Calculation of the ALMA Risk of Right Ventricular Failure After Left Ventricular Assist Device Implantation

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Right ventricular failure after continuous-flow left ventricular assist device (LVAD) implantation is still an unsolved issue and remains a life-threatening event for patients. We undertook this study to determine predictors of the patients who are candidates for isolated LVAD therapy as opposed to biventricular support (BVAD). We reviewed demographic, echocardiographic, hemodynamic, and laboratory variables for 258 patients who underwent both isolated LVAD implantation and unplanned BVAD because of early right ventricular failure after LVAD insertion, between 2006 and 2017 (LVAD = 170 and BVAD = 88). The final study patients were randomly divided into derivation (79.8%, n = 206) and validation (20.1%, n = 52) cohorts. Fifty-seven preoperative risk factors were compared between patients who were successfully managed with an LVAD and those who required a BVAD. Nineteen variables demonstrated statistical significance on univariable analysis. Multivariable logistic regression analysis identified destination therapy (odds ratio [OR] 2.0 [1.7–3.9], $p = 0.003$), a pulmonary artery pulsatility index <2 (OR 3.3 [1.7–6.1], $p = 0.001$), a right ventricle/left ventricle end-diastolic diameter ratio >0.75 (OR 2.7 [1.5–5.5], $p = 0.001$), an right ventricle stroke work index <300 mm Hg/ml/m^2 (OR 4.3 [2.5–7.3], $p < 0.001$), and a United Network for Organ Sharing modified Model for End-Stage Liver Disease Excluding INR score >17 (OR 3.5 [1.9–6.9], $p < 0.001$) as the major predictors of the need for BVAD. Using these data, we propose a simple risk calculator to determine the suitability of patients for isolated LVAD support in the era of continuous-flow mechanical circulatory support devices. *ASAIO Journal* 2018; 64:e140–e147.

Key Words: left ventricular assist device, right ventricular failure, score

Significant advances in the field of mechanical circulatory support (MCS) have yielded 1- to 3-year outcomes for continuous-flow (CF) left ventricular assist devices (LVADs) comparable with those of heart transplantation.[1,2] Despite newer technology and greater familiarity with patient management,[3,4] early right ventricular failure (RVF) is still an issue that significantly impacts survival post-LVAD implantation.[1–19]

We aimed to develop a simple and easily memorized risk stratification tool to determine whether a patient will tolerate an isolated LVAD, as opposed to requiring biventricular support (BVAD), institutionally defined as the "ALMA" score,* in the era of CF MCS devices.

Methods

Patient Population

This was a retrospective study of the medical records of patients who underwent either isolated LVAD (n = 170) or unplanned BVAD (n = 88) implantation between January 2006 and December 2017 at 2 MCS coworker institutions: S. Orsola University Hospital in Bologna and S. Camillo Hospital in Rome. Patients with complete data only, according to the official MCS datasets of both institutions, were analyzed. The contribution of the 2 centers has been comparable.

We excluded the pediatric population (<18 years of age) and patients who received total artificial heart support or first-generation pulsatile LVADs. The final study patients were divided into derivation (79.8%, n = 206) and validation (20.1%, n = 52) cohorts.

The device brand profiles for these patients are presented in **Table 1**. The majority of LVAD patients received the HeartMate II LVAS (Abbott/Thoratec Inc., Pleasanton, CA), whereas most of the unplanned BVAD patients received double CentriMag (Abbott/Thoratec Inc.) support.

Patients in the BVAD cohort included those who had sudden RVF after initial isolated LVAD implantation and required early insertion of a temporary or long-term RV assist device (RVAD).

The decision regarding RVAD insertion was based on individual patient assessment by the multidisciplinary team including experts in cardiology, cardiothoracic surgery, and cardiac anesthetic. The indication of RVAD included failure of weaning from cardiopulmonary bypass at the time of LVAD implantation and any sign of systemic low flow (*i.e.*, low urine output, low mix venous saturation, and rising lactate level) associated with elevated central venous pressure (CVP; >18 mm Hg) and "low-flow" LVAD estimation, despite escalating dose of inotropes/pressors and inhalating nitric oxide use. The decision of RVAD insertion was made before patients developed progressive end-organ dysfunction. RVAD placement technique has been described elsewhere by the same authors.[18] The mean time from primary LVAD implantation to RVAD implantation was 1.0 (0–2) day.

