INCIDENCE AND OUTCOMES OF LATE-ONSET RIGHT VENTRICULAR FAILURE IN PATIENTS WITH LEFT VENTRICULAR ASSIST DEVICE

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A thesis

submitted in partial fulfillment of the

requirements for the degree of

Master of Science

University of Washington

2023

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Abstract

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Introduction: Right Ventricular Failure (RVF) is an incompletely understood complication observed in patients undergoing durable left ventricular assist device (LVAD) implantation. Prior research has primarily concentrated on early post-implantation RVF. This study seeks to characterize the incidence and clinical features associated with late-onset RVF in LVAD patients.

Methods: This retrospective cohort study included individuals undergoing LVAD implantation at the University of Washington (2005-2021), with at least 30 days of support. Late-onset RVF was defined based on Mechanical Circulatory Support Academic Research Consortium criteria, occurring over 30 days post-implantation. The outcomes of interest were time to late-onset RVF and mortality on LVAD support. Potential causal factors were examined using cause-specific models accounting for the competing events, transplant, or cardiac recovery requiring LVAD explantation. Cox regression

models assessed the risk of death associated with late-onset RVF as a time-varying exposure after LVAD implantation.

Results: The cohort consisted of 497 LVAD recipients, with a median age of 56 years (interquartile range 45-64), 18% women, and 75% Caucasian. Late-onset RVF criteria were met in 120 subjects, resulting in an incidence rate of 15.6 events per 1,000 person-months. Cause-specific competing risk analysis, stratified by self-identified ancestor identity, revealed associations between higher body mass index (BMI), peripheral vascular disease, INTERMACS 1 or 2, and longer cardiopulmonary bypass time with late-onset RVF development. Conversely, ischemic cardiomyopathy and the use of temporary MCS before LVAD implantation were linked to a reduced likelihood of late-onset RVF. After adjustment, late-onset RVF was associated with an increased hazard of death (HR: 2.8, 95% CI: 2.0–4.0 $p<0.001$).

Conclusion: Within this cohort, late-onset RVF was a prevalent complication linked to elevated mortality. Peripheral vascular disease proved to be the most robust predictor for late-onset RVF, while temporary mechanical circulatory support prior to LVAD emerged as a protective factor against this complication. Future investigations should extend to different cohorts to better understand the impact of this complication.

INTRODUCTION

Approximately 6 million adults in the United States of America suffer from heart failure,[1] of which ~5% per year may progress to a terminal stage, termed advanced heart failure. Heart transplantation is the gold-standard treatment for advanced heart failure. However, given the limited number of organ donors, it is available to only a small fraction of patients that might benefit from this intervention. Surgically implanted left ventricular assist devices (LVADs) are a viable option for patients who cannot be transplanted before an irreversible complication or death occurs.[2-4] While LVADs have successfully saved many lives,[2, 4, 5] the development of right ventricular failure (RVF) is one of the complications observed in patients chronically supported with LVADs that may negate the clinical benefits of this intervention.[6-9] Depending on the definition of RVF utilized, 5-44% of people develop RVF early (<30 days) post-LVAD implantation,[10, 11] and early RVF is associated with poorer outcomes.[9] Both pre-surgical factors, such as baseline RV function, and post-operative factors, which include a rise in RV preload and changes in cardiac geometry and septal contractility, contribute to RVF development early in the post-LVAD implantation period.[11-14]

There is growing recognition that, in addition to RVF that develops early post-LVAD, some patients may have a delayed RVF presentation, known as late-onset RVF, that develops beyond the first 30 days post-LVAD implantation. The burden and outcomes associated with this complication, defined using a contemporary definition of RVF, have not been reported. This knowledge gap arises largely from the fact that post-LVAD RVF research has focused almost exclusively on early RVF. Only a few studies describe the prevalence of late-onset RVF, but the definitions utilized in those studies [15-19] are inconsistent with and differ from the most recent definition proposed by the Mechanical Circulatory Support (MCS) Academic Research Consortium (ARC).[20] In this study, we sought to describe the incidence of late-onset RVF and outcomes associated with this complication using the MCS-ARC definition. Further, we explored the potential etiologic factors associated with this event in patients with end-stage heart failure supported with LVAD.

METHODS

Study Design and Participants:

This retrospective cohort study included all adult (≥18 years) patients with advanced heart failure who underwent LVAD implantation between July 19, 2005 and September 22, 2021 at the University of Washington (UW) Medical Center. To ensure that included patients were at risk for late-onset RVF, we included those patients on LVAD support for >30 days.

Data Collection and Event Adjudication

Data were extracted through chart review of UW medical records. Baseline information was obtained at the index hospitalization for LVAD implantation. It included demographics, clinical, laboratory, imaging, hemodynamic measurements, and need for temporary mechanical support prior to LVAD implantation. Information regarding surgical approach and post-surgical events was collected.

To adjudicate incident cases of late-onset RVF in LVAD patients, patient medical records were reviewed following the recommended algorithm of the MCS-sARC.[20] Briefly, a late-onset RVF event was defined by the presence of either clinical signs or laboratory manifestations associated with elevated right-sided filling pressure, or low cardiac output at >30 days post-LVAD implantation. Need for an associated intervention for this event, which included the use of inotropes, intravenous diuretics, or right-sided MCS, was required **(Figure 1).** After LVAD implantation, patients were followed through the end of LVAD support or the last available record in the UW healthcare system. Outcomes, including transplant, death, and LVAD explantation due to cardiac recovery, were collected. Data were extracted from the medical records and stored in a HIPAA-compliant REDCap database. The study was approved by the University of Washington Institutional Review Board (STUDY00013718, approved 7/13/2021).

