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The Right Ventricular Failure Risk Score:

A Pre-Operative Tool for Assessing the Risk of Right Ventricular Failure in Left Ventricular Assist Device Candidates

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Abstract

Objectives—This study sought to develop a model that estimates the post-operative risk of right ventricular (RV) failure in left ventricular assist device (LVAD) candidates.

Background—Right ventricular failure after LVAD surgery is associated with increased morbidity and mortality, but identifying LVAD candidates at risk for RV failure remains difficult.

Methods—A prospectively collected LVAD database was evaluated for pre-operative clinical, laboratory, echocardiographic, and hemodynamic predictors of RV failure. Right ventricular failure was defined as the need for post-operative intravenous inotrope support for >14 days, inhaled nitric oxide for ≥48 h, right-sided circulatory support, or hospital discharge on an inotrope. An RV failure risk score (RVFRS) was created from multivariable logistic regression model coefficients, and a receiver-operating characteristic curve of the score was generated.

Results—Of 197 LVADs implanted, 68 (35%) were complicated by post-operative RV failure. A vasopressor requirement (4 points), aspartate aminotransferase ≥80 IU/l (2 points), bilirubin ≥2.0 mg/dl (2.5 points), and creatinine ≥2.3 mg/dl (3 points) were independent predictors of RV failure. The odds ratio for RV failure for patients with an RVFRS ≤3.0, 4.0 to 5.0, and ≥5.5 were 0.49 (95% confidence interval [CI] 0.37 to 0.64), 2.8 (95% CI 1.4 to 5.9), and 7.6 (95% CI 3.4 to 17.1), respectively, and 180-day survivals were 90 ± 3%, 80 ± 8%, and 66 ± 9%, respectively (log rank for linear trend p = 0.0045). The area under the receiver-operating characteristic curve for the RVFRS (0.73 ± 0.04) was superior to that of other commonly used predictors of RV failure (all p < 0.05).

Conclusions—The RVFRS, composed of routinely collected, noninvasive pre-operative clinical data, effectively stratifies the risk of RV failure and death after LVAD implantation.

Right ventricular (RV) failure is a major cause of morbidity and mortality in patients who have undergone placement of a left ventricular assist device (LVAD). Right ventricular failure results in poor filling of the left ventricle (LV) and poor LVAD output, often necessitating additional RV support in the form of inotropes or a right-sided mechanical device. When RV failure occurs, the perioperative mortality of LVAD surgery increases to 19% to 43% (1–3) and patients tend to have worse survival to (1,2,4–6) and after (7) cardiac transplant. Likewise, RV failure leads to increased morbidity, including delayed rehabilitation, increased transfusion requirements, and delayed or failed restoration of end-organ function (2,4). Thus, a pre-operative tool for identifying LVAD candidates at high risk for RV failure would be valuable.

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The complex pathophysiology of post-operative RV failure—RV myocardial dysfunction, ventricular interdependence, and elevated RV afterload—makes it difficult to predict. Previously identified univariable predictors of RV failure have been prognostically inconsistent when evaluated in independent samples (1,2,4–12). Using a large LVAD database, we evaluated over 80 pre-operative variables to identify independent predictors of RV failure. We then created a right ventricular failure risk score (RVFRS) to better stratify RV failure risk in LVAD candidates.

Methods

A prospectively collected database of patients receiving an LVAD at the University of Michigan between October 1996 and August 2006 was evaluated. A retrospective analysis of pre-operative clinical, echocardiographic, laboratory, and hemodynamic data was performed to determine risk for RV failure after LVAD implantation. Right ventricular failure was defined prospectively as the post-operative need for: 1) intravenous inotrope support for >14 days (1, 2,12); 2) inhaled nitric oxide (iNO) for ≥48 h; 3) right-sided circulatory support (extracorporeal membrane oxygenation [ECMO] or right ventricular assist device [RVAD]); or 4) hospital discharge with an intravenous inotrope. The decision to implement each of these interventions was based on signs of clinically significant RV dysfunction and was at the discretion of the treating physician. Data from patients with temporary right-sided circulatory support (ECMO or an extracorporeal RVAD) placed before LVAD implant were included in the primary analyses.

Variables evaluated

Clinical data evaluated included demographics; the occurrence of a pre-operative myocardial infarction, arrest, or post-cardiotomy shock; the need for life support, including mechanical ventilation, renal replacement therapy, or temporary LV mechanical bridge (defined as a Tandem Heart [CardiacAssist Inc., Pittsburgh, Pennsylvania], ECMO, or Abiomed BVS-5000 [Abiomed Inc., Danvers, Massachusetts]); or the requirement for pre-operative intra-aortic balloon pump or continuous intravenous inotrope (milrinone, dobutamine, or dopamine), vasopressor (norepinephrine, vasopressin, or phenylephrine), or antiarrhythmic therapies immediately before LVAD placement.

Echocardiograms were obtained in 193 patients (98%) before LVAD implant. Echocardiographic data included LV ejection fraction and dimensions, valvular insufficiency (graded as mild, moderate, moderate-severe, and severe insufficiency), and the presence of mild, moderate, or severe RV dysfunction. Right heart catheterizations were obtained <24 h before LVAD implant and before anesthesia induction. Hemodynamic data included measurements of right atrial (RA), pulmonary artery (PA), and pulmonary capillary wedge pressures. Cardiac output was assessed by thermodilution. Systemic vascular resistance, transpulmonary gradient, pulmonary vascular resistance (PVR), and RV stroke work index (RVSWI) were calculated. In patients undergoing extracorporeal right-sided circulatory support before LVAD implant, hemodynamic measurements were obtained immediately before implantation of RV support.

Pre-operative laboratory data were obtained <24 h before surgery and included a complete blood count, liver enzymes, serum electrolytes, albumin, and coagulation parameters. Patients requiring renal replacement therapy were assigned a creatinine of 6.0 mg/dl.

