patients' demographics, comorbidities, clinical status, operative details, and postoperative. Patients were analyzed in two groups, those who experienced RHF per our definition between 7 and 14 days post-peratively

Table 1 Incidence of postoperative RHF in patients undergoing LVAD implantation at UAB, 2017–2020

Surgery year	7-day postoperative		
	No RHF	RHF	Total
2017	12 37.50%	20 62.50%	32
2018	14 42.42%	19 57.58%	33
2019	15 38.46%	24 61.54%	39
2020	3 30.00%	7 70.00%	10
Total	44 38.60%	70 61.40%	114

$P = 0.91$ indicating that the incidence of RHF remains stable over time

and those who did not. Continuous variables were presented as mean (standard deviation) and compared between patients with and without RHF using Student's *t*-test. Categorical variables are presented numerically (percentage) and compared using the chi-square test. We used multivariable logistic modeling to identify risk factors associated with postoperative RHF and estimate each risk factor's odds ratio (OR) and 95% confidence interval (CI). All data analyses were conducted using SAS 9.4 (Cary, NC, USA).

Results

Baseline characteristics (Table 1), demographics (Table 2), and risk factors (Table 3) of the study population were obtained from the institutional Society of Thoracic

Table 2 Demographics in patients undergoing LVAD implantation at UAB, 2017–2020

Demographics	Overall ($n = 114$)	RHF ($n = 70$)	No RHF ($n = 44$)	*p*-value
Age (year)	51.4 ± 11.1	50.6 ± 11.6	52.5 ± 10.3	0.3882
White	66 (61.1%)	38 (57.6%)	28 (66.7%)	0.3448
Black	41 (38.0%)	27 (40.9%)	14 (33.3%)	0.4290
Hispanic	1 (0.9%)	1 (1.6%)	0 (0.0%)	0.4157
BMI	30.5 ± 6.0	29.9 ± 5.8	31.4 ± 6.4	0.1953
BMI: (0:18.5)	1 (0.9%)	0 (0.0%)	1 (2.4%)	0.2079
BMI: [18.5:25]	19 (17.6%)	17 (25.8%)	2 (4.8%)	0.0052
BMI: (25:30)	33 (30.6%)	16 (24.2%)	17 (40.5%)	0.0742
BMI: (30,:45)	53 (49.1%)	33 (50.0%)	20 (47.6%)	0.8093
BMI: > 45	2 (1.9%)	0 (0.0%)	2 (4.8%)	0.0735

*p-values comparing patients with RHF vs. no RHF. **For continuous variables mean +/−SD, *t*-test. **For categorical variables *n* (%), chi-square test

Table 3 Preoperative characteristics in patients undergoing LVAD implantation at UAB, 2017-2020

Pre-operative Characteristics	Overall (n=114)	RHF (n=70)	No RHF (n=44)	*p*-value
Pre-op SysPAP (mmHg)	49.7 ± 12.7	51.3 ± 12.3	47.2 ± 13.0	0.0931
Pre-op DiaPAP (mmHg)	25.9 ± 7.9	26.8 ± 6.8	24.5 ± 9.3	0.1239
Pre-op CVP (mmHg)	9.9 ± 5.5	10.4 ± 5.6	9.1 ± 5.4	0.2191
Pre-op PAPi (mmHg)	3.4 ± 2.7	3.1 ± 2.1	3.8 ± 3.4	0.2100
Pre-op PWP (mmHg)	27.3 ± 9.9	28.5 ± 9.6	25.5 ± 10.1	0.1195
Pre-op CVP/PWP	0.4 ± 0.5	0.4 ± 0.2	0.5 ± 0.8	0.2774
History of Hypertension	74 (68.5%)	45 (68.2%)	29 (69.0%)	0.9248
Hyperlipidemia	76 (70.4%)	44 (66.7%)	32 (76.2%)	0.2907
History of diabetes	52 (48.6%)	29 (43.9%)	23 (56.1%)	0.2212
Current Smoker	10 (9.3%)	5 (7.7%)	5 (11.9%)	0.4648
Chronic Lung Disease	26 (24.1%)	13 (19.7%)	13 (31.0%)	0.1823
Pre-op Medication: ACEI or ARB	14 (13.3%)	8 (12.7%)	6 (14.3%)	0.8147
Pre-op Creatinine mg/dL	1.2 ± 0.3	1.2 ± 0.3	1.1 ± 0.3	0.2500