Covariates and Data Analyses

Baseline characteristics were summarized as counts and percentages for categorical variables, and either means and standard deviations or medians and interquartile ranges for quantitative variables. Baseline information was obtained either immediately prior to LVAD implantation or during surgery. Time-to-event analyses were performed, for which the follow-up time starts at the date of LVAD implantation and ends at the time of either LVAD explantation due to recovery, heart transplant, death, or at last follow-up for patients still on LVAD support. The primary and secondary outcomes were, respectively, time to late-onset RVF development and time to death on LVAD support. We assessed whether each covariate met the proportional hazards assumption for the cause-specific hazard model and time-varying Cox regression model.[21]

Because the occurrence of transplant, death, or cardiac recovery requiring LVAD explantation precluded the possibility of a late-onset RVF event, these outcomes were competing events for our primary outcomes of interest **(Figure 2)**. Thus, to account for competing events, the cumulative incidence function (CIF) of late-onset RVF was estimated using non-parametric methods. To model the potential causal relationship between several prespecified factors and late-onset RVF, we used cause-specific hazards.[22] The cause-specific model included the following variables assessed at the time of LVAD implantation: age at LVAD implant; sex at birth; self-identified ancestor identity; BMI; history of diabetes; history of peripheral arterial disease; ischemic cardiomyopathy as the etiology of the heart failure; right ventricular (RV) dysfunction on echocardiogram; INTERMACS category (1-2 versus >2); device type; transpulmonary gradient prior to LVAD; the use of temporary mechanical support prior to LVAD; and cardiopulmonary bypass time. Since self-identified ancestor identity did not meet the proportional hazard assumption for this model, the analysis was performed stratified by self-identified ancestor identity.

To assess whether late-onset RVF, a time-varying exposure, is a risk factor for death among patients on LVAD support, a time-varying Cox regression model was utilized. To adjust for possible confounding effects from certain covariates, the model was

controlled for sex at birth, self-identified ancestor identity, BMI, history of diabetes mellitus, history of peripheral arterial disease, ischemic cardiomyopathy as the etiology of the heart failure, smoking, chronic CKD, and device type. For this analysis, age was modified to spline with a knot at 50 years to meet the proportional hazard assumption for this model.

Little's test was used to assess whether data was missing completely at random.[23] For multivariable analyses, missing data were handled using a complete case analysis approach.

All statistical analyses were performed using R version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Study population characteristics

A total of 497 advanced HF patients who were on LVAD support for more than 30 days were included in these analyses. The median age at implant for the cohort was 57 (IQR: 45-64) years; most were white males and INTERMACS profile ≤2. As shown in **Table 1**, a total of 4 (0.8%) patients were on VA-ECMO, and 261 (52.5%) were on another temporary MCS device before LVAD implantation**.** Pre-LVAD implantation echocardiographic and hemodynamic information are described in **Table 2**.

A total of 243 patients (48.9%) received the LVAD as destination therapy. Most LVAD patients received a HeartMate 2 device (53.3%), and most surgeries were performed via a median sternotomy approach (85.3%). Of the patients that underwent LVAD implantation, 9 (1.8%) required a temporary RV MCS device placement. As shown in **Table 3**, at the end follow-up, most patients had either been transplanted or expired while on LVAD**.**

Late-Onset RVF

A total of 120 patients supported with LVAD developed late-onset RVF during follow-up. The estimated cumulative incidence of late-onset RVF was 24.1 (95% CI 20.4 to 28.2) cases per 100 individuals at risk. The incidence rate of late-onset RVF in the study population was 15.6 (95% CI 12.9 to 18.7) new cases per 1,000 person-months at risk. Accounting for competing events, the cumulative incidence of late-onset RVF at 20 months follow-up was 18.6% (95% CI 15.3 to 22.2) (**Figure 3**).

Stratified by Black race and accounting for competing events death on LVAD support, our models identified transplant and LVAD explant due to recovery, higher BMI, peripheral vascular disease, INTERMACS 1 or 2, and longer cardiopulmonary bypass time as associated with a higher risk of developing late-onset RVF. Conversely, the presence of ischemic cardiomyopathy and the use of temporary mechanical support (excluding VA ECMO) before LVAD implantation were associated with a lower risk of late-onset RVF (**Table 4**).

Survival Associated with Late-Onset RVF in LVAD patients.

Survival was significantly reduced among patients with late-onset RVF as compared to those without this complication (**Figure 4**). In an unadjusted analysis, the presence of RVF was associated with an increased risk of dying on LVAD support (hazard ratio [HR]: 2.7, 95% confidence interval [CI]: 1.9–3.8, $p<0.001$). After multivariable adjustment for potential confounders, the presence of late RVF remained significantly associated with a higher risk of dying on LVAD support (HR: 2.8, 95% CI: 2.0–4.0, $p<0.001$, **Table 5**).

DISCUSSION

This retrospective cohort study, conducted at a high-volume center, identified that late-onset RVF is a common complication in LVAD patients and correlates significantly with increased risk for mortality. Notably, several factors, including higher BMI, INTERMACS profile 1 or 2 at LVAD implantation, history of peripheral vascular disease, and prolonged cardiopulmonary bypass time during LVAD implantation, were associated with elevated risk for late-onset RVF. Conversely, a diagnosis of ischemic cardiomyopathy or the application of temporary MCS before LVAD placement were linked to a reduced risk for late-onset RVF.

With the evolution of LVAD technology and medical treatments, risks for many LVAD-related complications, such as stroke, gastrointestinal bleeding, driveline infection, and device thrombosis, have decreased over the years.[4, 24, 25] Unfortunately, post-LVAD RVF lacks established medical treatment options.[26] Although most research has focused on RVF occurring immediately or early after LVAD implantation, known as early RVF, there is growing recognition of a delayed form of this complication, referred to as late-onset RVF. Thus far, risk factors for late-onset RVF remain poorly characterized.