Statistical analysis

Data analysis was performed using SPSS version 14.0 (SPSS Inc., Chicago, Illinois). Laboratory and hemodynamic data were evaluated as continuous and, as appropriate,

dichotomous variables. Dichotomization of variables occurred at 25th (platelets, albumin), 50th (RVSWI, PA pressure), or 75th percentiles (PVR, aspartate aminotransferase [AST], bilirubin, blood urea nitrogen, creatinine, white count). Continuous data were evaluated for normality, and between-group comparisons were performed using either the Student *t* or the Mann-Whitney *U* test for normal and non-normal data, respectively. Categorical data were compared with the Fisher exact test for 2 × 2 tables or Pearson chi-square otherwise. Stepwise forward multivariable logistic regression analyses were performed on univariable predictors of RV failure (entry criterion $p \leq 0.1$). An RVFRS was devised by rounding the exponentiated regression model coefficients to the nearest 0.5. A receiver-operating characteristic curve of the RVFRS was created, and the area under the curve (AUC) for the score was calculated. The AUCs were also calculated for previously published univariable predictors of RV failure (RA and PA systolic pressures, PVR, transpulmonary gradient, RVSWI, and severe RV failure on echocardiogram) (1,5–12). The AUC for the RVFRS was then compared to each of the other AUCs (13). Kaplan-Meier survival curves were created to evaluate post-LVAD survival (defined as continued LVAD support at the time of last follow-up, LVAD explant with survival >1 year without repeat LVAD or transplant, or cardiac transplant) and, in those patients listed for transplant, freedom from death on the transplant list. Survival between groups was analyzed by log rank for linear trend. Unless otherwise specified, all data are expressed as mean ± standard deviation.

This study was approved by the University of Michigan Medicine Institutional Review Board, and written informed consent was obtained before patient participation.

Results

There were 197 LVADs implanted during the period of study, with 94% placed as a bridge to transplant and 6% for destination therapy. Implanted pumps included the HeartMate 1000 IP (n = 15, 8%), HeartMate VE (n = 65, 33%), HeartMate XVE (n = 77, 39%), HeartMate II (n = 28, 14%), Thoratec IVAD (n = 7, 4%), Thoratec VAD (n = 2, 1%) (all manufactured by Thoratec Corp, Pleasanton, California), Novacor ([n = 1, 1%], WorldHeart Corp., Oakland, California) and Micromed ([n = 2, 1%], MicroMed Cardiovascular Inc., Houston, Texas) devices. Indications for LVAD included heart failure of nonischemic (n = 95, 48%) or ischemic (n = 102, 52%) etiologies. Thirty-six (35%) patients in the latter group had acute ischemic heart failure, 16 (44%) of whom developed shock after bypass surgery. Eight (4%) subjects required pre-operative RV mechanical support (Abiomed BVS 5000). An LV mechanical bridge was required in 45 (22%) and 55 (28%) were supported with a pre-operative intra-aortic balloon pump. Before LVAD implantation, 16 (8%) patients required renal replacement therapy and 47 (24%) were on a ventilator.

Sixty-eight (35%) LVAD operations were complicated by post-operative RV failure. Right ventricular failure was diagnosed based on the need for post-operative right-sided circulatory support in 29 (43%), prolonged post-operative inotropes in 45 (69%), prolonged iNO in 33 (49%), and/or discharge to home on inotropes in 6 (9%). No patient met the definition of RV failure based solely on a home inotrope requirement. Four patients (6%) met RV failure criteria because of an isolated requirement for prolonged iNO. Of the 29 patients requiring RV circulatory support after LVAD implantation, 17 (59%) received an Abiomed, 4 (14%) a Thoratec RVAD, and 8 (27%) were supported with ECMO.

The presence of RV failure for each of the pre-operative recipient demographics and associated odds ratios (OR) for univariable predictors of RV failure with a $p \leq 0.1$ are shown in Table 1. Smaller body surface area, history of a stroke, and absence of a prior sternotomy were the only demographic predictors of RV failure.

Table 2 depicts the pre-operative events and medical interventions that occurred in the LVAD sample. The odds of RV failure were 2-fold higher in patients who experienced an arrest at any time in the pre-operative period ($p = 0.03$). The odds of RV failure were also higher in patients needing renal replacement therapy or ventilatory support ($p \leq 0.001$). Subjects requiring a temporary mechanical LV bridge before LVAD surgery had 3-fold higher odds of RV failure than those who did not, with 68% of patients on ECMO and 64% of patients with a Tandem Heart subsequently developing post-LVAD RV failure ($p = 0.001$). Post-cardiotomy shock was not associated with an increased risk of RV failure.

The need for pre-operative mechanical extracorporeal RVAD support was not associated with increased risk of RV failure after LVAD placement (Table 2) ($p = 0.45$). Of the 8 patients supported with a pre-operative RVAD, 4 experienced persistent RV failure during or after LVAD implantation, of whom 3 required replacement of the RVAD at the time of LVAD implantation (mean duration of RVAD support after LVAD implant = 11 ± 9 days). One subject experienced recurrent RV failure, defined by the need for prolonged inotropes (17 days) and inhaled iNO (4 days).

Pre-operative intravenous medications

Patients requiring pre-operative intravenous vasopressor or antiarrhythmic therapies were more likely to have RV failure after LVAD implantation (Table 3). Likewise, higher dose requirements for vasopressin ($p = 0.001$) and phenylephrine ($p = 0.018$) were associated with RV failure. Right ventricular failure developed less frequently in individuals supported with milrinone and in those requiring higher milrinone doses ($p \leq 0.009$), possibly reflecting poor tolerance of the vasodilatory properties of this agent in a patient sample with overall increased vasopressor requirements.

Pre-operative echocardiography and cardiopulmonary hemodynamic measurements

In Table 4, pre-operative echocardiographic and hemodynamic data are presented. The only echocardiographic parameter that portended increased odds of RV failure was the presence of severe RV systolic dysfunction ($p = 0.01$). Patients with lower RVSWI, cardiac index, and PA systolic and mean pressures were more likely to develop RV failure ($p < 0.05$). When evaluated categorically, a PA systolic pressure <50 mm Hg ($p = 0.035$) and RVSWI <450 mm Hg·ml/m^2 ($p = 0.012$) were predictive of RV failure. The RA pressure, PVR, and transpulmonary gradient were not predictive of RV failure.

Pre-operative laboratory measurements

Table 5 depicts pre-operative laboratories. There were increased odds of RV failure in patients with higher blood urea nitrogen, creatinine, glucose, white blood cell count, AST, and total bilirubin, whereas the risk of RV failure was decreased in patients with higher platelet counts ($p < 0.05$ for each). Categorical evaluation of the laboratory parameters revealed increased odds of RV failure in patients with a creatinine ≥2.3 mg/dl (OR 5.56), blood urea nitrogen ≥48 mg/dl (OR 2.06), white blood cell count ≥12.2 k/mm^3 (OR 2.71), platelet count ≤120 k/mm^3 (OR 3.36), albumin ≤3.0 g/dl (OR 1.86), AST ≥80 IU/l (OR 3.20), and bilirubin ≥2.0 mg/dl (OR 3.59) (all $p < 0.05$).