*p-values comparing patients with right heart failure vs no right heart failure. **For continuous variables mean +/−SD, *t*-test. **For categorical variables n(%), chi-square test. *PAP* pulmonary arterial pressure, *CVP* central venous pressure, *PAPi* pulmonary artery pulsatility index, *PWP* pulmonary wedge pressure, *ACEI* angiotensin-converting enzyme inhibitors, *ARB* angiotensin receptor blocker

Surgeons database. The groups were similarly matched regarding operative details such as additional valve surgeries, intraoperative IABP pre-induction, and CPB time (Table 5). Demographic data were not strongly correlated with RV outcomes after LVAD implantation. There was no significantly increased risk for RHF post-LVAD among white (57.6% vs. 66.7%, $P = 0.35$), Black (40.9% vs. 33.3%, $P = 0.43$), and Hispanic (1.6% vs. 0%, $P = 0.42$) patients. A significantly increased risk of RHF was found only in patients with a BMI between 18.5 and 25 kg/m^2 (17.6% vs. 4.8%, $P = < 0.01$). Age was not found to be a significant variable in patient outcomes (50.6 ± 11.6 vs. 52.5 ± 10.3, $P = 0.39$).

Of the 114 patients who underwent planned isolated LVAD surgery, 70 (61.4%) experienced RHF. Between the patients who did and did not experience RHF post-LVAD, no difference was seen in the prevalence of a history of hypertension (68.5% vs. 69%, $P = 0.93$), hyperlipidemia (66.7% vs. 76.2%, $P = 0.29$), diabetes (43.9% vs. 56.1%, $P = 0.22$), chronic lung disease (CLD) (19.7% vs. 31.0%, $P = 0.18$), or smoking status (7.7% vs. 11.9%, $P = 0.47$) (Table 3). The use of ACE or ARB and preoperative creatinine was not found to correlate with RHF (12.7% vs. 14.3%, $P = 0.81$; 1.2 ± 0.3 vs. 1.1 ± 0.3, $P = 0.25$) (Table 3). A history of coronary artery disease (CAD) treated with percutaneous coronary intervention (PCI) was more prevalent in those who did not experience RHF post-LVAD than in those who did (19.7% vs. 40.5%, $P = 0.02$) (Table 4). A history of myocardial infarction (MI) was also more prevalent in the patients without RHF post-LVAD than those with RHF post-LVAD (21.9% vs. 47.6%, $P < 0.01$) (Table 4).

Of those patients who experienced RHF post LVAD, 10 (14.2%) required RVAD. There was no significant difference in the model of LVAD among those 70 patients who experienced RHF and those who did not: HeartMate 3 (17.1% vs 22.7%; $P = 0.46$), HeartWare HVAD (HW) (70% vs 65.9%; $P = 0.65$), and HeartMate 2 (12.9% vs 11.4%; $P = 0.81$) (Table 5).

Elevated PAPi was not associated with the occurrence of RHF among planned LVAD recipients. Average PAPi among patients who experienced post-op RHF did not significantly differ from PAPi among those patients who

Table 4 History of cardiac interventions and cardiac status in patients undergoing LVAD implantation at UAB, 2017–2020

History of cardiac interventions and cardiac status	Overall ($n = 114$)	RHF ($n = 70$)	No RHF ($n = 44$)	*p*-value
History of CVA	6 (5.6%)	4 (6.1%)	2 (4.8%)	0.7739
History of PCI	30 (27.8%)	13 (19.7%)	17 (40.5%)	0.0188
History of MI	34 (32.1%)	14 (21.9%)	20 (47.6%)	0.0055
Non-ST elevation MI (non-STEMI)	7 (6.1%)	3 (4.3%)	4 (9.1%)	0.2982
NYHA class II	1 (1.0%)	1 (1.7%)	0 (0.0%)	0.4238
NYHA class III	10 (10.2%)	6 (10.0%)	4 (10.5%)	0.9332
NYHA class IV	87 (88.8%)	53 (88.3%)	34 (89.5%)	0.8617
Ejection fraction (%)	23.8 ± 3.1	23.5 ± 2.9	24.2 ± 3.5	0.2402