Demographic, clinical, and outcome data were used from the patients' charts pre-LVAD. Interagency Registry of

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Table 1. Type of Device Brand Utilized in the Isolated LVAD (n = 170) Support Population and Device Combinations Utilized in the Unplanned BVAD (n = 88) Support Population Stratified by Derivation Cohort (LVAD, n = 135; Unplanned BVAD, n = 71), and Validation Cohort (LVAD, n = 35; Unplanned BVAD, n = 17)

Isolated LVAD		Unplanned BVAD		
Derivation Cohort				
LVAD device	n	RVAD device	LVAD device	n
HeartMate II	56	CentriMag	CentriMag	34
HeartWare HVAD	33	CentriMag	HeartMate II	27
CentriMag	23	CentriMag	HeartWare HVAD	6
HeartMate 3	15	HeartWare HVAD	HeartWare HVAD	3
Jarvik 2000	6	CentriMag	HeartMate 3	1
Heart Assist 5	1			
Berlin Heart Incor	1			
Validation Cohort				
LVAD device	n	RVAD device	LVAD device	n
HeartWare HVAD	18	CentriMag	CentriMag	10
CentriMag	12	CentriMag	HeartWare HVAD	5
HeartMate 3	4	HeartWare HVAD	HeartWare HVAD	1
HeartMate II	1	CentriMag	HeartMate 3	1

BVAD, biventricular assist device; LVAD, left ventricular assist device; RVAD, right ventricular assist device.

Mechanically Assisted Circulatory Support (INTERMACS)[1] profiles were assessed just before LVAD placement. Laboratory, echocardiographic, and hemodynamic data (acquired during right heart catheterization) were obtained within 3 ± 2, 6 ± 5, and 8 ± 7 days before surgery, respectively.

Preoperative circulatory support was defined as a preoperative need for an intraaortic balloon pump or extracorporeal membrane oxygenation.

A total of 57 variables were compared between the LVAD and unplanned BVAD cohorts. All patients included in the analysis had sufficient data. The primary outcome was severe RVF within 30 days of LVAD implantation, defined as receiving short- or long-term right-sided circulatory support despite maximal dosage of continuous inotropic support and NO ventilation. The secondary outcome was all-cause mortality.

The study was approved by the institutional review boards of both hospitals.

Echocardiographic Assessment

Transthoracic echocardiographic measurements were performed using Xcelera (Philips Healthcare) and TomTec Imaging Systems software. RV systolic function was qualitatively described as (in order of severity) normal or mildly, moderately, markedly, or severely reduced. Left- and right-sided chamber dimensions and functional parameters were measured according to established guidelines.[5,6,13] The right ventricle/left ventricle (RV/LV) diameter ratio was calculated as the end-diastolic RV basal diameter/end-diastolic diameter.[13] The tricuspid annular plane systolic excursion was measured on the apical 4-chamber view by manually tracking the lateral wall tricuspid annulus from maximal systolic excursion *via* maximal diastolic relaxation and atrial contraction.[5,6,12]

Hemodynamics on Right Heart Catheterization

The mean right atrial pressure, pulmonary artery (PA) systolic, diastolic, and mean pressures, and the pulmonary capillary wedge pressure (PCWP) were measured using a PA catheter during right heart catheterization. Cardiac output was assessed using thermodilution. The transpulmonary gradient was computed as mean PA pressure – mean PCWP.[14,15] The RV stroke work index (RVSWi) was calculated as (mean PA pressure – mean right atrial pressure) × stroke volume index, where the stroke volume index was determined as the cardiac index divided by the heart rate.[14,15] The pulmonary artery pulsatility index (PAPi)[14] was calculated as [(systolic PA pressure – diastolic PA pressure)/central venous pressure].

Laboratory Parameters

Pre-MCS laboratory parameters and end-organ function were assessed by calculating the Model for End-Stage Liver Disease Excluding International Normalized Ratio (INR) score (MELD-XI; function of creatinine and total bilirubin levels) as follows: MELD-XI = 11.76 (log creatinine) + 5.112 (log total bilirubin) + 9.44.[16]

Statistical Analysis

Patient characteristics are described as means (SD) or medians for continuous variables and frequency (percentage) for categorical variables. Differences between patient groups were evaluated for continuous variables by the Student's *t*-tests or nonparametric Mann–Whitney *U* tests and for categorical variables with the χ^2 test.

Univariate logistic regression analysis was applied to relate a broad range of preoperative parameters to the study outcome, including demographics, clinical values, comorbidities, echocardiographic, hemodynamic, and laboratory parameters. Variables with a value of $p < 0.10$ entered the multivariate stage, and a logistic regression model was constructed to predict early post-LVAD right heart failure (RHF), applying the stepwise forward method, with a value of $p = 0.05$, a modelentry criterion.

We used the receiver-operating characteristic (ROC) curve area under the curve (AUC) analysis to calculate the best cutoff point for its association with RHF.

The relative magnitude of the model regression coefficients from statistically significant variables in the final multivariable model was not weighted. Instead, a simple and practical risk model was generated, in which each of the five variables identified in the final multivariable model was assigned a score of 0 or 1 (overall "ALMA" minimum and maximum scores of 0 and 5, respectively).

The model discrimination abilities were evaluated by the c index of the final multivariate model. ROC curve analysis of the "ALMA" risk score was compared with published risk scores and with individual known markers of RHF. Finally, we validated the risk model in the validation cohort.