RVFRS

All clinical, echocardiographic, laboratory, and hemodynamic variables with a univariable $p \leq 0.1$ for predicting RV failure were entered into multivariable analyses. Remaining independent ($p \leq 0.1$) predictors of RV failure included a vasopressor requirement (OR 3.9, 95% confidence interval [CI] 1.5 to 9.8), AST ≥80 IU/l (OR 2.1, 95% CI 0.96 to 4.5), bilirubin ≥2.0 mg/dl (OR 2.4, 95% CI 1.1 to 5.2), and creatinine ≥2.3 mg/dl (OR 2.9, 95% CI 1.1 to 7.7).

These variables, therefore, were selected as the components of the RVFRS. The RVFRS was calculated as the sum of the points awarded for the presence of each of the 4 pre-operative variables, with a vasopressor requirement assigned 4 points, AST ≥80 IU/l assigned 2 points, bilirubin ≥2.0 mg/dl assigned 2.5 points, and creatinine ≥2.3 mg/dl (or renal replacement therapy) assigned 3 points.

Applying the RVFRS in this sample (Table 6), the odds of RV failure for patients (n = 30) with an RVFRS ≥5.5 were 15-fold greater than those (n = 142) with an RVFRS ≤3.0, and about 3-fold greater than subjects (n = 25) with a RVFRS of 4.0 to 5.0. Of the 129 patients who did not develop RV failure, 113 had an RVFRS ≤3.0 (specificity = 88%); the absence of RV failure was correctly identified in 113 of 142 patients with an RVFRS ≤3.0 (negative predictive value = 80%). Among 68 patients with RV failure, an RVFRS ≥5.5 identified 24 (sensitivity = 35%). However, 24 of 30 patients with an RVFRS ≥5.5 developed RV failure (positive predictive value = 80%).

The AUC for the RVFRS (Fig. 1) was 0.73 ± 0.04. Receiver-operating characteristic curves were also generated for commonly used predictors of RV failure, including RVSWI, transpulmonary gradient, PVR, RA, and PA systolic pressures, and severe RV failure on echocardiography (Fig. 1, Table 7) (1,5,7–12). Comparison of the AUC of the RVFRS with that of the other previously identified predictors shows that the RVFRS is a more discriminative predictor of RV failure (all $p < 0.05$).

Survival and RVFRS

During the 180 ± 236 days of follow-up, 4 (2%) patients were permanently weaned from LVAD support without death or transplant, 17 (9%) remained supported, 39 (20%) died, and 137 (70%) were transplanted. Twenty-six (38%) patients with post-operative RV failure died compared with 13 (10%) without complicating RV failure (OR death 5.5, 95% CI 2.6 to 11.8). Of these deaths, 21 (81%) and 6 (46%), respectively, occurred in the operating room. Figure 2 depicts the Kaplan-Meier survival curves for the high (RVFRS ≥5.5), medium (RVFRS 4.0 to 5.0), and low (RVFRS ≤3.0) risk score strata. The 180-day post-LVAD survivals were 66 ± 9%, 80 ± 8%, and 90 ± 3% for the high, medium, and low RVFRS strata, respectively, with a log rank for linear trend $p = 0.0045$, showing the increased mortality risk associated with higher RVFRS.

In those individuals (n = 185) bridged to transplant with an LVAD, freedom from death on the transplant list was 54 ± 11% and 89 ± 5% for patients with (n = 65) and without (n = 120) RV failure, respectively, at 1 year ($p < 0.005$). Freedom from death on the transplant list for high, medium, and low strata RVFRS was 66 ± 9%, 53 ± 22%, and 85 ± 5%, respectively, at 1 year (log rank $p = 0.002$).

Discussion

Right ventricular failure after LVAD surgery is associated with increased post-operative morbidity and mortality. However, criteria for RV support are poorly defined because definitions of RV failure vary and its prediction is difficult (14). Using extensive information from a prospectively collected LVAD database, we created an RVFRS that stratifies an LVAD candidate's risk of RV failure and post-operative death. The RVFRS is composed of noninvasive, routinely collected clinical pre-operative data, providing critical patient-specific operative morbidity and mortality estimates that are invaluable during the pre-operative patient/family education encounter. Although more evaluation is necessary, the RVFRS may also aid in the selection of those patients who may benefit from planned biventricular support. Further, because present options for permanent biventricular support offer limited mobility and quality of life, the RVFRS may assist in identifying poor candidates for permanent LVAD support. In

this analysis, the destination therapy sample was small (n = 12) and more studies will be needed to clarify the model's role in this population.

Because various mechanisms underlie the development of RV failure after LVAD implantation (i.e., increased after-load, pre-load, ventricular interdependence, RV ischemia), measures reflective of the consequences of RV dysfunction, rather than diagnostic of poor RV contractility, are likely to be most useful in predicting RV failure. Although other studies have identified many pre-operative variables associated with post-operative RV failure (1,2,4–12), data are limited by an ambiguous definition (4) or low prevalence of RV failure (5,7,10) and exclusion of patients with normal pre-operative RV ejection fractions (6). Furthermore, many prior studies relied solely on univariable analyses (2,4–6,11). Multivariable techniques, as used in this study, afford simultaneous evaluation of many risk factors that, when evaluated separately, may suggest different outcomes for an individual patient (15).

Several intuitively appealing pre-operative hemodynamic and laboratory parameters have been associated with increased risk of RV failure, including reduced RVSWI (5,7,10,12) or PA pressure (5,7,10,11), and elevated RA pressure (1,8,9), AST (5,11), bilirubin (2,4,6), and creatinine (4,6,11). Elevations in RV afterload and pre-load with reductions in RV contractility are reflected in hemodynamic measurements, whereas renal and hepatic laboratory abnormalities reflect congestion and hypoperfusion in those with RV dysfunction. Pre-operative elevation of RA pressure was predictive of RV failure in 2 retrospective analyses (1,9), but subsequent studies (including ours) have not validated this risk (2,4–6,11). Fukamachi et al. (5) analyzed pre-operative risks for RV failure occurring in 11 of 100 HeartMate 1000 IP and VE patients. Increased AST and lower mean PA pressure and RVSWI were associated with increased risk of RV failure (5). Likewise, Kavarana et al. (2) evaluated 69 LVAD patients (21 with RV failure) and found that higher pre-operative bilirubin was a significant predictor of RV failure, whereas lower RVSWI and higher AST achieved a nonsignificant predictive trend. In the current study, all of the previously mentioned variables were associated with significantly increased risk for RV failure, but only AST and bilirubin remained independently predictive after multivariable analysis. When the AUC of the RVFRS was compared with that of previously published predictors (1,5,7,9–12) of RV failure, the RVFRS showed superior risk discrimination.