**p*-values comparing patients with RHF vs. no RHF. **For continuous variables mean +/−SD, *t*-test. **For categorical variables *n* (%), chi-square test. *RCVA* cerebrovascular accident, *PCI* percutaneous coronary intervention, *MI* myocardial infarction, *NYHA* New York Heart Association

Table 5 Operative details in patients undergoing LVAD implantation at UAB, 2017–2020

Operative details	Overall ($n = 114$)	RHF ($n = 70$)	No RHF ($n = 44$)	*p*-value
Aortic valve procedure	3 (2.8%)	2 (3.0%)	1 (2.4%)	0.8413
Tricuspid valve procedure	11 (10.2%)	7 (10.6%)	4 (9.5%)	0.8561
Procedure time (as defined skin-to-skin time), min	307.3 ± 103.6	315.8 ± 104.1	294.0 ± 102.5	0.2865
Cardiopulmonary bypass time (minutes)	121.4 ± 44.0	123.7 ± 43.1	117.8 ± 45.6	0.4998
Lowest intra-op hematocrit (%)	25.1 ± 4.2	25.3 ± 4.4	24.7 ± 3.9	0.4136
Intraoperative transfusion	104 (97.2%)	64 (97.0%)	40 (97.6%)	0.8571
Intraoperative use of IABP pre-induction	73 (67.6%)	44 (66.7%)	29 (69.0%)	0.7966
HeartMate 3	22 (19.3%)	12 (17.1%)	10 (22.7%)	0.4620
HVAD	78 (68.4%)	49 (70.0%)	29 (65.9%)	0.6473
HeartMate 2	14 (12.3%)	9 (12.9%)	5 (11.4%)	0.8130

**p*-values comparing patients with RHF vs. no RHF. **For continuous variables mean +/−SD, *t*-test. **For categorical variables *n* (%), chi-square test. *HVAD* HeartWare ventricular assist device. *IABP* intra-aortic balloon pump

did not (3.1 ± 2.1 vs. 3.8 ± 3.4, $P = 0.21$) (Table 3). Pre-op CVP/PWP did not differ significantly between RHF and non-RHF patients (0.4 ± 0.2 vs. 0.5 ± 0.8, $P = 0.28$) (Table 3). There was a nonsignificant correlation between elevated preoperative PWP and those with post-LVAD RHF versus those without (*OR* = 1.05, 95% *CI*: 1.00, 1.10) (Table 7). However, no correlation was found between RHF and either risk score calculated using PWP:PAPi ($P = 0.12$) and CVP/PWP ($P = 0.28$) (Table 3). Preoperative systolic pulmonary artery pressure (SysPAP), which was factored into calculating PAPi, was elevated in patients with post-LVAD RHF compared to those without (51.3 ± 12.3 vs. 47.2 ± 13.0, $P = 0.09$) (Table 3), but this difference was not statistically significant.

The postoperative outcomes in both groups are shown in Table 6. The operative mortality was defined as all deaths occurring during the hospitalization in which the operation was performed, regardless of length of stay, and all deaths occurring after discharge from the hospital, but before the end of the 30th postoperative day, in accordance with the STS National Database Taskforce. Operative mortality was greater in patients with RHF (8.6% vs. 0%, $P = 0.04$). There were no differences in renal failure, stroke, reoperation, readmission, or wound infection (Table 6). Reoperation included reoperations for any cardiac reason, including late insertion of RVAD, sternal wound closure and washout, and bleeding.

Table 7 Parameters associated with postoperative RHF in patients undergoing LVAD implantation at UAB, 2017–2020

Parameter	OR (95% *CI*)	*p*-value
Age (year)	0.98 (0.94, 1.02)	0.38
Female	1.39 (0.51, 3.78)	0.52
Device type: HVAD vs. other	0.88 (0.35, 2.18)	0.78
Device strategy: destination vs. bridge to transplantation	0.91 (0.37, 2.24)	0.84
Pulmonary wedge pressure	1.05 (1.00, 1.10)	0.04