We plotted Kaplan–Meier curves for the occurrence of up to 2-year all-cause mortality according to the presence or absence of post-LVAD RHF and stratified by the "ALMA" RHF risk score categories. The log-rank test was used to examine time to mortality differences in the Kaplan–Meier analyses. A 2-tailed value of $p < 0.05$ was considered statistically significant.

All statistics were undertaken with SPSS statistics version 24 (IBM Corp, Armonk, NY).

Results

Univariable Analysis

The individual variables with distinct differences between the isolated LVAD and unplanned BVAD cohorts were revealed by univariable analysis (**Tables 2** and 3). Both the LVAD and BVAD cohorts presented mostly an INTERMACS profile 2–3 (**Table 2**). Patients in the unplanned BVAD cohort were more likely to be female, to have a higher body mass index, and to have undergone cardiac surgery previously. Patients who underwent BVAD implantation were more likely to require mechanical ventilation or continuous veno-venous hemofiltration. Thereafter, the destination therapy (DT) strategy was the main treatment goal compared with patients who tolerated isolated LVAD therapy (**Table 2**).

Concerning the preoperative echocardiographic parameters, severe tricuspid regurgitation and high RV sphericity index values were found in the unplanned BVAD cohort preoperatively (**Table 3**). In terms of hemodynamics, a lower RVSWi and PAPi and higher CVP/PCWP ratio were detected by right heart catheter evaluations in the unplanned BVAD cohort (**Table 3**). On the other hand, pulmonary hypertension seemed to be protective in the LVAD patients. Regarding laboratory values, an elevated white blood cell count and MELD-XI score were significantly more frequent among

Table 2. Demographic and Laboratory Parameters, Baseline Risk Profiles, Univariable Analysis (Derivation and Validation Cohorts)

	Derivation Cohort			Validation Cohort		
	Isolated LVAD	Unplanned BVAD	*p*	Isolated LVAD	Unplanned BVAD	*p*
Age (y)	54.1 ± 1.6	57.3 ± 2.6	NS	53.1 ± 1.7	56.1 ± 1.4	NS
Gender (female, %)	15 (11.1)	22 (30.1)	0.05	9 (25.7)	6 (35.2)	0.05
Etiology						
Ischemic DCMP (n, %)	87 (64.4)	19 (26.7)	0.03	22 (62.8)	4 (23.5)	0.02
Nonischemic DCMP (n, %)	48 (35.5)	52 (73.2)	0.03	13 (37.1)	11 (64.7)	0.03
BMI (kg/m^2)	25.8 ± 3.2	29.8 ± 4.3	NS	24.5 ± 2.1	28.7 ± 3.1	NS
BMI >30 (n, %)	18 (13.3)	29 (40.8)	0.04	7 (20)	7 (41.1)	0.04
ICD (n, %)	98 (72.5)	58 (81.6)	NS	30 (85.7)	14 (82.3)	NS
Prior cardiac surgery (n, %)	13 (9.6)	18 (25.3)	0.04	4 (11.4)	5 (29.4)	0.03
Stroke/TIA (n, %)	7 (5.1)	4 (5.6)	NS	3 (8.5)	1 (5.8)	NS
Diabetes (n, %)	35 (25.9)	17 (23.9)	NS	8 (22.8)	4 (23.5)	NS
Atrial fibrillation (n, %)	45 (33.3)	21 (29.5)	NS	10 (28.5)	5 (29.4)	NS
Peripheral vasculopathy (n, %)	47 (34.8)	17 (23.9)	NS	12 (34.2)	3 (17.6)	NS
Hemoglobin (g/dL)	12.1 ± 1.3	11.5 ± 1.1	NS	13.1 ± 1.2	11.8 ± 1.3	NS
Hematocrit	32.5 ± 5.6	30.2 ± 6.1	NS	33.4 ± 4.8	31.1 ± 5.1	NS
Leukocytes (×1000/ml)	6.9 ± 4.7	13.3 ± 3.9	0.04	5.9 ± 3.6	12.3 ± 4.1	0.02
Platelets (×1000/ml)	156.5 ± 119.5	160.7 ± 117.6	NS	149.3 ± 112.4	162.5 ± 110.3	NS
Creatinine (mg/dl)	1.36 ± 0.6	1.67 ± 1.4	NS	1.25 ± 0.8	1.66 ± 1.2	NS
BUN (mg/dl)	42.1 ± 28.7	58.1 ± 38.8	NS	39.5 ± 20.6	60.1 ± 28.5	NS
Total bilirubin (mg/dl)	1.2 ± 0.3	1.8 ± 0.6	NS	1.3 ± 0.6	1.8 ± 0.9	NS
AST (U/L)	22.1 ± 8.8	29.7 ± 10.7	NS	20.1 ± 6.6	28.6 ± 9.8	NS
ALT (U/L)	26.2 ± 15.6	34.7 ± 12.7	NS	25.1 ± 14.4	35.5 ± 11.5	NS
INR	1.32 ± 0.62	1.83 ± 0.81	NS	1.28 ± 0.58	1.78 ± 0.61	NS
MELD-XI >17 (n, %)	10 (7.4)	22 (30.1)	0.001	6 (17.1)	6 (35.2)	0.001
Mechanical ventilation (n, %)	25 (18.5)	48 (67.6)	0.002	8 (22.8)	6 (35.2)	0.05
CVVH (n, %)	7 (5.1)	22 (30.9)	0.003	3 (8.5)	4 (23.5)	0.002
i.v. Inotropic agents	82 (60.7)	48 (67.6)	NS	23 (65.7)	11 (64.7)	NS
IABP (n, %)	61 (45.1)	36 (50.7)	NS	18 (51.4)	8 (47.1)	NS
ECMO (n, %)	4 (2.9)	—	—	2 (5.7)	—	—
INTERMACS level 1 (n, %)	4 (2.9)	—	—	2 (5.7)	—	—
INTERMACS level 2–3 (n, %)	102 (75.5)	58 (81.6)	NS	25 (71.4)	11 (64.7)	NS
INTERMACS level 4 (n, %)	29 (21.4)	13 (18.3)	NS	8 (22.8)	4 (23.5)	NS
LVAD indication						
DT (n, %)	30 (22.2)	32 (45.1)	0.02	9 (25.7)	7 (41.1)	0.03
BTC (n, %)	105 (77.7)	39 (54.9)	0.02	26 (74.2)	8 (47.1)	0.02
Device brand						
CentriMag (n, %)	23 (17.1)	34 (47.8)	0.02	12 (34.2)	10 (58.8)	0.02
HeartMate II (n, %)	56 (41.4)	27 (38.1)	NS	1 (2.8)	—	—
HeartWare HVAD (n, %)	33 (24.4)	9 (12.6)	NS	18 (51.4)	6 (35.2)	0.03
HeartMate 3 (n, %)	15 (11.1)	1 (1.4)	0.02	4 (11.4)	1 (5.8)	0.02
Jarvik 2000 (n, %)	6 (4.4)	—	—	—	—	—
Heart Assist 5 (n, %)	1 (0.7)	—	—	—	—	—
Berlin Heart Incor (n, %)	1 (0.7)	—	—	—	—	—