As previously highlighted by Kormos et al. (6), it is likely that nonhemodynamic pre-operative clinical factors are more predictive of RV failure than inherent measurements of RV function. Several univariable clinical predictors for RV failure have been previously identified, including female gender, smaller body surface area, nonischemic etiology of cardiomyopathy, and pre-operative circulatory or inotropic support (1,4–7,10). In our sample, over 40 clinical parameters were analyzed, but only a pre-operative vasopressor requirement remained independently predictive of RV failure. Of the 4 variables in the RVFRS, a vasopressor requirement has the greatest weight (4 points), reflecting the importance of underlying pre-operative hemodynamic instability in the pathophysiology of RV failure.

Consistent with previous studies (1,4–7), the presence of RV failure in this sample was associated with nearly 6-fold higher odds of post-operative LVAD death. Overall survival decreased with increasing RVFRS strata. Likewise, in the bridge-to-transplant group, survival to transplant was lower for subjects with higher RVFRS. Thus, in addition to identifying patients at high risk for post-LVAD RV failure, the RVFRS identified subjects at higher risk for postoperative death and those less likely to survive to transplant.

Study limitations

Our patient sample had clinical characteristics and a prevalence of RV failure similar to those reported for other cohorts (1,2,16). However, cohort studies are subject to bias and confounding

that may have influenced our results. We tried to adjust for confounding variables through multivariable analysis, but it is unlikely that all confounders were identified. Furthermore, there is no means of identifying and adjusting for all the patient selection biases involved with LVAD candidacy and referral in an unblinded evaluation. Because this is a single-center study, study power was limited. However, this is the largest cohort of LVAD subjects analyzed with RV failure. Because of sample-size limitations, we used a $p \leq 0.1$ as variable selection criteria in RVFRS development. We recognize that the use of a less rigorous standard may affect future validation of the model. Of the 68 cases of RV failure, 58 occurred in first-generation HeartMate devices, with only 3 occurring in nonpulsatile LVADs. Thus, testing of the RVFRS in an independent patient sample with a variety of devices is necessary.

Another weakness of post-LVAD RV failure studies is the lack of a uniform definition for RV failure. Our diagnosis was predicated on the medical judgment of the treating physician, which is likely to vary between providers. Because every attempt was made to include all patients experiencing RV failure in the post-operative period, the definition of RV failure was broader in this study than in others that only included patients requiring RVAD assistance—the most extreme form of RV dysfunction (4,5,7,10). Prolonged inotrope support is known to be associated with increased morbidity and/or mortality in patients with post-LVAD RV dysfunction, independent of RVAD requirements (2,6,12). We prospectively selected >14 days of inotrope support as an RV failure criterion in an attempt to identify those patients with clinically relevant RV dysfunction, requiring inotropes for additional RV support outside of that which is usual in the early postoperative period. This definition was consistent with that used in prior studies (1,2) and was the inotrope criterion used by the Interagency Registry of Mechanically Assisted Circulatory Support until 2007 (17).

The need for home inotropes was included prospectively in the RV failure definition to identify patients with a delayed presentation of RV failure. No patient met the definition of RV failure based on this criterion alone, and its inclusion in the definition of RV failure in future studies warrants reexamination.

Last, prolonged iNO administration was a defining criterion because it is used by many as a hemodynamic bridge after LVAD placement. Nitric oxide has been shown to reduce PA pressures and improve LVAD flow in the setting of RV dysfunction (18), reducing the need for mechanical RV support (16). In this study, all but 4 patients on prolonged iNO met other inclusion criteria for RV failure, mainly a need for prolonged inotrope therapy. However, despite being on an inotrope, 2 patients on prolonged iNO died of RV failure before reaching the 14-day inotrope requisite and would not have been properly categorized in this analysis otherwise.

We did not exclude patients with pre-LVAD extracorporeal RV support. In these 8 patients, pre-operative extracorporeal RVAD support did not predict the development of post-LVAD RV failure, with 4 RVADs successfully explanted at the time of LVAD operation. This may reflect the benefit of reduced RV afterload and pre-load after LVAD placement in select individuals. In a separate analysis, exclusion of these 8 patients did not affect the discriminative ability of the RVFRS to predict RV failure (data not shown).

The RVFRS offers a high specificity for excluding RV failure and may be useful when devising an operative strategy for LVAD candidates, especially in those individuals with high RVFRSs. However, RV failure occurred in 20% of patients in the lowest strata (RVFRS ≤ 3), so we were unable to identify a truly low-risk group of patients. The RVFRS is one of several factors that physicians can consider in the complex evaluation of LVAD candidacy and operative risk. As with all clinical tools, the RVFRS is not meant to replace, but rather should supplement clinical judgment.

Conclusions

In conclusion, the RVFRS is the first model for pre-operative risk stratification of RV failure in LVAD candidates. The RVFRS is composed of easily obtained pre-operative clinical and laboratory data, and offers a high specificity for excluding the occurrence of RV failure after LVAD implant. Higher RVFRS in this sample also identified individuals at an increased risk of post-operative death. Validation of this model in an independent sample using a variety of devices and candidates is warranted before it is widely implemented.

Abbreviations and Acronyms

AST	aspartate aminotransferase
AUC	area under the curve
CI	confidence interval
ECMO	extracorporeal membrane oxygenation
iNO	inhaled nitric oxide
LV	left ventricle/ventricular
LVAD	left ventricular assist device
OR	odds ratio
PA	pulmonary artery
PVR	pulmonary vascular resistance
RA	right atrial
RV	right ventricle/ventricular
RVAD	right ventricular assist device
RVFRS	right ventricular failure risk score(s)
RVSWI	right ventricular stroke work index