It has been reported that between 5% and 45% of LVAD recipients experience late-onset RVF.[15 16-19, 27] A significant challenge in understanding the burden of late-onset RVF lies in the inconsistent definitions of this complication. However, irrespective of the definition, this complication is consistently associated with worse outcomes.[6, 16, 17, 19] Interestingly, late-onset RVF also has been linked to increased post-transplant mortality, indicating that risk for adverse outcomes may persist beyond the period of LVAD support.[15]

Various attempts have been made to define post-LVAD RVF, encompassing criteria such as the duration of pharmacological inotropic/vasopressor support, the necessity for temporary RV MCS, or multidimensional criteria such as the INTERMACS definition.[28] For this study, we adopted the most recent definition proposed by the MCS-ARC.[20] Unlike previous definitions, this latest one is more comprehensive and rigorous, requiring the presence of either clinical or laboratory findings suggestive of elevated right-sided

filling pressures or low cardiac output, in addition to requiring need for an intervention involving hospitalization and treatment such as diuretics, inotropes, or RV MCS.

Since transplant and death on LVAD support are common events that could compete with late-onset RVF, traditional survival analyses performed without accounting for competing events may yield biased results. Therefore, we opted to incorporate these events in our cause-specific hazard models to better identify factors that may be causally associated with late-onset RVF development. Additionally, we addressed competing events when estimating the incidence of late-onset RVF events, and also used late-onset RVF as a time-varying exposure when evaluating its association with death on LVAD support. Although our findings may not be directly comparable with other published studies, given that ours is the first study to follow the MCS-ARC definition of late-onset RVF and both accounts for competing events and uses RVF as a time-varying exposure, some of our observations align with previous reports.

For instance, a study by Kapelios*, et al.*, [29] found that 24% had prevalent RVF at 1 month, with 5.1% presenting with *de novo* RVF by 3 months. Additionally, they observed that persistent RVF was associated with an increased risk of mortality. That study found associations between late-onset RVF and centrifugal flow pumps, pre-implant blood urea nitrogen (BUN), severely depressed RV function on echocardiogram, and previous repair or replacement of the tricuspid valve. Rame*, et al.*,[27] reported incidences at 3, 6, and 12 months post-implant of, respectively, 5%, 6%, and 6% for mild RVF, and of 5%, 3%, and 3% for moderate RVF. Rich*, et al.*,[19] included patients enrolled in the HeartMate II trial, and reported that 8% of their patients developed this complication, with higher preoperative BUN and increased central venous pressure–to–pulmonary capillary wedge pressure ratio (RA/PCW) associated with late-onset RVF. Takeda, *et al.*,[17] found that diabetes mellitus, BMI, and BUN were significant predictors of late RVF. As compared to previous reports, our study identified a higher cumulative incidence of this complication among LVAD patients. However, due to the methodological differences mentioned earlier, direct comparisons are challenging. Notably, we did not find associations of diabetes mellitus or dysfunctional RV on echocardiogram with this complication. We did not include BUN nor the central venous pressure–to–

pulmonary capillary wedge pressure ratio, centrifugal flow pumps, or previous repair/replacement of the tricuspid valve in our analysis due to unreliable reporting of these variables or because they were out of the scope of the current study.

The association of high BMI with RV dysfunction has been reported previously in a variety of scenarios, including in LVAD patients.[30, 31] The exact mechanisms by which obesity leads to post-LVAD RVF are unclear and most likely multifactorial. The RV remodeling and dysfunction observed in patients with obesity could be mediated by an increased RV workload due to a higher circulating volume, preload, or obstructive sleep apnea, among other factors, including increases in sympathetic nervous system and renin-angiotensin-aldosterone system activation.[32-35] Interestingly, we found an association between peripheral vascular disease and higher rates of late-onset RVF, while ischemic cardiomyopathy was associated with lower rates of the same complication. On its face, this finding seems counterintuitive, as both are manifestations of atherosclerotic cardiovascular disease. One potential explanation may be that, rather than ischemic cardiomyopathy being “protective”, non-ischemic cardiomyopathies predispose to RVF, due to the presence of underlying genetic factors that may affect the both the LV and RV. To our knowledge, this is the first report of associations of peripheral vascular disease or ischemic cardiomyopathy with late-onset. Although the association of peripheral vascular disease is strong, this finding should be taken cautiously as identification of this comorbidity was obtained from medical records rather than from a formal adjudication process. The association of worse INTERMACS profile at LVAD implantation with worse post-surgical outcomes is known. However, our finding that a worse INTERMACS profile is associated with a higher rate of late-onset RVF has not been reported previously. Mechanistically, the association INTERMACS 1 or 2 at LVAD implantation may reflect that overall poorer patient health predisposes to late-onset RVF, as does for other post-LVAD complications. Conversely, support with a left-sided temporary mechanical circulatory support device before LVAD implantation appeared strongly protective for late-onset RVF development. A potential explanation for this finding is that even though the patient is sick enough to require temporary mechanical support, its use allows organ perfusion optimization and stabilization prior to LVAD implantation. Finally,

we observed that longer cardiopulmonary bypass time also was associated with this complication. It is well known that longer cardiopulmonary bypass time can elicit an inflammatory response,[36] that could eventually result in RV failure. Additionally, longer cardiopulmonary bypass time might also represent a longer and perhaps more complex surgery, longer organ malperfusion, and requiring more blood transfusions and other interventions that could contribute to the eventual development of late-onset RVF.