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; BSA, body surface area; BUN, blood urea nitrogen; BVAD, biventricular assist device; BTC, bridge to candidacy; CVVH, continuous veno-venous hemofiltration; DCMP, dilated cardiomyopathy; DT, destination therapy; ECMO, extracorporeal membrane oxygenation; IABP, intraaortic baloon pump; ICD, intracardiac defibrillator; INR, international normalized ratio; INTERMACS, Interagency Registry of Mechanically Assisted Circulatory Support; i.v., intravenous; LVAD, left ventricular assist device; MELD-XI, Model for End-Stage Liver Disease Excluding International Normalized Ratio; TIA, transitory ischemic attack.

Table 3. Hemodynamic and Echocardiographic Factors, Univariable Analysis (Derivation and Validation Cohorts)

	Derivation Cohort			Validation Cohort		
	Isolated LVAD	Unplanned BVAD	*p*	Isolated LVAD	Unplanned BVAD	*p*
HR (beats/min)	88.1 ± 22.1	95.2 ± 20.6	NS	86.3 ± 20.5	97.1 ± 15.4	NS
LV EF (%)	17.3 ± 9.1	20.1 ± 8.2	NS	15.1 ± 7.5	18.3 ± 6.6	NS
CO (l/min)	3.36 ± 0.96	3.18 ± 0.74	NS	3.12 ± 0.82	3.26 ± 0.68	NS
CI (l/min/m^2)	1.90 ± 0.4	2.03 ± 0.7	NS	1.85 ± 0.6	1.99 ± 0.5	NS
SvO2 (%)	60.2 ± 12.6	57.2 ± 7.7	NS	58.1 ± 10.4	56.4 ± 6.3	NS
MSAP (mm Hg)	78.3 ± 10.1	81.3 ± 12.1	NS	80.5 ± 9.9	80.1 ± 10.5	NS
MPAP (mm Hg)	29.9 ± 5.91	21.2 ± 7.01	NS	30.7 ± 6.55	22.7 ± 5.07	NS
TPG	9.36 ± 3.88	7.29 ± 3.53	NS	8.54 ± 2.77	7.55 ± 3.23	NS
PVR (WU)	2.79 ± 1.31	2.15 ± 1.05	NS	2.95 ± 1.45	2.11 ± 1.16	NS
PH (severe*) (n, %)	52 (38.5)	8 (11.2)	0.03	13 (37.1)	2 (11.7)	0.02
RVSWi (mm Hg/ml/m^2)	528 ± 210.5	304 ± 208.2	0.001	516 ± 181.3	299 ± 188.1	0.001
TAPSE (mm)	16.9 ± 3.1	9.6 ± 3.1	0.04	15.9 ± 5.3	8.8 ± 5.1	0.05
TR ≥ 3+ (n, %)	13 (9.6)	23 (32.3)	0.03	4 (11.4)	6 (35.2)	0.03
PAPi <2 (n, %)	9 (6.6)	28 (39.4)	0.001	3 (8.5)	6 (35.2)	0.001
CVP/PCWP >0.63 (n, %)	12 (8.8)	29 (40.8)	0.002	2 (5.7)	5 (29.4)	0.001
RV S/L ratio >0.63 (n, %)	11 (8.1)	31 (43.6)	0.001	2 (5.7)	5 (29.4)	0.001
RV/LV ratio >0.75 (n, %)	12 (8.8)	32 (45.1)	0.001	2 (5.7)	5 (29.4)	0.001