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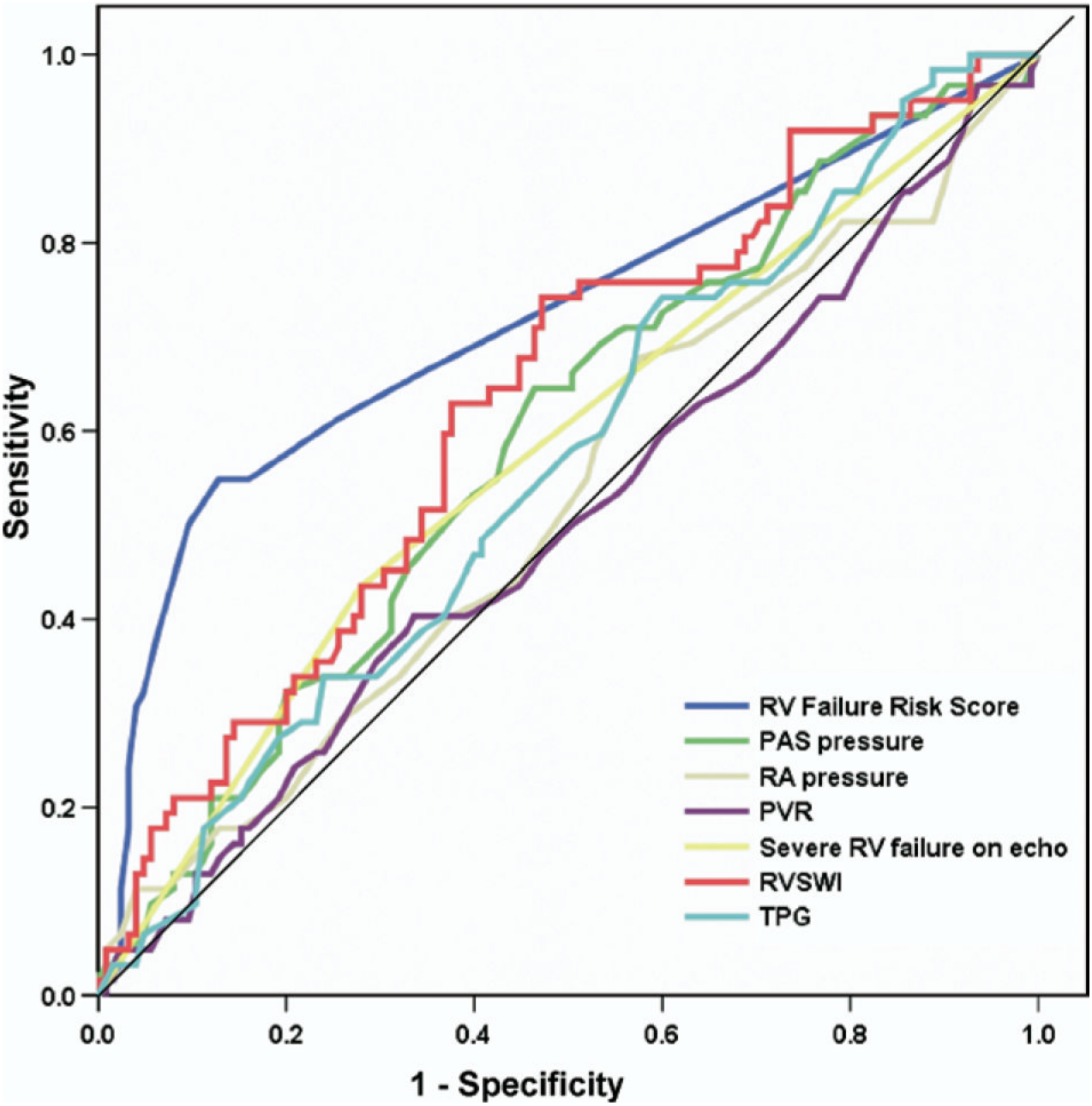

Figure 1. ROC Curve of the RVFRS and Other Univariable Predictors of RV Failure

Table 7 shows the areas under the receiver-operating characteristic (ROC) curve for the predictors. PAS = pulmonary artery systolic; PVR = pulmonary vascular resistance; RA = right atrial; RV = right ventricular; RVFRS = right ventricular failure risk score; RVSWI = right ventricular stroke work index; TPG = transpulmonary gradient.