This study has the inherent limitations of a retrospective observational study reliant on data extracted from medical records. Another potential limitation is the possibility of changes over time in the medical management of LVAD patients. However, during the period of LVAD implantation studied, the field saw no significant changes in medical management. The study also is limited by the changing landscape of LVAD models implanted over time, with differing mechanisms and complication rates. While HeartMate II dominated in the early years, HeartMate 3 and HeartWare prevailed in the latter part. Despite the demonstrated clinical superiority of the latter two devices,[4, 37, 38] there is, at present, no data specifically suggesting that device type affects risk for RVF. Also, while definition of RVF includes objective findings extracted from medical records, some physical exam findings used for adjudication, such as elevated jugular venous pressure or ascites, may be underreported. Similarly, the accuracy of comorbidities that lacked a careful adjudication process is less certain. Further, other covariates can be subjective, inter-reader dependent, and or operator-dependent, such as the echocardiographic assessment of the RV and hemodynamic evaluation. Therefore, the interpretability of the association of these covariates with late-onset RVF should be taken cautiously. Finally, though the sample size is relatively small, it is larger than prior studies, thereby enhancing the statistical power to detect associations with RVF events.

In summary, this single-center retrospective cohort study of LVAD patients from a large volume medical center found that late-onset RVF is common and has risk-associations with multiple baseline and perioperative factors. These factors generally reflect either worse overall health condition at the time of surgery or a more complex surgical intervention. Additionally, the study found that late-onset RVF is associated with a

significantly higher mortality risk. Though retrospective, this study is the first to use the most current definition of RVF and is the largest to date examining risk factors and mortality associated with late-onset RVF. Further studies are necessary better to characterize this complication in a broader patient population.

FIGURES

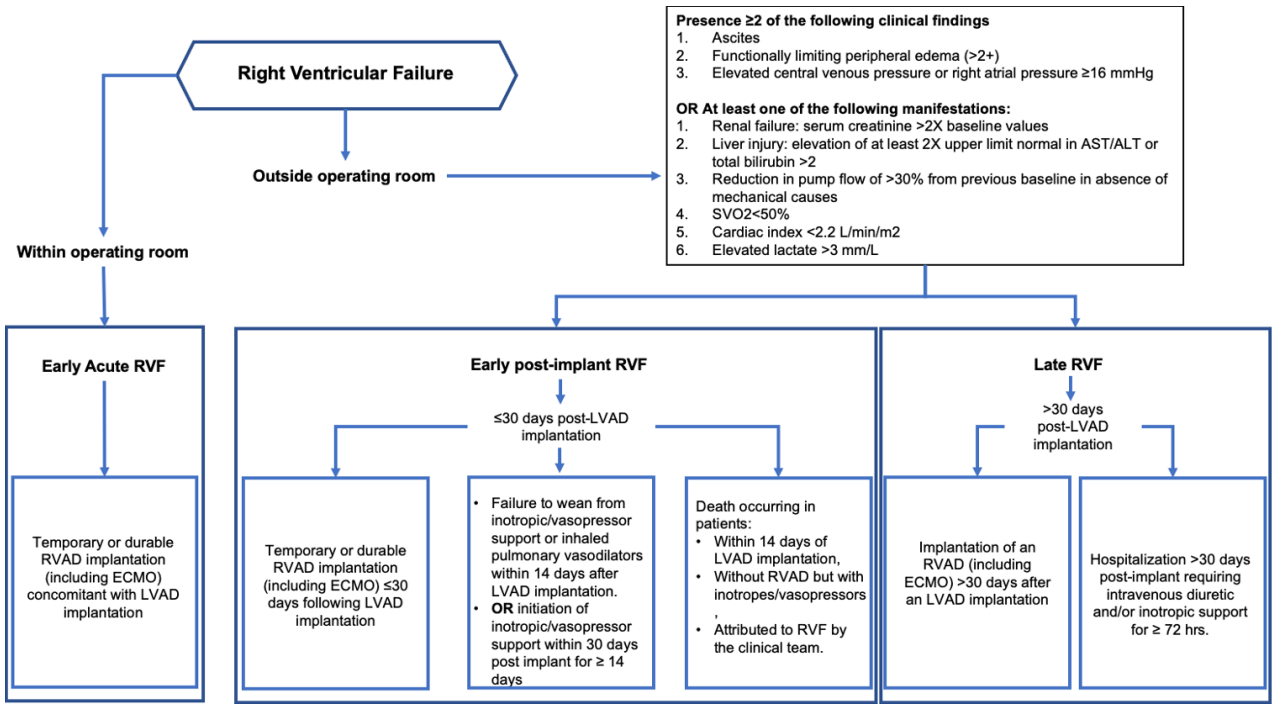

Figure 1: Algorithm for adjudicating early or late-onset RVF based on MCS ARC definition. ECMO: extracorporeal membrane oxygenator; RVAD: right ventricular assist device; and SVO2: mixed venous oxygen saturation.