BVAD, biventricular assist device; CI, cardiac index; CO, cardiac output; CVP, central venous pressure; HR, heart rate; LVAD, left ventricular assist device; LV EF, left ventricular ejection fraction; MSAP, mean systemic arterial pressure; MPAP, mean pulmonary arterial pressure; PAPi, pulmonary artery pulsatility index; PCWP, pulmonary capillary wedge pressure; PH, pulmonary hypertension; RV, right ventricle; RVSWi, right ventricular stroke work index; RV/LV ratio, right to left ventricular end-diastolic diameter ratio; RV S/L ratio, right ventricular short/long axis ratio; SvO2, mixed venous oxygen saturation; TAPSE, tricuspid annulus plane systolic excursion; TR, tricuspid regurgitation; WU, wood units.
*According to the International Society for Heart and Lung Transplantation (ISHLT) classification.[1]

patients in the unplanned BVAD than in the isolated LVAD cohort (**Table 2**).

Multivariable Logistic Regression Analysis

A stepwise multivariable logistic regression model was created by incorporating the significant variables identified by univariate analysis. Variables predictive of the need for unplanned BVAD included DT intention, PAPi <2, RVSWi <300 mm Hg/ml/m^2, RV/LV ratio >0.75, and MELD-XI score >17 (**Table 4**).

The ALMA Risk Score

Similar to the CRITT score method,[11] for simplicity and efficiency of use, a five-point risk score was developed based on the clinical variables identified in the multivariable logistic regression model (**Table 4**). Instead of weighting variables with coefficients based on their odds ratios, each variable is given a binary response. Therefore, a patient who satisfies the at-risk criterion (*e.g.*, PAPi <2) is assigned a score of 1 for that variable *versus* 0 if not. Thus, 1 or 0 point is allotted for each of the following five variables in the institutionally defined "ALMA" score:* DT intention, PAPi <2, RVSWi <300 mm Hg/ml/m^2, RV/LV ratio >0.75, and MELD-XI score >17.

The model fit and predictive power of the five-point risk score were satisfactory when applied to the ventricular assist device data obtained from patients from the University of Bologna, S. Orsola Hospital, or Rome S. Camillo Hospital.

The predicted rate of RVF was significantly (p for linear trend <0.001) increased from 9% for a score of less than 2, to 57.1% for a score of 2–3, and to 100% for a score of 4–5 (**Figure 1**). The c index was 0.77 in the derivation *versus* 0.71 in the validation cohort (p = 0.063; **Figure 2**). In the resulting ROC curves, a score of 3.0 points provided a sensitivity of 82.5% and a specificity of 87.1% for the entire sample. The Hosmer–Lemeshow goodness-of-fit p value was 0.62 in the validation cohort, which reflects an appropriate fit for the data in this cohort. ROC curve comparison with other individual known hemodynamic, echocardiographic markers of RV failure, and other published scores (**Figure 2**) demonstrated a good performance and a high AUC for the ALMA-RVF score (**Table 5**).

Based on this model, we recommend an isolated LVAD for patients with a score of 0 or 1 and a BVAD for those with a score of 4 or 5. Patients with a score of 2 are in the gray area and may be able to tolerate an isolated LVAD with appropriate pharmacologic and/or primary temporary RVAD support, preferably associated with tricuspid valve repair (TVR).[18–20] Patients

Table 4. Results of Multivariable Logistic Regression Analysis

Characteristics	OR	95% CI	χ^2 Value (χ^2 =56.8)	Coefficients	*p*
DT	2.0	1.7–3.9	4.5	0.47	0.003
PAPi <2	3.3	1.7–6.1	12.4	0.73	0.001
RV/LV ratio >0.75	2.7	1.5–5.5	6.5	0.72	0.001
RVSWi <300 (mm Hg/ml/m^2)	4.3	2.5–7.3	17.3	1.16	<0.001
MELD-XI >17	3.5	1.9–6.9	16.01	1.06	<0.001

CI, confidence interval; DT, destination therapy; MELD-XI, Model for End-Stage Liver Disease Excluding International Normalized Ratio; PAPi, pulmonary artery pulsatility index; RV/LV ratio, right to left ventricular end-diastolic diameter ratio; RVSWi, right ventricular stroke work index.

