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DECISION TREE FOR ADJUVANT RIGHT VENTRICULAR SUPPORT IN PATIENTS RECEIVING A LEFT VENTRICULAR ASSIST DEVICE

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Abstract

Background—Right ventricular (RV) failure is a significant complication following implantation of a left ventricular assist device (LVAD). It is therefore important to identify patients at risk a-priori. However, prognostic models derived from multivariate analyses have had limited predictive power.

Methods—This study retrospectively analyzed 183 patient records of LVAD recipients between May 1996 and Oct. 2009; 27 of which later required a right ventricular assist device ($RVAD^+$) and 156 remained on LVAD only ($RVAD^-$) until the time of transplantation or death. A decision tree model was constructed to represent combinatorial nonlinear relationships of the preoperative data that are predictive of the need for RVAD support.

Results—An optimal set of eight preoperative variables were identified: transpulmonary gradient, age, right atrial pressure, international normalized ratio, heart rate, white blood cell count, alanine aminotransferase and the number of inotropic agents. The resultant decision tree, comprised of 28 branches and 14 leaves, identified $RVAD^+$ patients with 85% sensitivity, $RVAD^-$ patients with 83% specificity, and exhibited an area under the ROC curve of 0.87.

Conclusions—The decision tree model developed in this study exhibited several advantages over existing risk scores. Quantitatively, it provided improved prognosis of RV support by encoding the nonlinear, synergic interactions among preoperative variables. Because of its intuitive structure, it more closely mimics clinical reasoning and therefore can be more readily interpreted. Further development with additional multi-center, longitudinal data may provide a valuable prognostic tool for triage of LVAD therapy, and potentially improve outcomes.

Keywords

left/right ventricular assist device; right ventricular failure; decision tree; machine learning; decision support

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INTRODUCTION

Mechanical circulatory support for end-stage heart failure has become an established therapeutic option with significant survival benefit. However, patients receiving a left ventricular assist device (LVAD) alone periodically develop postoperative right ventricular (RV) failure necessitating pharmacological or mechanical support. This applies to approximately 10 to 30% of all LVAD patients[1–4], and is associated with increased morbidity and mortality[5]. Severe RV failure results in renal and hepatic dysfunction due to elevated central venous pressure as well as under-filling of the LVAD[6]. Postoperative RV failure also adversely affects outcomes of patients who are ultimately bridged to transplant[3, 7, 8].

Conversely, implanting an RVAD bears its own risk of increased morbidity[9], effectively doubling the likelihood of thrombosis, infection, and mechanical failure. Therefore, the prediction of RV failure prior to VAD implantation is critically important to optimal course of treatment and clinical outcome. This prognosis is sometimes obscured by the complex interaction between pre-operative conditions, intra-operative factors, and immediate post-operative hemodynamic status[9–11]. Consequently, previous predictors of RV failure based on uni- and multi-variate statistical analyses[1, 3, 5, 11–16] have not provided adequate sensitivity and specificity for practical use. For example, a popular right ventricular failure risk score (RVFRS)[11] that has demonstrated high positive predictive value (80%) of RV failure in LVAD candidates (based on a threshold value of 5.5), reports an overall sensitivity of only 35%. Furthermore the performance of this index is prognostically inconsistent when evaluated on independent samples. Thus there remains a need for a more accurate, sensitive, specific, and robust method to identify LVAD candidates at risk for RV failure.

This study aimed to develop an improved prognostic tool by capitalizing on recent advances in data mining and machine learning theory. These techniques are gaining popularity to predict future trends and discover unknown patterns in clinical outcomes, including breast cancer, pneumonitis[17, 18] and others[19–21]. The *Decision Tree* is one such algorithm that has been used extensively in medicine[22–25]. It has proven to be reliable and effective, providing high classification accuracy with a simple representation of gathered knowledge. Because of its tree structure, it can be readily interpreted and therefore more likely to be adopted than, say, an ambiguous numerical risk score[26]. This study employed the decision tree algorithm in combination with *over-sampling* and *feature selection* techniques to identify and represent the nonlinear interactions between preoperative variables.