HVAD HeartWare ventricular assist device

Discussion

Right heart failure after LVAD placement remains a devastating and enigmatic complication. Despite the widespread use of hemodynamic variables as predictors for RHF post-LVAD in the clinical setting, the body of research surrounding their efficacy is heterogenous. One hurdle to an adequate predictive score for RHF post-LVAD may be the moving target of concretely defining RHF. The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) defines right heart failure (RHF) as signs and symptoms of persistent right ventricular (RV) dysfunction after left ventricular assist device (LVAD) implantation [14]. Established precedent exists which defines RHF as inotrope use for at least 14 days or RVAD implantation. Our study adhered partially to this established definition for the purpose of our study, as it has been frequently used to define RHF after LVAD implantation [4, 15, 16].

The most recent definition of RHF requires both the documentation of elevated central venous pressure (CVP) and manifestations of elevated CVP, including renal or hepatic dysfunction. RHF severity has also been graded based on the duration of medical therapy and the need for RVAD placement. RHF is further stratified by duration of inotrope requirement as mild (< 7 days), moderate (8–14 days), severe (> 14 days), or severe acute

Table 6 Postoperative outcomes in patients undergoing LVAD implantation at UAB, 2017–2020

Postoperative outcomes	Overall ($n = 114$)	RHF ($n = 70$)	No RHF ($n = 44$)	*p*-value
Post-op reoperation	82 (75.2%)	51 (78.5%)	31 (70.5%)	0.3421
Post-op eGFR (MDRD)	51.0 ± 22.4	48.5 ± 24.7	55.0 ± 17.7	0.1422
Post-op eGFR [0, 30 (mL/min)]	19 (17.6%)	14 (21.2%)	5 (11.9%)	0.2156
Post-op eGFR [30, 60 (mL/min)]	58 (53.7%)	38 (57.6%)	20 (47.6%)	0.3117
Post-op eGFR > 60 (mL/min)	31 (28.7%)	14 (21.2%)	17 (40.5%)	0.0310
Post-op renal failure	11 (10.2%)	9 (13.6%)	2 (4.8%)	0.1371
Newly post-op dialysis	7 (6.5%)	6 (9.1%)	1 (2.4%)	0.1674
Operative mortality	6 (5.3%)	6 (8.7%)	0 (0.0%)	0.0444
Length of stay (days)	24.4 ± 26.8	27.0 ± 32.8	20.3 ± 11.5	0.2019
Stroke	7 (6.5%)	6 (9.1%)	1 (2.4%)	0.1674
Reop due to bleeding	4 (3.7%)	4 (6.1%)	0 (0.0%)	0.1040
Postoperative transfusion	86 (79.6%)	57 (86.4%)	29 (69.0%)	0.0294
Readmission	32 (31.7%)	19 (31.7%)	13 (31.7%)	0.9966
Wound infection	1 (0.9%)	1 (1.5%)	0 (0.0%)	0.4229

**p*-values comparing patients with RHF vs. no RHF. **For continuous variables mean +/−SD, *t*-test. **For categorical variables *n* (%), chi-square test. *eGFR* estimated glomerular filtration rate, *RHF* right heart failure

(RVAD implantation) [14, 17]. A modified grading system for the severity of early right heart failure (ERHF) is associated with 1 year survival and functional capacity after CF-LVAD. Outcomes were only meaningfully worse among patients requiring RVAD or more protracted inotropes of ≥ 21 days [18]. Muslem et al. found that 1- and 2-year survival rates were significantly lower among patients with severe (inotropes > 14 days) and severe acute RHF (need for unplanned RVAD or early death due to RHF) but were not significantly different for patients with mild and moderate ERHF [19]. These findings add to those reported by LaRue et al. and support the concept that ERHF exists on a continuum of severity with respect to clinically relevant morbidity and mortality after CF-LVAD. Given these results, inotrope use for less than 14 days may not be clinically meaningful and should not be categorized as RHF for risk prediction and clinical outcomes [20]. Based in this new perception of the postop RHF as a continuum of an inevitable outcome, we modified the definition of RHF for this study to exclude all patients with mild RHF, i.e., inotrope and/or no requirement during the first week only.