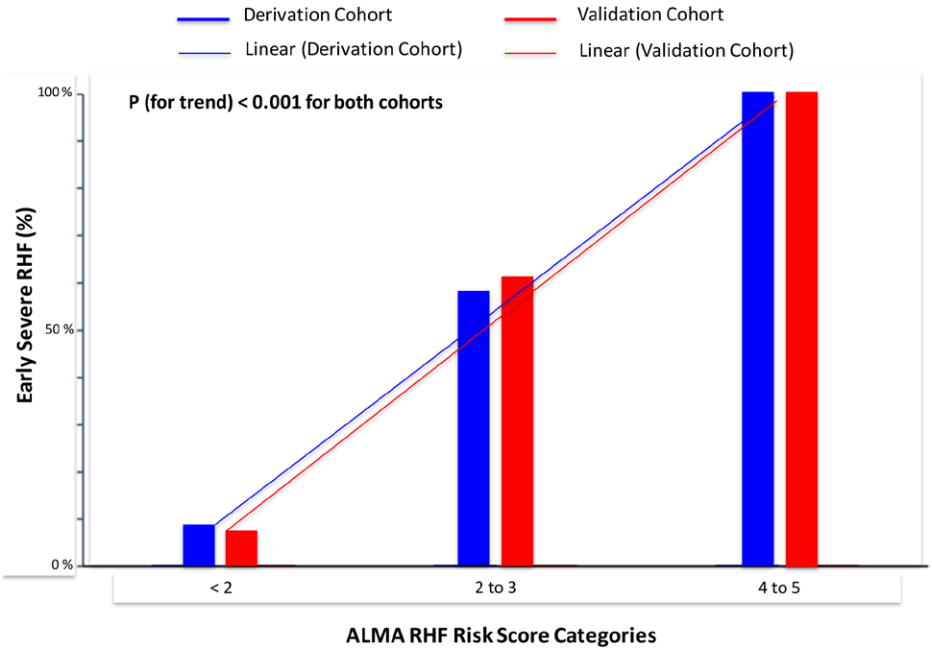

Figure 1. Frequency of early right heart failure (RHF) stratified by ALMA RHF risk score in the derivation cohort (DC) and the validation cohort (VC).

with a score of 3 have a high risk of BVAD need, but it might be speculated and investigated the same radical treatment as described above for patients with a score of 2.[18–20]

Comment

Preoperative RV function is an established prognosticator of RVF post-LVAD implantation.[1–16,18–20] RV failure is multifactorial and depends on RV preload, RV afterload, RV contractility, and ventricular geometric mechanical interdependence. Existing risk prediction models are derived from retrospective studies based on demographics, presence of end-organ dysfunction, hemodynamics, echo imaging, and prior open thoracic procedures.[1–22] Notably, most scores are derived from patient populations supported by earlier-generation pulsatile-flow pumps and hence are not fully representative of the present-day LVAD population.[5,17] The usefulness of RVF risk prediction models is limited primarily because of no standardized definition of RVF, small study sample sizes, and their modest discrimination in derivation cohorts.[5,17] Differences in the results of risk stratification tools among studies can also be caused by differences in the study duration, indications for LVAD therapy, and surgical strategies.[5,17]

As incorporated in the INTERMACS definition,[1] most of the hemodynamic factors were strong risk factors for postimplant RVF.[17] Surrogates of reduced RV contractility, that is, low PA systolic pressure, and RVSWi remain risk markers but have not yielded substantial predictive information by themselves.[5,7,14,15]