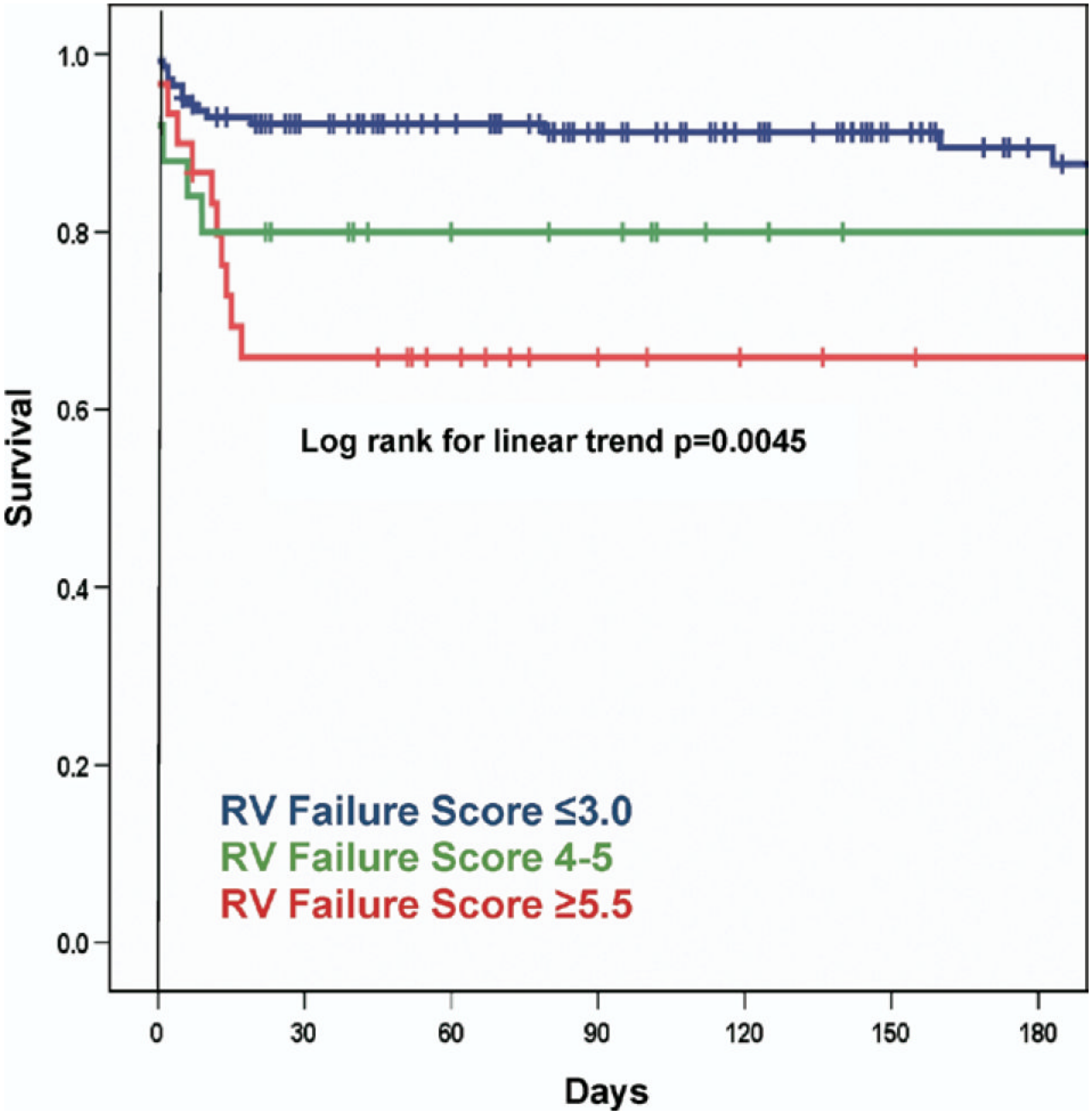

Figure 2. Kaplan-Meier Survival Curve for Each RV Failure Risk Score Strata

The 180-day post-left ventricular assist device survival curves for each score strata are displayed. RV = right ventricular.

Table 1

Baseline Pre-Operative Clinical Demographics and the Occurrence of RV Failure After LVAD Surgery for Each Variable

	RV Failure (n = 68)	No RV Failure (n = 129)	p Value*	Odds RV Failure (95% CI)
Age, yrs	51.3 ± 12.8	49.2 ± 13.2	0.28	
Male	51 (33)	105 (67)	0.36	
Female	17 (42)	24 (59)		
BSA, m^2	1.93 ± 0.21	2.0 ± 0.24	0.063	3.39 (0.89–12.99)
BMI, kg/m^2	26.6 ± 4.8	26.8 ± 5.2	0.76	
Race			0.31	
Caucasian	60 (37)	103 (63)		
African American	7 (25)	21 (75)		
Other	1 (17)	5 (83)		
Etiology for heart failure			0.77	
Ischemic	34 (33)	68 (67)		
Nonischemic	34 (36)	61 (64)		
NYHA functional class	4.0 ± 0.0	4.0 ± 0.1	0.55	
III	0 (0)	2 (100)		
IV	68 (35)	127 (65)		
Diabetes mellitus (+)	13 (27)	36 (74)	0.30	
Diabetes mellitus (−)	50 (35)	93 (65)		
Hypertension (+)	21 (32)	45 (68)	1.00	
Hypertension (−)	37 (31)	81 (67)		
Hyperlipidemia (+)	23 (30)	54 (70)	0.75	
Hyperlipidemia (−)	35 (33)	72 (67)		
TIA/CVA (+)	9 (56)	7 (44)	0.048	2.99 (1.06–8.46)
TIA/CVA (−)	52 (30)	121 (70)		
Prior sternotomy (+)	17 (25)	52 (75)	0.041	0.49 (0.26–0.95)
Prior sternotomy (−)	51 (40)	77 (60)		
Blood type			0.32	
O, n = 79	24 (30)	55 (70)		
A, n = 86	35 (41)	51 (59)		
B, n = 22	5 (23)	17 (77)		
AB, n = 10	4 (40)	6 (60)		
Reason for LVAD			0.55	
Bridge to transplant	65 (35)	120 (65)		
Destination therapy	3 (25)	9 (75)		

Values are expressed as n (%) unless otherwise specified. Percents reflect row values. Odds ratios are shown for univariable predictors with $p \leq 0.1$.

(+) = condition present; (−) = condition absent; BMI = body mass index; BSA = body surface area; CI = confidence interval; LVAD = left ventricular assist device; NYHA = New York Heart Association functional class at admission; RV = right ventricular; TIA/CVA = transient ischemic attack/cerebrovascular accident.

*p value for between-group comparisons.

Table 2

Occurrence of RV Failure Based on Pre-Operative Clinical Events and Medical Interventions

	RV Failure (n = 68)	No RV Failure (n = 129)	p Value*	Odds RV Failure (95% CI)
Code ≤24 h of admission (+)	10 (56)	8 (44)	0.067	2.61 (0.98–6.96)
Code ≤24 h of admission (−)	58 (32)	121 (68)		
Code >24 h of admission (+)	16 (46)	19 (54)	0.18	
Code >24 h of admission (−)	52 (32)	110 (68)		
Code, any time pre-operative (+)	22 (48)	24 (52)	0.035	2.09 (1.07–4.11)
Code, any time pre-operative (−)	46 (31)	105 (70)		
MI ≤1 week of LVAD (+)	15 (42)	21 (58)	0.42	
MI ≤1 week of LVAD (−)	53 (33)	108 (67)		
Pre-operative ICU stay (+)	65 (34)	127 (66)	0.34	
Pre-operative ICU stay (−)	3 (60)	2 (40)		
Length of pre-operative ICU stay, days	7.7 ± 6.0	7.4 ± 6.9	0.37	
Post-cardiotomy shock (+)	9 (52)	8 (47)	0.11	
Post-cardiotomy shock (−)	59 (33)	121 (67)		
IABP (+)	22 (40)	33 (60)	0.32	
IABP (−)	46 (32)	96 (68)		
Life support (+)†	35 (57)	26 (43)	<0.005	4.20 (2.21–7.98)
Life support (−)	33 (24)	103 (76)		
Bridge to bridge	25 (56)	20 (44)	0.001	3.17 (1.60–6.29)
None, n = 152	43 (28)	109 (72)		0.32 (0.16–0.63)
ECMO, n = 19	13 (68)	6 (32)		
Abiomed, n = 15	5 (33)	10 (67)		
Tandem Heart, n = 11	7 (64)	4 (36.4)		
Time on bridge, days	5.5 ± 2.6	5.3 ± 2.5	0.85	
Ventilator support (+)	26 (55)	21 (45)	0.001	3.18 (1.62–6.26)
Ventilator support (−)	42 (28)	108 (72)		
Time on ventilator support, days	4.7 ± 3.4	5.5 ± 3.0	0.32	
Renal replacement therapy (+)	13 (81)	3 (19)	<0.005	9.93 (2.72–36.24)
Renal replacement therapy (−)	55 (30)	126 (70)		
Pre-operative RVAD (+)	4 (50)	4 (50)	0.45	
Pre-operative RVAD (−)	64 (34)	125 (66)		

Values are expressed as n (%) unless otherwise specified. Percents reflect row values. Odds ratios are shown for univariable predictors with $p \leq 0.1$.