Right heart failure (RHF) remains a common complication after continuous-flow left ventricular assist device (CF-LVAD) implantation. Several case series have reported that RHF occurs in 17–39% of LVAD recipients [1–3]. Specifically, severe RV failure has been associated with a threefold increase in the risk of death at 6 months and is associated with significantly longer hospitalizations [4, 16]. Determining which patients are at the highest risk of developing RHF after CF-LVAD surgery remains a challenging problem. To accomplish this goal would be to allow for earlier treatment for RV protection, precise RVAD indication, and improved outcomes in the at-risk population and patient selection.

Preoperative prediction of post-LVAD RHF is difficult not only because of the complexity of factors involved in RV function and neurohormonal and inflammatory activation but also because of the complex interactions between the risk factors related to the RV potential for recovery. All the risk factors and parameters (hemodynamic and laboratory data, ECHO) used in all studies were not sufficiently reliable to classify patients with and without a definitive risk of RHF after LVAD implantation. Currently available measurements are usually insufficient to identify patients with acceptable accuracy who will develop RHF after LVAD implantation [15, 16]. A growing body of research presents evidence of a relationship between hemodynamic measurements and RHF after LVAD implantation [3, 13, 21, 22]. Hemodynamic measures that reflect deleterious changes in RV function offer an attractive alternative to diagnostic measures of poor RV contractility in their consistency across an otherwise broad range of etiologies of RHF. These measures are also often available prior to surgery and can be gathered at different points in preoperative and postoperative care to create a dynamic, longitudinal picture of RV function.

The preoperative evaluation of the status of the right ventricle at our home institution, beside the clinical evaluation of the patient, is based in 3 areas:

1. Hemodynamic parameters: pulmonary arterial compliance index (PACi) + CVP/PCWP
2. Echocardiographic parameters: TAPSE, RV stroke work index (SWIRV) (mmHg mL/m2), and, as of recently, the RV global longitudinal strain (GLS)
3. RVF scores: Michigan

Due to the complex and multivariate nature of the systems at play in the development of RVF in LVAD candidates, the most reliable means of prediction are likely to be those which incorporate measures of different risk factors for post-LVAD RVF as well as descriptive measures of RV functionality via composite variables. RHC-derived hemodynamic measures as well as scoring systems which appropriately weigh composite preoperative data have been the most reliably predictive for postoperative RVF [1]. Such scores may incorporate laboratory data reflecting severe end-organ consequences of congestive heart failure and ECHO variables reflecting RV impairment or structural alteration (such as reduced tricuspid annulus peak systolic excursion (TAPSE), increase RV/LV diameter ratio, severe tricuspid regurgitation, decreased RV-RA pressure gradient, and increased CVP & CVP/PWCP, and low PACi) [23]. However, per the meta-analysis by Dandel et al., these parameters were not identified in all studies as significant risk factors for RVF [24]. Comprehensive review of the current research landscape suggests that commonly used and obtained clinical values and derivations thereof are generally unable to accurately identify those LVAD candidates who will develop RVF after LVAD implantation, nor can a single-risk algorithm stand in for the multivariate problem of difficult prediction [24].

Recently, the sonographic measurement of RV strain outperformed more invasive hemodynamic measures and clinical predictors as a predictor of post-LVAD implant right ventricular failure and may serve as a useful tool in risk-stratifying patients for device selection [25]. The European Registry for Patients with Mechanical Circulatory Support (EUROMACS) score is likely the best model at this time for RVF prediction post-left ventricular assist device implantation. However, in some retrospective analyses, EUROMACS-RHF risk score did not predict early RHF. While the EUROMACS score stands out among others as a potential predictor for RHF after

LVAD implantation, the literature suggests that its predictive capabilities cannot sufficiently solve the unmet need for an optimized risk score [26, 27].

Hemodynamic variables that correlate with RHF include elevated right atrial (RA) pressure and elevated RA to pulmonary capillary wedge pressure ratio (RA:PCWP). The pulmonary artery pulsatility index (PAPi) is a measure of RHF in acute myocardial infarction [10]. The numerator of the index is defined as the PA pulse pressure, which may serve as a surrogate marker of RV contractile function. The PAPi contrasts with the CVP/PCWP ratio which examines left-sided and right-sided filling pressures because the denominator of the index (RA pressure) serves as a marker of RV preload. By combining these parameters into a single index, PAPi provides insight into the RV loading conditions and mechanics [11].