METHODS

Study Design

This study retrospectively analyzed 183 de-identified patient enrolled in Artificial Heart Program at the University of Pittsburgh Medical Center (UPMC) from May 1996 to Oct. 2009. These patients initially received an LVAD, but 27 (15%) later required a RVAD ($RVAD^+$) and 156 (85%) remained on LVAD until the time of transplantation or death ($RVAD^-$). Multiple devices were used throughout this time period (Table 1 and Table 2) including: BVS 5000 and AB 5000 (Abiomed, Danvers, MA), Bio-Medicus Perfusion System (Medtronic, Inc., Minneapolis, MN), Novacor (Worldheart, Salt Lake City, Utah), CentriMag, HeartMate XVE, Thoratec IVAD, Thoratec PVAD, HeartMate II (Thoratec, Pleasanton, CA), Jarvik 2000 (Jarvik Heart, Inc., New York, NY), and Ventrassist (Ventracor Limited, Chatswood, Australia). Among these, the initial pulsatile-flow LVADs comprised 78.1% (n=143) of the total cohort with 121 $RVAD^+$ and 22 $RVAD^-$ patients; continuous-flow LVADs comprised 21.9% (n=40) with 35 $RVAD^+$ and 5 $RVAD^-$ patients, respectively.

A total of 39 preoperative variables were selected based on a survey of the literature and their availability in the patient records, categorized as follows: patient demographics (n=6), hemodynamics (n=14), blood chemistry and hematologic laboratory values (n=13) and medications (n=6) including digoxin, angiotensin-converting enzyme inhibitors/angiotensin II receptor antagonists, beta-blocker, antiarrhythmics and inotropic agents (See Table 3.) Data were reviewed retrospectively the UPMC Transplant Patient Management System (TPMS), a password-protected, HIPAA compliant, IRB approved, web-based data repository for all patients who receive mechanical circulatory support. Data were extracted from preoperative day 14 to 1. For variables with multiple values, the value closest to the time of surgery was used. In circumstances where data elements were missing, various interpolation techniques (mean, median, nearest neighbor) were implemented, indicated in Table 3. The primary end point was whether the LVAD patient received an RVAD implantation subsequent to the index LVAD surgery and the secondary end point was 1-year survival.

Analysis

The set of pre-operative variables was first ranked by Chi-Square analysis, and then combined into incrementally sized subsets (n=1, 2,…, 39). Further analyses were performed on each of the subsets to determine the optimal set that provided sufficient information without overfitting. A well-known decision tree algorithm, C4.5, was employed, implemented in an open-source software library[27] (WEKA, J48, University of Waikato, New Zealand). This analysis uses recursive partitioning methods to separate the two groups of patients into distinct subsets by identifying the significant nonlinear interactions among the pre-operative variables and automatically constructing the decision branches. The corresponding breakpoints for each of the variables were selected with the criterion of maximization the purity of the cohort after splitting. The algorithm also includes a “pruning” procedure to reflexively eliminate unnecessary branches, reduce the estimated errors and generalize the model. The objective function for this analysis was to minimize the error between predicted and historical decision of RVAD implantation ($RVAD^{+}$/$RVAD^{-}$, defined above.) It was assumed here that the clinical cost of failing to initially implant an RVAD in a patient who develops RV failure is comparable to the cost of implanting an RVAD unnecessarily. Synthetic Minority over Sampling Technique (SMOTE)[28–30] was applied to supplement the $RVAD^{+}$ data to compensate for the imbalanced ratio of $RVAD^{+}$ to $RVAD^{-}$ in the current cohort (1:6) and avoid unintended bias in the calculation of error rate.

Ten-fold cross-validation was used to evaluate the predictive performance of decision tree model, whereby the data was divided into 10 mutually exclusive subsets, nine of which were used for training and one for evaluation. This was repeated ten times, thereby employing ten different, but overlapping training sets, and 10 unique testing sets. The performance measures for evaluation of the decision tree analysis were: (1) true positive rate, $RVAD^{+/+}$ (in which the algorithm agrees with historical clinical decision to implant an RVAD); (2) true negative rate, $RVAD^{-/-}$ (in which both agree to forgo an RVAD), (3) false positive rate, $RVAD^{-/+}$ (in which the model predicts RVAD implantation while historical decision forwent RVAD), and (4) false negative rate, $RVAD^{+/-}$ (in which the model prediction disagreed with the historical decision of RVAD implantation.) Additional measures of performance were the area under the receiver operating characteristic (ROC) curve and kappa statistics. The *specificity* and *sensitivity* of the model were defined as the $RVAD^{-/-}$ and $RVAD^{+/+}$ rates, respectively. To investigate the dependence of late-RVAD implantation on the generation of the initial LVAD, the above analysis was repeated on the subgroups of patients with initial pulsatile-flow LVAD (n=143) and initial continuous-flow LVAD (n=40).

The performance in terms of survival was provided by Kaplan-Meier analysis. Differences in actuarial survival were evaluated using log-rank test. For comparison, the University of Michigan Right Ventricular Failure Risk Score (RVFRS)[11] was also calculated for each patient, which stratified the cohort according to the published definition. Standard ROC curves were constructed to illustrate overall sensitivity and specificity.