ECMO = extracorporeal membrane oxygenation; IABP = intra-aortic balloon pump; ICU = intensive care unit; MI = myocardial infarction; RVAD = right ventricular assist device (extracorporeal); other abbreviations as in Table 1.

*p value for between-group comparisons.

†Defined as need for ventilator, renal replacement therapy, or ECMO/Tandem Heart/Abiomed.

Table 3

Pre-Operative Intravenous Medication Requirements and Incidence of RV Failure After LVAD Implantation

IV Support	RV Failure	No RV Failure	p Value*	Odds RV Failure (95% CI)
IV inotrope (+),†	55 (32)	115 (68)	0.13	
IV Inotrope (−)	13 (48)	14 (52)		
>1 inotrope (+)	23 (32)	50 (69)	0.54	
>1 inotrope (−)	45 (36)	79 (64)		
Milrinone (+)	30 (26)	86 (74)	0.004	0.40 (0.22–0.72)
dose, μg/kg/min‡	0.206 ± 0.258	0.302 ± 0.251	0.009	0.22 (0.065–0.72)
Milrinone (−)	39 (47)	43 (53)		
Dobutamine (+)	19 (41)	26 (59)	1.00	
dose, μg/kg/min‡	3.46 ± 4.76	2.62 ± 3.85	0.38	
Dobutamine (−)	41 (35)	77 (65)		
Dopamine (+)	19 (41)	26 (59)	0.37	
dose, μg/kg/min‡	1.38 ± 3.29	0.76 ± 1.72	0.27	
Dopamine (−)	50 (33)	103 (67)		
Vasopressor (+),§	18 (67)	9 (33)	<0.005	4.80 (2.02–11.41)
Vasopressor (−)	50 (29)	120 (71)		
Norepinephrine (+)	4 (40)	6 (60)	0.74	
dose, μg/kg/min‡	0.005 ± 0.022	0.004 ± 0.022	0.72	
Norepinephrine (−)	64 (34)	123 (66)		
Vasopressin (+)	10 (77)	3 (23)	0.002	7.24 (1.92–27.30)
dose, U/h‡	0.529 ± 1.37	0.074 ± 0.590	0.001	1.72 (1.15–2.56)
Vasopressin (−)	58 (32)	126 (69)		
Phenylephrine (+)	7 (64)	4 (36)	0.050	3.59 (1.01–12.72)
dose, μg/min‡	10.4 ± 40.9	3.8 ± 22.6	0.018	1.01 (0.997–1.018)
Phenylephrine (−)	61 (3)	125 (67)		
IV antiarrhythmic (+)	19 (53)	17 (47)	0.019	2.56 (1.22–5.33)
IV antiarrhythmic (−)	49 (30)	112 (70)		
Amiodarone (+)	10 (39)	16 (62)		
Lidocaine (+)	3 (100)	0 (0)		

Values are expressed as n (%) unless otherwise specified. Percents reflect row values. Odds ratios are shown for univariable predictors with $p \leq 0.1$.

IV = intravenous; other abbreviations as in Table 1.

*p value for between-group comparisons.

†Inotrope defined as milrinone, dobutamine, or dopamine.

‡Untreated patients assigned dose of zero.

§Vasopressor defined as phenylephrine, norepinephrine, or vasopressin.

Table 4

Echocardiographic and Cardiopulmonary Hemodynamic Measurements Before LVAD Implantation With Associated RV Failure

	RV Failure	No RV Failure	p Value*	Odds RV Failure (95% CI)
Echocardiographic parameters				
LViDd, mm	67.1 ± 12.7	70.1 ± 11.1	0.12	
LViDs, mm	60.8 ± 13.2	62.5 ± 12.4	0.42	
Mitral regurgitation severity†	2.0 ± 1.3	2.1 ± 1.5	0.97	
Tricuspid regurgitation severity†	1.7 ± 1.2	1.4 ± 1.1	0.10	1.25 (0.97–1.61)
Aortic insufficiency severity†	0.2 ± 0.7	0.2 ± 0.7	0.91	
Ejection fraction, %	13.6 ± 6.8	13.6 ± 5.4	0.85	
Left ventricular mass, g	332.9 ± 103.1	360.6 ± 138.6	0.20	
RV dysfunction, n (%)			0.067	
None, n = 30	8 (27%)	22 (73%)		
Mild, n = 36	12 (33%)	24 (67%)		
Moderate, n = 58	16 (28%)	42 (72%)		
Severe, n = 69	32 (46%)	37 (54%)	0.012	2.21 (1.20–4.07)‡
Electrocardiogram				
Rhythm, n (%)			0.35	
Sinus, n = 128	41 (32%)	87 (68%)		
Paced, n = 41	14 (34%)	27 (66%)		
Afibrillation/flutter, n = 28	13 (46%)	15 (54%)		
QRS, ms	144.4 ± 43.6	131.8 ± 44.8	0.82	
Vital signs				
Temperature, °C	37.3 ± 0.9	37.2 ± 0.6	0.16	
Systolic blood pressure, mm Hg	96.9 ± 13.7	99.1 ± 15.6	0.33	
Diastolic blood pressure, mm Hg	62.0 ± 13.4	61.3 ± 11.4	0.68	
Mean arterial pressure, mm Hg	73.6 ± 11.3	74.0 ± 11.3	0.85	
Heart rate, beats/min	93.6 ± 16.4	92.6 ± 18.0	0.72	
Cardiopulmonary hemodynamics				
Right atrial pressure, mm Hg	12.5 ± 6.3	11.9 ± 5.8	0.62	
Mean PA pressure, mm Hg	30.5 ± 9.3	33.5 ± 9.2	0.040	0.97 (0.94–0.99)
PA systolic pressure, mm Hg	45.2 ± 14.4	49.9 ± 14.6	0.036	0.98 (0.96–0.99)
≥50	22 (25%)	66 (75%)	0.030	0.49 (0.56–0.91)
<50	41 (41%)	60 (59%)		
PA diastolic pressure, mm Hg	23.2 ± 7.5	25.3 ± 7.6	0.082	0.97 (0.93–1.00)
Pulmonary capillary wedge pressure, mm Hg	22.2 ± 7.3	23.7 ± 7.9	0.21	
Cardiac index, l/min/m^2	2.1 ± 0.6	2.3 ± 0.6	0.049	0.61 (0.37–1.00)
Systemic vascular resistance, dynes•s•cm^{-5}	1,334 ± 546	1,180 ± 382	0.11	
Pulmonary vascular resistance, WU	2.3 ± 1.6	2.3 ± 1.5	0.96	