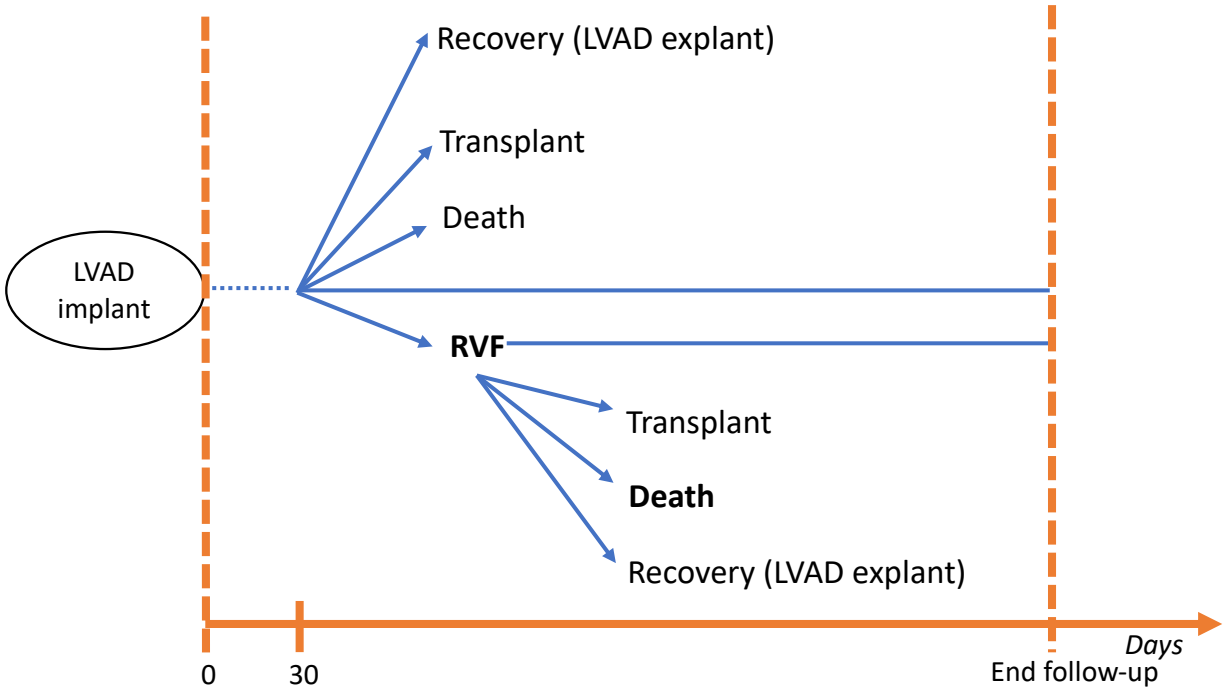

Figure 2: Diagram illustrating potential outcomes and competing events over time for a patient supported with an LVAD.

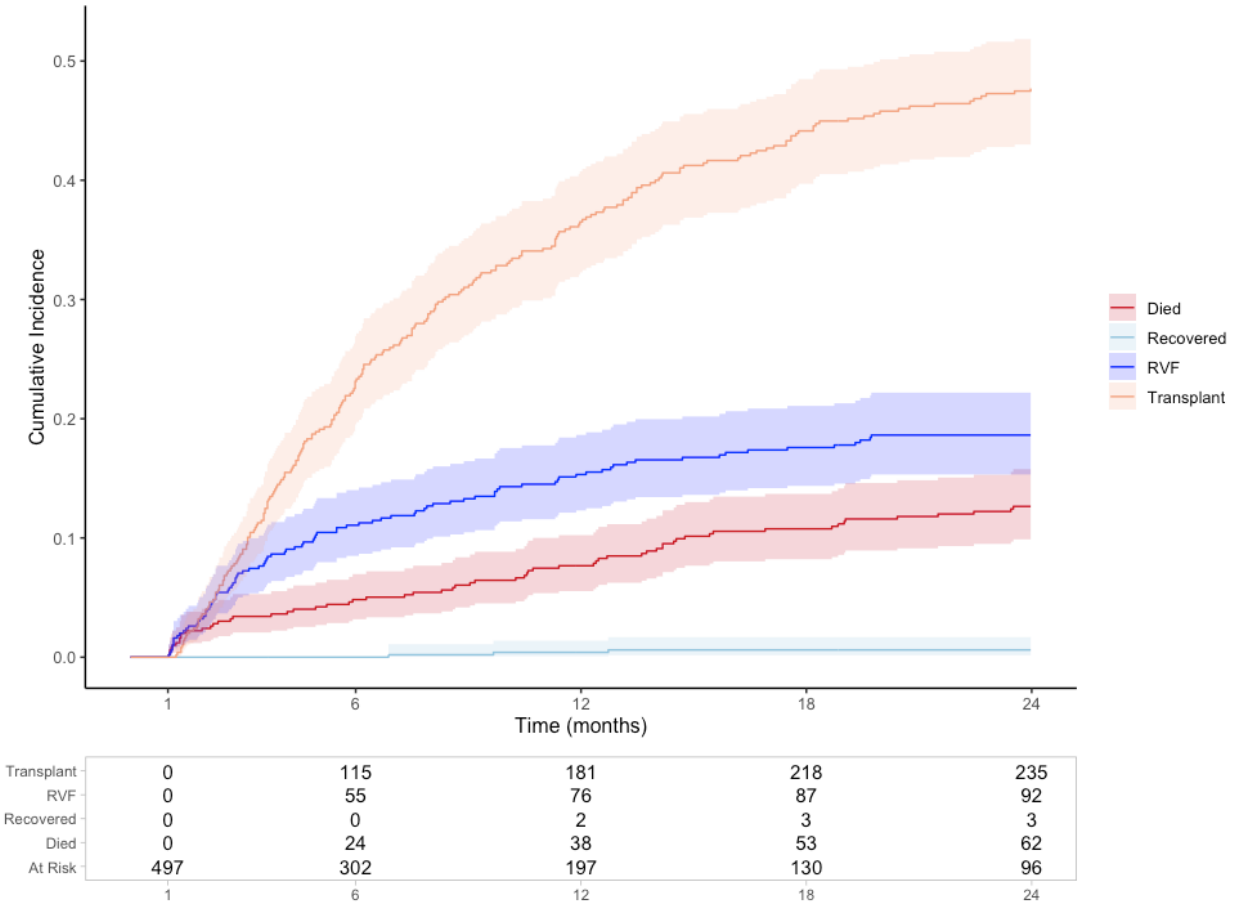

Figure 3: Competing risk analysis and cumulative incidence function plot employing the sub-distribution function in patients who underwent LVAD implantation. The potential outcomes or competing events considered in this model comprise heart transplantation (transplant), late-onset RVF (RVF), cardiac recovery necessitating LVAD explantation (recovered), and death while on LVAD support (died). Note that the event count commences 30 days post-LVAD implantation.