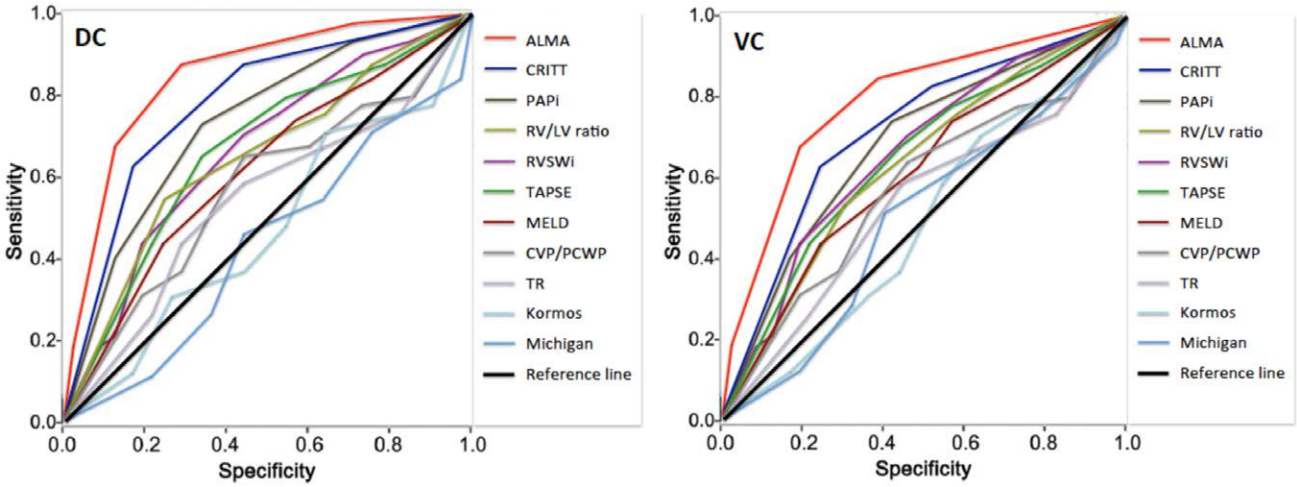

Figure 2. Receiver-operating characteristic (ROC) curve analysis derived from the derivation cohort (DC) and validation cohort (VC) stratified by current published scores[17] and single risk parameters (Table 5). CVP, central venous pressure; MELD, Model for End-Stage Liver Disease; PAPi, pulmonary artery pulsatility index; PCWP, pulmonary capillary wedge pressure; RVSWi, right ventricular stroke work index; RV/LV ratio, right to left ventricular end-diastolic diameter ratio; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation.

Table 5. Discriminatory Power of Commonly Used Indices and Scores[2,5–9,11–17] in Predicting Early Severe Right Ventricular Failure After Continuous-Flow Only LVAD Implantation (Figure 2)

Variable	AUC	95% CI	*p*
ALMA score	0.77	0.60–0.88	—
CRITT score[11]	0.74	0.62–0.86	NS
PAPi[14]	0.70	0.49–0.87	0.05
RV/LV ratio[2,13]	0.69	0.52–0.81	0.046
RVSWi[7]	0.69	0.56–0.81	0.047
TAPSE[12]	0.68	0.45–0.93	0.040
MELD score[16]	0.67	0.48–0.72	0.043
CVP/PCWP[15]	0.66	0.50–0.79	0.041
Severe TR (≥3+)[2]	0.65	0.49–0.77	0.031
Kormos score[9]	0.63	0.46–0.79	0.024
Michigan score[8]	0.60	0.48–0.75	0.028

AUC, area under the curve; CI, confidence interval; CVP, central venous pressure; MELD, Model for End-Stage Liver Disease; PAPi, pulmonary artery pulsatility index; PCWP, pulmonary capillary wedge pressure; RV/LV ratio, right to left ventricular end-diastolic diameter ratio; RVSWi, right ventricular stroke work index; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation.

A CVP/PCWP ratio >0.63 was shown to be an independent predictor of early RVF risk in the HeartMate II Bridge-to-Transplantation Pivotal Trial, with an overall low discrimination (0.68).[5,9,15]

Echocardiography is emerging as a feasible tool for evaluating parameters of RV dysfunction.[5,6,12,13,17] Puwanant *et al*.[12] demonstrated a 91% specificity and 46% sensitivity for a low tricuspid annular plane systolic excursion, with a cutoff of 7.5 mm, in predicting post-LVAD RVF. The RV/LV diameter ratio, as a surrogate of disproportionate RV remodeling analogous to the CVP/PCWP ratio, showed a strong association with RVF in some studies.[2,5,13] Moreover, the Stanford University team[14] noticed that the PAPi is a better predictor of RVF after LVAD in patients receiving inotropes when compared with the CVP/PCWP ratio. This may be because of the effect inotropes have in unloading the LV and lowering PCWP, which may increase the CVP/PCWP in patients receiving inotropes, making CVP/PCWP less predictive of RVF in that cohort. Vivo *et al*.[13] demonstrated that based on ROC curve analysis, an RV/LV diameter ratio >0.75 (AUC = 0.68) was as optimal as those obtained from the risk scoring systems of Matthews (AUC = 0.69)[8] and Kormos (AUC = 0.63)[9] in predicting RVF alone or both RVF and death.

To resume all current scores, similar to the CRITT model[11] but by adopting some of the current and accurate methods and metrics to assess RV function preoperatively,[17] we attempted to create a reliable risk stratification tool applicable to patients with end-stage heart failure.