	RV Failure	No RV Failure	p Value*	Odds RV Failure (95% CI)
≥2.8	22 (37%)	38 (63%)	0.51	
<2.8	40 (30%)	88 (70%)		
Transpulmonary gradient, mm Hg	8.3 ± 4.4	9.8 ± 5.6	0.13	
PA input resistance	15.0 ± 8.0	16.1 ± 7.5	0.79	
RVSWI, mm Hg•ml/m^2	404 ± 275	555 ± 318	0.002	
<450	40 (43%)	54 (57%)	0.009	2.32 (1.24–4.32)
≥450	23 (24%)	72 (76%)		

Percents reflect row values. Odds ratios are shown for univariable predictors with $p \leq 0.1$.

LViDd = left ventricular internal diastolic diameter; LViDs = left ventricular internal systolic diameter; PA = pulmonary artery; RVSWI = right ventricular stroke work index; WU = Wood units; other abbreviations as in Table 1.

*p value for between-group comparisons.

†Valve insufficiency graded on a 4-point scale (1 = mild, 2 = moderate, 3 = moderate-severe, 4 = severe).

‡Odds of post-operative RV failure with severe RV failure on pre-operative echocardiography.

Table 5

Pre-Operative Laboratory Values and Associated Post-Operative RV Failure

	RV Failure	No RV Failure	p Value*	Odds RV Failure (95% CI)
Sodium, mEq/l	134 ± 7	133 ± 6	0.44	
Potassium, mEq/l	4 ± 1	4 ± 1	0.69	
Bicarbonate, mEq/l	27 ± 5	27 ± 4	0.25	
Blood urea nitrogen, mg/dl	43 ± 26	32 ± 17	0.001	1.03 (1.01–1.04)
≥48	24 (47%)	27 (53%)	0.040	2.06 (1.07–3.96)
<48	44 (30%)	102 (70%)		
Creatinine, mg/dl	2.4 ± 1.8	1.5 ± 0.9	<0.005	1.68 (1.30–2.18)
≥2.3	20 (69%)	9 (31%)	<0.005	5.56 (2.36–13.06)
<2.3	49 (29%)	120 (71%)		
Glucose, mg/dl	149 ± 60	131 ± 45	0.039	1.007 (1.001–1.013)
White blood cell count, k/mm^3	12 ± 5	9 ± 3	<0.005	1.15 (1.06–1.25)
≥12.2	26 (52%)	24 (48%)	0.003	2.71 (1.40–5.24)
<12.2	42 (29%)	105 (71%)		
Hemoglobin, g/dl	12 ± 2	12 ± 2	0.94	
Platelets, k/mm^3	165 ± 84	206 ± 88	0.001	0.99 (0.99–1.00)
≤120	27 (56%)	21 (44%)	<0.005	3.36 (1.71–6.59)
>120	41 (28%)	107 (72%)		
Total protein, g/dl	6.3 ± 1.1	6.5 ± 0.9	0.23	
Albumin, g/dl	3.1 ± 0.7	3.3 ± 0.6	0.055	0.64 (0.40–1.01)
≤3.0	33 (43%)	43 (57%)	0.046	1.86 (1.02–3.40)
>3.0	35 (29%)	85 (71%)		
LDH, IU/l	488 ± 340	361 ± 410	<0.005	1.001 (1.000–1.002)
AST, IU/1	96 ± 96	73 ± 169	<0.005	1.00 (0.999–1.003)
≥80	27 (55%)	22 (45%)	0.001	3.20 (1.64–6.25)
<80	41 (28%)	107 (72%)		
ALT, IU/1	128 ± 200	84 ± 160	0.16	
Alkaline phosphatase, IU/l	119 ± 64	106 ± 48	0.15	
Total bilirubin, mg/dl	3.2 ± 4.5	1.2 ± 0.8	<0.005	1.68 (1.29–2.19)
≥2.0	27 (57%)	20 (43%)	<0.005	3.59 (1.82–7.10)
<2.0	41 (27%)	109 (73%)		
INR, s	1.2 ± 0.2	1.2 ± 0.3	0.38	
PTT, s	45.7 ± 19.0	43.5 ± 20.2	0.16	

Percents reflect row values. Odds ratios are shown for univariable predictors with $p \leq 0.1$.

ALT = alanine aminotransferase; AST = aspartate aminotransferase; INR = International normalized ratio of the prothrombin time; LDH = lactic acid dehydrogenase; PTT = partial thromboplastin time; other abbreviations as in Table 1.

* p value for between-group comparisons.

Table 6

Right Ventricular Failure Risk Score and Likelihood of RV Failure by Score Strata

Risk Score	n	RV Failure (n)	No RV Failure (n)	Likelihood Ratio (95% CI)
≤3.0	142	29	113	0.49 (0.37–0.64)
4.0–5.0	25	15	10	2.8 (1.4–5.9)
≥5.5	30	24	6	7.6 (3.4–17.1)

Risk Score is derived by summing points awarded for the presence of a vasopressor requirement (4 points), AST ≥80 IU/l (2 points), bilirubin ≥2.0 mg/dl (2.5 points), and creatinine ≥2.3 mg/dl (3 points).

Abbreviations as in Table 1.

Table 7

Area Under the Receiver-Operating Characteristic Curve of the RV Failure Risk Score and Other Commonly Used Predictors of RV Failure

	AUC (95% CI)	*p Value
RV failure risk score	0.73 (0.65–0.81)	—
Severe RV failure on echocardiograph	0.59 (0.51–0.68)	0.004
RVSWI	0.63 (0.55–0.72)	0.011
PVR	0.50 (0.41–0.59)	<0.001
TPG	0.56 (0.48–0.65)	<0.001
PA systolic pressure	0.59 (0.51–0.68)	0.017
RA pressure	0.53 (0.44–0.61)	<0.001

AUC = area under the curve; PVR = pulmonary vascular resistance; RA = right atrial; TPG = transpulmonary gradient; other abbreviations as in Table 1 and 4.

* p value comparing the AUC of the RV Failure Risk Score to that of the respective predictor.