RESULTS

Baseline data and comparison between $RVAD^{-}$ (n=156) and $RVAD^{+}$ (n=27) groups are summarized in Table 3. The RVAD+ group included 8 (30%) CentriMag, 3 (11%) Abiomed BVS 5000, 1 (4%) Biomedicus RVAD and 15 (55%) Thoratec PVAD. The demographics, hemodynamic and laboratory data were typical of patients with advanced heart failure and were similar between $RVAD^{-}$ and $RVAD^{+}$ groups. The $RVAD^{+}$ group was younger (50 versus 53; p=0.04) and had a higher proportion of women (37% versus 15% overall; p=0.01). Pearson product-moment pairwise analysis identified 2 variables that were significantly positively correlated with the need of post-RVAD individually: female gender and elevated white blood cell (WBC) count ($RVAD^{-}$: 9.4 ±3.9*10^{9}/L vs. $RVAD^{+}$: 11.8 ±7.3*10^{9}/L). Pre-operative weight was inversely correlated with the late-use of RVAD, ($RVAD^{-}$: 89.3 ±21.7 kg vs. $RVAD^{+}$: 76.0 ±17.3 kg). The corresponding correlation coefficients and 95% confidence intervals are summarized in Table 4, which demonstrates significant differences between groups ($p<0.05$) but generally weak correlations ($\ll 1$).

Decision Tree Model

Feature selection resulted in 8 pre-operative variables comprising the decision tree model for the complete cohort: transpulmonary gradient (TPG), age, right atrial pressure (RAP), international normalized ratio (INR), heart rate (HR), white blood cell count (WBC), alanine aminotransferase (ALT) and the number of inotropic agents (# inotrope). Pearson product-moment pairwise analysis identified seven significant correlations ($p<0.05$): # inotrope was positively correlated with WBC, which indicated that elevated WBC was associated with a greater number of inotropic agents. Similar observations were found between WBC and RAP, ALT and RAP, INR and ALT as well as INR and RAP. Yet, RAP and HR were inversely correlated with age, which reflects younger patients tending to have greater RAP and HR in this cohort. Figure 1 shows the corresponding correlation coefficients as well as 95% confidence intervals.

The resulting decision tree built upon the above dataset with 5X synthetic $RVAD^{+}$ samples is provided in Figure 2. In this model, TPG is the initial splitting feature with a breakpoint of 7 mmHg. The branch of TPG ≤ 7 mmHg predicts no need of RVAD support; and the branch of TPG > 7 mmHg leads to age as the secondary splitting feature with a breakpoint of 59. On the third level, there exist different thresholds of RAP depending on age: 18 mmHg (≤ 59yo), 10 mmHg (> 59yo). This demonstrates the apparent nonlinear relationship among these pre-operative features. Thereafter, additional splits unveil the complicated patterns embedded in the $RVAD^{+}$ and $RVAD^{-}$ data sets. The tree eventually terminates in a total of 14 leaves representing one of two outcomes ($RVAD^{-}$ or $RVAD^{+}$). This model indicates that elevated INR and/or WBC are common to the branches with increased risk of the need of RVAD support. This model achieved 85% sensitivity, 83% specificity (See Table 5a.)

Receiver operating characteristic curves were generated for both the decision tree model and the RVFRS calculated for this cohort (See Figure 3.) Comparison of AUC showed that decision tree exhibited better performance than RVFRS on this cohort of patients (AUC: 0.87 versus 0.54.) The figure also depicts the RVFRS ROC curve reported in Matthews *et al.* in which the reported AUC is 0.73[11]. Applying this weighted score on the present cohort,

it was found that 18.5% $RVAD^{+}$ patients were identified as high risk, 64.1% $RVAD^{-}$ as low risk leaving 22.2% $RVAD^{+}$ patients and 19.2% $RVAD^{-}$ patients as medium risk.

Survival Outcome

Kaplan Meier 1-year survival curves of the two groups of patients with respect to historical decisions of $RVAD^{-}$ and $RVAD^{+}$ are provided in Figure 4 (log rank p = 0.0008). Thirty-day post-LVAD survival for the $RVAD^{-}$ and $RVAD^{+}$ groups were 89% and 78% respectively. The corresponding survivals at 90 days were 78% and 60%, respectively, and at 180 days 73% and 37%. Survival at 1 year was 51% and 19%, respectively. Figure 5 provides the survival curves for the subset of patients belonging to $RVAD^{-/-}$ and $RVAD^{+/+}$ groups. Compared to Figure 4, short-term post-LVAD survivals between the groups were similar: 89%, 84% at 30 days and 77%, 65% at 90 days respectively. However, the 1-year survivals are much more distinct: 51% for $RVAD^{-/-}$ and 0% $RVAD^{+/+}$. The overall curves were found to be statistically different (log rank p = 0.0108).