Although many previously published risk models for RVF involve complex calculations,[5,17] the ALMA score* is very easy to use and remember. Despite the small sample size of the current study, the ALMA score* might emerge as a competitive risk stratification tool in terms of the ROC analysis results and predictive accuracy (**Table 5**; **Figure 2**).[2,5–9,11–17]

In terms of practice patterns, in our opinion, patients with an ALMA score* of 2 and 3 should be treated with the most recent surgical approaches and technologies to try to improve the current outcomes (**Figure 3**).[19] Previously, we showed that primary and prompt temporary CentriMag RVAD support in long-term LVAD recipients provides encouraging results compared with patients undergoing permanent BVAD/total artificial heart.[17,18] This may allow certain patients to be on LVAD support alone, despite preoperative biventricular dysfunction.[17,18–20]

Despite the controversy over concomitant TVR in the literature,[17,21] at our institutions, primary temporary RVAD support with TVR at the time of LVAD insertion resulted in improved early RV function with consequent higher probability of weaning from temporary RVAD.[17,19] Additionally, a minimally invasive approach to LVAD placement may contribute to further stabilize RV contractility as a result of the partial integrity of the pericardium.[17,22]

Predicting the outcome after CF LVAD placement is challenging. More sophisticated risk assessments using several continuous (rather than dichotomized) variables that build

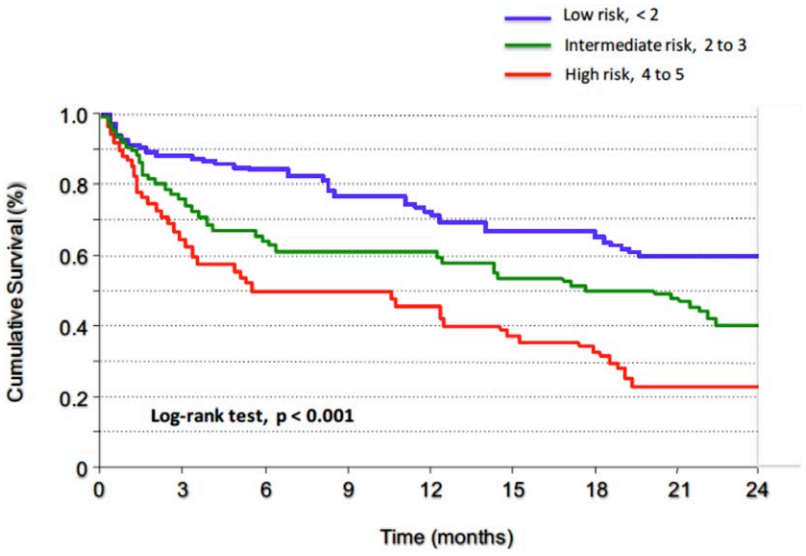

Figure 3. Two-year Kaplan–Meier estimates of death in overall study population resulting from any cause stratified by ALMA right heart failure (RHF) risk score strata.

upon already established clinical tools and employ patient data from multiple centers are needed.[5,17] Given the cost, morbidity, and mortality associated with RV failure after LVAD, in the near future, we should be able to identify the patients who will benefit most from CF LVAD placement.[17]

Limitations

This was a double-center, retrospective study, which investigated not a huge volume population sample. Only patients with complete data insertion into both official institutional MCS datasets were used for this study. Preimplant hemodynamic, echo, and laboratory parameters were not collected simultaneously before LVAD, and these parameters can evolve slightly with changes in medical therapy or a patient's clinical state. However, there was no correlation between the ALMA score* calculation and the time between clinical assessment and implantation.

Statistically, the predictors have been reduced from 57 to 19. The stepwise regression was repeated from several starting points for checking, and the procedure always converged to the same 5 variables, as well. We tried to weigh these variables as well, but the analysis provided no better predictive value thus supporting the binary model of our suggested easy scoring system.

We resulted to have a high rate of post-LVAD RVF managed mechanically with an RVAD in overall studied population if compared with the recent literature.[17] This, in our opinion, depends on our historical high volume of CentriMag implants.[23] Additionally, the CentriMag population has been more unstable preoperatively and at higher risk of post-LVAD RVF if compared with the implantable long-term LVAD (particularly newer generation) population, thus providing 2 potentially different kind of MCS recipients (paracorporeal *vs*. implantable),[17,19,23] even if not significantly in the current study. The other point is our radical and quicker decision for temporary RVAD implantation by time (even according to both institutions experience, learning curve, and clinical results as already described elsewhere[19]) with the aim to support the RV in the very early phase, thus getting the chance to wean certain patients and leave them on implantable LVAD support only despite a preoperative moderate RV dysfunction.[17,19] This resulted to provide a high volume of "unplanned BVAD" by time. For completeness, planned BVAD population, in the same study period, encountered only 44 patients, and the outcomes have been poor as partially reported elsewhere.[19]

Despite the above-mentioned limitations, we think our institutional score might contribute in providing a first indicative provisional screening before any current CF LVAD placement.

Appendix

*"ALMA" stands both for "ALMA" Mater Studiorum Bologna University and "[A]ntonio [L]oforte & [M]ontalto [A]ndrea" MCS research network.

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