The presumed utility of these measures is largely due to the phenomenon by which CF-LVAD activation alters RV mechanics by increasing RA pressure, altering the RV geometry, and shifting the interventricular septum leftward, thereby reducing RV contractile function [11].

In spite of this relationship, our results demonstrate that PAPi and CVP/PCWP as hemodynamic indices are not strongly predictive of postoperative RHF after continuous-flow LVAD implantation. In particular, we report several key findings. First, a large single-center series of CF-LVAD implants illustrates that RHF remains a common problem after LVAD implantation. Second, we report that preoperative PAPi and CVP/PWP are not conclusive determinants of postoperative RHF. These findings suggest that this simple hemodynamic calculation is not sufficient for identifying patients at high risk of developing RHF after CF-LVAD surgery in contrast to what previous studies have concluded [3, 11, 17, 28, 29].

Inconsistent with these previous observations, we report a 61% overall incidence of RHF [1, 2, 20]. Virtually, all patients receive inotropes in the days immediately following LVAD implantation. In a 2017 study by Cowger et al., a meta-analysis of the prevalence of post-LVAD RHF was 35%, although the definition of RHF post-LVAD differed from our study (14 days inotropic support vs. 7 days inotropic support, respectively), thereby creating broader inclusion criteria for RHF [20]. The increased prevalence of RHF at our institution, even after excluding mild RHF, compared to prior studies is likely due to both the changing definition of RHF as well as the baseline severity of disease of the patient population at a large, tertiary care center.

Furthermore, our results suggest that using shorter durations of post-implant inotropes may fail to accurately identify patients with clinically important ERHF. Our data suggest a limited utility of the PaPi score and RA:PCWP as indicators of RHF after CF-LVAD implantation, despite their common utilization in the field of cardiac surgery.

Study limitations

The limitations of our study include its single-center design and relatively small sample size. A second limitation is the retrospective nature of the study; a prospective study is required to determine the practical utility of our findings. Third, although our analysis is a large analysis of postoperative RHF in modern CF-LVADs, our patient population represents a small subset of the overall VAD population from a single center. As a tertiary center serving largely INTERMACS-1 patients from across the southeast, our patient population is especially sick and likely less generalizable as a consequence. Further studies are needed to validate these findings in a larger prospective cohort. Lastly, we included patients with inotrope support by postoperative day 7; therefore, there is concern that using this criterion, with its shorter duration of inotropic support, to define RHF could ultimately dilute the population of patients with true and clinically relevant RHF.

Conclusions

Clinical application of the PAPi and CVP/PCWP index to stratify patients based on the likelihood of postoperative RHF before isolated LVAD is limited. Our study did not show that either of these hemodynamic indices could improve patient selection for isolated LVAD implantation versus BiVAD implantation or identify which patients may benefit from aggressive pre- and perioperative management of RVD.

Abbreviations

CFLVAD: Continuous-flow left ventricular assist device; CVP: Central venous pressure; ΔpRV-RA: Right heart pressure gradient; ERHF: Early right heart failure; EUROMACS: European Registry for Patients with Mechanical Circulatory Support; eGFR: Estimated glomerular filtration rate; GLS: Global longitudinal strain; HVA: HeartWare ventricular assist device; HW: HeartWare; IABP: Intra-aortic balloon pump; LAIRV: Right ventricle load adaptation index; LV: Left ventricle; LVAD: Left ventricular assist device; PACi: Pulmonary arterial compliance index; PAPi: Pulmonary artery pulsatility index; PWP: Pulmonary wedge pressure; RHF: Right heart failure; RV: Right ventricle; SysPAP: Systolic pulmonary artery pressure.

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Authors' contributions

EOH and KDL contributed to the final version of the manuscript with edits and guidance from PV. KDL performed data collection. RX designed and executed data analysis and interpretation. CH and JD assisted with project design and, along with SP and EG, contributed to project development throughout including interpretation of results. The authors read and approved the final manuscript.

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Availability of data and materials
De-identified data supporting the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
Ethics approval and consent to participate were granted by the Institutional Review Board (IRB-300002865).

Consent for publication
Not applicable

Competing interests
The authors declare that they have no competing interests.

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