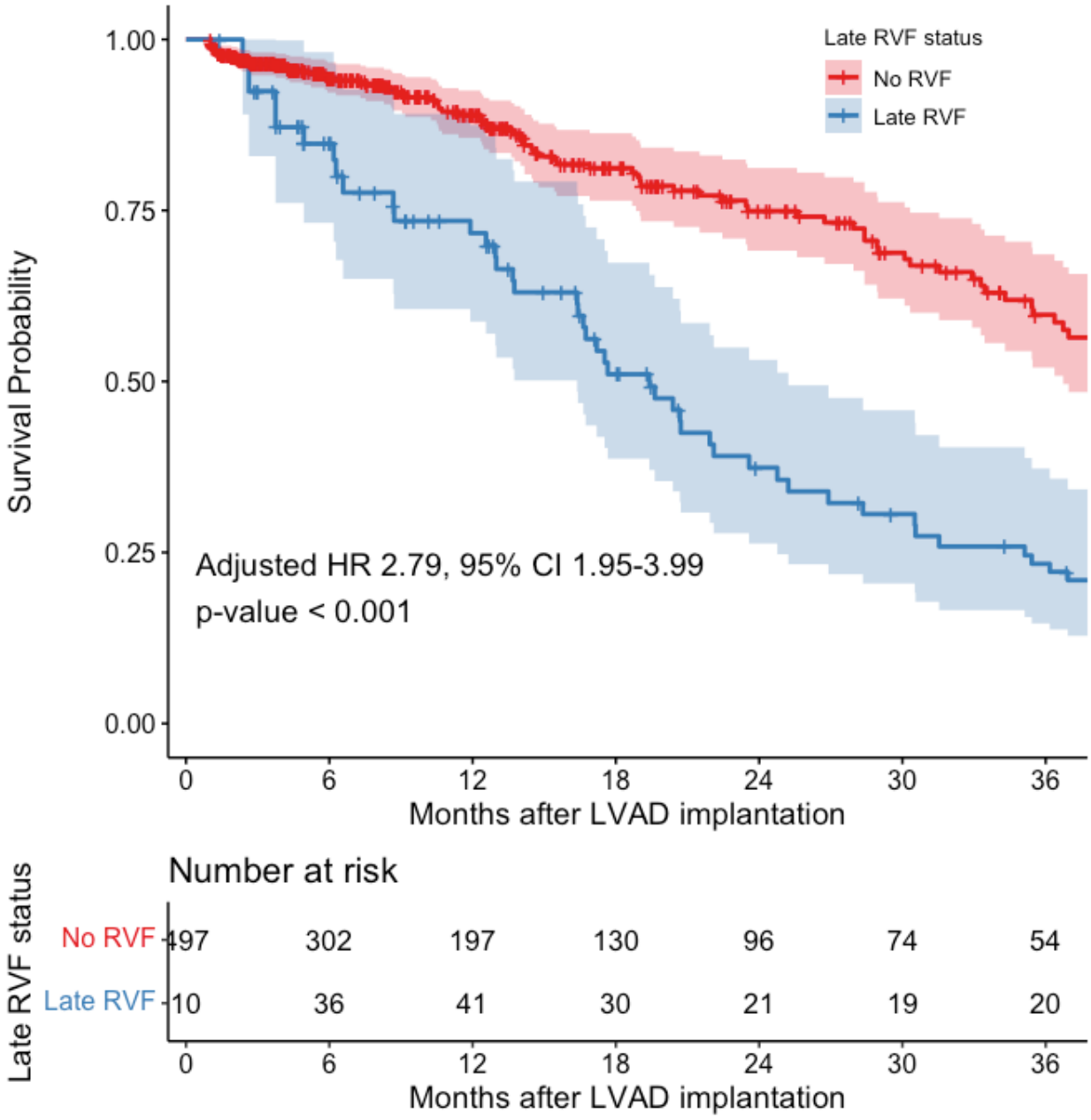

Figure 4: Kaplan-Meier curve depicting the survival probability of patients supported with LVAD, stratified by right ventricular failure status. In this analysis, cardiac recovery, heart transplantation, and the end of follow-up were considered censoring events.

TABLES

Characteristics	**N** = 497	**Black**, N = 56	**White**, N = 373	**Other**, N = 62	**p-value**
Age (years)	57 (45, 64)	51 (42, 59)	58 (47, 65)	50 (41, 59)	**<0.001**
Female	90 (18.1%)	12 (21.4%)	60 (16.1%)	16 (25.8%)	0.14
Self-identified ancestor identity					
African American or Black	56 (11.3%)	56 (100%)	0 (0%)	0 (0%)	
American Indian and Alaska Native	18 (3.6%)	0 (0%)	0 (0%)	18 (29%)	
Asian	21 (4.2%)	0 (0%)	0 (0%)	21 (33.9%)	
Native Hawaiian or Pacific Islander	14 (2.8%)	0 (0%)	0 (0%)	14 (22.6%)	
Hispanic/Latino	9 (1.8%)	0 (0%)	0 (0%)	9 (14.5%)	
White	373 (75.1%)	0 (0%)	373 (100%)	0 (0%)	
Unknown	6 (1.2%)	0 (0%)	0 (0%)	(0%)	
Body Mass Index (kg/m^2)	26.9 (23.9, 31.1)	27.8 (25.4, 33.2)	26.7 (23.8, 31.0)	26.9 (23.9, 31.2)	0.1
Unknown	2 (0.4%)	0 (0%)	1 (0.3%)	1 (1.6%)	
Diabetes	167 (33.6%)	22 (39.3%)	122 (32.7%)	23 (37.1%)	0.6
Unknown	7 (1.4%)	0 (0%)	3 (0.8%)	0 (0%)	
Peripheral Vascular Disease	32 (6.4%)	4 (7.1%)	27 (7.2%)	1 (1.6%)	0.2
Unknown	9 (1.8%)	0 (0%)	5 (1.3%)	0 (0%)	
Current or past smoker	284 (57.1%)	29 (51.8%)	215 (57.6%)	38 (61.3%)	0.7
Unknown	10 (2%)	2 (3.6%)	4 (1.1%)	0 (0%)	
Estimated GFR (mL/min/1.73m^2)	68 (49, 89)	70 (48, 89)	68 (48, 89)	65 (50, 89)	0.9
Unknown	7 (1.4%)	0 (0%)	1 (0.3%)	0 (0%)	
Ischemic Cardiomyopathy	164 (33.0%)	12 (21.4%)	134 (35.9%)	16 (25.8%)	**0.026**
Unknown	1 (0.2%)	0 (0%)	1 (0.3%)	0 (0%)	
INTERMACS					
1	41 (8.2%)	4 (7.1%)	31 (8.3%)	4 (6.5%)	
2	158 (31.8%)	17 (30.4%)	114 (30.6%)	24 (38.7%)	
3	196 (39.4%)	22 (39.3%)	149 (39.9%)	24 (38.7%)	
4	55 (11.1%)	8 (14.3%)	41 (11%)	6 (9.7%)	
5	34 (6.8%)	4 (7.1%)	28 (7.5%)	2 (3.2%)	
6	10 (2%)	1 (1.8%)	7 (1.9%)	2 (3.2%)	
7	3 (0.6%)	0 (0%)	3 (0.8%)	0 (0%)	
Pre-LVAD temporary (Excluding VA-ECMO)	261 (52.5%)	30 (53.6%)	200 (53.6%)	26 (41.9%)	0.2
Pre-LVAD RV MCS (Including VA-ECMO)	6 (1.2%)	0 (0%)	5 (1.3%)	1 (1.6%)	>0.9
Pre-LVAD VA-ECMO	4 (0.8%)	0 (0%)	3 (0.8%)	1 (1.6%)	0.7

Table 1: Pre-surgical information including all patients that underwent LVAD implantation stratified by Self-identified ancestor identity. Data are presented as median (interquartile range) or numbers (%). GFR: Glomerular filtration rate; VA-ECMO: Venoarterial extracorporeal membrane oxygenation; and MCS: mechanical circulatory support.

Characteristics	**N** = 497	**Black**, N = 56	**White**, N = 373	**Other**, N = 62	**p-value**
Echocardiographic					
Ejection Fraction (%)	19 (15, 24)	20 (15, 25)	19 (14, 24)	19 (16, 24)	0.2
Unknown	6 (1.2%)	0 (0%)	5 (1.3%)	1 (1.6%)	
LV end diastolic diameter (cm)	7.20 (6.50, 7.83)	7.30 (6.60, 8.18)	7.20 (6.50, 7.80)	7.10 (6.50, 7.70)	0.4
Unknown	13 (2.6%)	2 (3.6%)	9 (2.4%)	1 (1.6%)	
Hemodynamics					
Right atrial pressure (mmHg)	8.0 (5.0, 13.0)	8.0 (5.0, 13.0)	8.0 (5.0, 13.0)	8.0 (5.0, 13.0)	>0.9
Unknown	25 (5%)	3 (5.4%)	20 (5.4%)	1 (1.6%)	
Pulmonary artery systolic pressure (mmHg)	47 (39, 58)	50 (41, 60)	47 (38, 57)	49 (43, 60)	0.2
Unknown	17 (3.4%)	1 (1.8%)	14 (3.8%)	1 (1.6%)	
Pulmonary artery diastolic pressure (mmHg)	24 (19, 29)	25 (19, 30)	24 (18, 28)	25 (21, 30)	**0.03**
Unknown	17 (3.4%)	1 (1.8%)	14 (3.8%)	1 (1.6%)	
Mean pulmonary artery pressure (mmHg)	32 (26, 38)	34 (27, 40)	31 (25, 38)	34 (29, 40)	0.057
Unknown	17 (3.4%)	1 (1.8%)	14 (3.8%)	1 (1.6%)	
Cardiac Index by Fick (L/min/m^2)	2.07 (1.70, 2.40)	2.00 (1.70, 2.37)	2.10 (1.79, 2.45)	2.05 (1.69, 2.25)	0.3
Unknown	51 (10.3%)	5 (8.9%)	40 (10.7%)	3 (4.8%)	
Pulmonary artery pulsatility index	2.87 (1.91, 4.63)	2.92 (1.90, 4.33)	2.87 (2.00, 4.67)	2.80 (1.80, 4.44)	0.9
Unknown	27 (5.4%)	3 (5.4%)	21 (5.6%)	1 (1.6%)	
Right atrial pressure/PCWP	0.40 (0.28, 0.54)	0.42 (0.25, 0.51)	0.40 (0.28, 0.53)	0.39 (0.27, 0.60)	>0.9
Unknown	28 (5.6%)	4 (7.1%)	22 (5.9%)	1 (1.6%)	
RV stroke work index Fick	654 (488, 825)	711 (549, 841)	633 (487, 798)	663 (470, 894)	0.3
Unknown	51 (10.3%)	5 (8.9%)	40 (10.7%)	3 (4.8%)	
Transpulmonary Gradient (mmHg)	9.7 (6.7, 13.3)	11.2 (8.7, 14.3)	9.3 (6.0, 12.3)	11.3 (7.7, 15.0)	**0.008**
Unknown	20 (4%)	2 (3.6%)	16 (4.3%)	1 (1.6%)	
Pulmonary vascular resistance by Fick	2.32 (1.52, 3.40)	2.71 (1.59, 3.49)	2.15 (1.41, 3.23)	2.75 (2.01, 3.98)	**0.003**
Unknown	52 (10.5%)	6 (10.7%)	40 (10.7%)	3 (4.8%)	

Table 2: Hemodynamic and echocardiographic features before LVAD implantation stratified by self-identified ancestor identity. Data are presented as median (interquartile range) or numbers (%). LV: left ventricular; and PCWP: Pulmonary capillary wedge pressure.

Characteristics	**N** = 497	**Black**, N = 56	**White**, N = 373	**Other**, N = 62	**p-value**
Intention Destination therapy	243 (48.9%)	28 (50%)	184 (49.3%)	31 (50%)	0.2
LVAD type					0.6
HM2	265 (53.3%)	31 (55.4%)	197 (52.8%)	31 (50%)	
HM3	62 (12.5%)	6 (10.7%)	51 (13.7%)	5 (8.1%)	
HW	170 (34.2%)	19 (33.9%)	125 (33.5%)	26 (41.9%)	
Surgical Approach					>0.9
Lateral Thoracotomy	73 (14.7%)	8 (14.3%)	55 (14.7%)	10 (16.1%)	
Sternotomy	424 (85.3%)	48 (85.7%)	318 (85.3%)	52 (83.9%)	
ICU length of stay (days)	6 (4, 10)	8 (5, 14)	6 (4, 9)	7 (4, 10)	0.061
Length of stay (days)	32 (23, 47)	37 (25, 56)	31 (23, 46)	32 (24, 48)	0.14
Cardiopulmonary bypass time (mins)	89 (70, 112)	86 (64, 110)	89 (70, 112)	95 (76, 112)	0.2
Unknown	9 (1.8%)	3 (5.4%)	4 (1.1%)	2 (3.2%)	
RV MCS placed during or after LVAD implantation	9 (1.8%)	2 (3.6%)	6 (1.6%)	1 (1.6%)	0.4
Status end follow-follow up					0.6
Transplant	293 (59%)%)	33 (58.9%)	222 (59.5%)	36 (58.1%)	
Deceased	160 (32.1%)	16 (28.6%)	119 (31.9%)	21 (33.9%)	
Explant due to recovery	8 (1.6%)	1 (1.8%)	5 (1.3%)	2 (3.2%)	
On LVAD support	36 (7.2%)	6 (10.7%)	27 (7.2%)	3 (4.8%)	

Table 3: Surgical and post-surgical characteristics of those patients that underwent LVAD implantation stratified by self-identified ancestor identity. Data are presented as median (interquartile range) or numbers (%). HM2: HeartMate II™ LVAD; HM3: HeartMate 3 LVAD; HW: HeartWare™; ICU: intensive care unit; MCS: mechanical circulatory support; RV: Right ventricular; and LVAD: left ventricular assist device.

Characteristic	HR	95% CI	p-value
Age at implant (years)	1	0.99, 1.02	0.24
Female sex at birth	1	0.57, 1.57	0.9
Dysfunctional right ventricle on echocardiogram	0.9	0.35, 2.24	0.8
Body Mass Index (kg/m2)	1	1.00, 1.07	**0.033**
Ischemic cardiomyopathy as etiology	0.6	0.40, 0.96	**0.034**
Diabetes Mellitus	1.2	0.80, 1.84	0.4
Peripheral vascular disease	2	1.02, 3.74	**0.044**
INTERMACS 1 or 2 vs the rest	1.6	1.07, 2.48	**0.024**
HeartMate 3	0.9	0.49, 1.56	0.6
Transpulmonary gradient	1	0.99, 1.06	0.2
Pre-LVAD temporary MCS (excluding ECMO)	0.3	0.21, 0.52	**<0.001**
Cardiopulmonary bypass time (every 5 mins)	1	1.02, 1.07	**<0.001**

Table 4: Cause-specific competing risk analysis for RVF in LVAD patients. HR: Hazard ratio; and CI: confidence interval.

	Unadjusted			Adjusted		
Characteristic	**HR**	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**
Right ventricular failure	2.7	1.92, 3.80	**<0.001**	2.8	1.95, 3.99	**<0.001**
Age in year spline at 50 years				1	1.00, 1.01	0.2
Female				1.3	0.85, 2.08	0.2
Body Mass Index				1	0.95, 1.01	0.13
Ischemic cardiomyopathy as etiology				1.2	0.82, 1.63	0.4
Diabetes Mellitus				1.2	0.80, 1.67	0.4
Peripheral vascular disease				1.3	0.74, 2.18	0.4
Smoking history				1.6	1.12, 2.32	**0.011**
History of chronic kidney disease				1.4	1.01, 2.00	**0.044**
HeartMate 3				0.7	0.39, 1.37	0.3
Black race				0.8	0.47, 1.43	0.5

Table 5: Time-Varying Cox regression model for right ventricular failure as exposure and mortality on LVAD as outcome. HR: Hazard ratio; and CI: confidence interval.

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