Comparison of First and Second Generation LVAD

In the subgroup of patients receiving continuous flow continuous-flow (second generation) LVAD the incidence of late-RVAD implantation was relatively lower than those who received a pulsatile-flow (first generation) LVAD: 12.5% versus 15.4%. The performance of the *aggregate* model (Figure 2) with this sub-group was: 80% sensitivity and 86% specificity, which was similar to the full cohort. (See Table 5b.) The decision tree model developed exclusively on the continuous-flow cohort re-prioritized the predictive variables, promoting the importance of body mass index (BMI), cardiac output (CO), and diastolic pulmonary artery pressure (PA_Dia). It also demoted the prognostic values of INR and WBC. It exhibited 100% sensitivity and 97% specificity based on 10-fold cross validation. However, when tested on the pulsatile-flow LVAD group, it exhibited only 18% sensitivity ($RVAD^{+/+}$) and 84% specificity ($RVAD^{-/-}$). Similarly, the model developed exclusively with the subset of patients with initial pulsatile-flow (first generation) LVAD performed poorly when tested on the continuous-flow LVAD group, exhibiting 20% sensitivity ($RVAD^{+/+}$) and 89% specificity ($RVAD^{-/-}$).

DISCUSSION

The complex pathophysiology of post-operative RV failure[11] and care[31] makes the pre-operative prediction of RV failure difficult and hinders the optimal course of treatment for an individual candidate[8, 10, 31, 32]. In lieu of sole univariate analysis or traditional linear multivariate analysis, the current study sought to develop a decision tree to facilitate the identification of patients who may require RV support. As contrasted to a weighted combination of independent variables, the decision tree is better able to represent the complicated, nonlinear relationships and synergy between variables that underlie the development of RV failure after LVAD implantation. An added benefit of the decision tree model is its ability to graphically illustrate the prediction logic – as compared a purely mathematically derived index that requires “blind faith” of the decision-maker.

The decision tree presented here includes predictive pre-operative variables that are supported by previous right ventricular failure studies and further reveals potentially counter-intuitive dependencies on variables not previously emphasized. For example, the first splitting variable found by the model, elevated TPG, has been previously identified as a significant predictor of right ventricular dysfunction after LVAD implantation[33]. However, the decision tree model further qualifies this splitting criterion for instances in which TPG is greater than 7 mmHg, in which case additional factors should be taken into consideration. While this cut point would not appear to be clinically relevant, particularly with respect to

historical linear analyses, the current study suggests that even modest elevation of TPG may impart risk when taken into consideration with other variables. Likewise, age, also identified by Fukamachi to be an important predictor[15], appears twice in the decision tree, in each case further qualified by subordinate variables. INR, also previously correlated with RV failure[2, 11, 16], is incorporated into the decision tree in a somewhat complex fashion. For example, for a patient with TPG > 7 mmHg, age < 59, and RAP > 18 mmHg, and elevated INR > 2.6 the model indicates the need of an RVAD; yet for a patient with the same profile except RAP < 18 mmHg, the prediction is much more complicated, and depends on HR, WBC, ALT and # inotropes. This interdependence of variables may possibly reflect their causality: for example it is less likely that elevated INR contributes directly to RV failure than it is indicative of other underlying pathologies that adversely effect outcomes. Accordingly, the model does *not* imply that altering a patient's INR would affect the risk of RV failure. Rather, it is more likely that prevailing condition leading to a high INR is further associated with multiple other physiologic abnormalities that eventually culminate in RV failure. Being a retrospective study, it is impossible to eliminate the bias potentially introduced by the "human in the loop."

The present study also revealed that multiple decision tree structures may provide equivalent results. (See, for example the decision tree of Figure 6 which is a variant of the present model with comparative performance to the model shown in Figure 2.) This non-uniqueness can be considered an asset inasmuch as it accommodates multiple sets of data elements. Therefore the user may select from an assortment of decision trees most consistent with the (limited) data available.

Although not reported here, it is intuitive that the performance of the decision tree would deteriorate as data elements are excluded. Conversely, the addition of more sensitive indices of RV function, such as echo-derived ejection-phase metrics[34] would *improve* the decision tree. But again, in practical situations, the data are often incomplete; and therefore the decision tree can make the best use of the limited data available – in contradistinction to existing functional scores that cannot be computed without each of the component data elements.

It is important to note that the objective function for this study was the "error" between prediction and eventual decision, as contrasted with a definitive measure of RV failure. Therefore, the model as it stands serves essentially to replicate expert judgment prior to LVAD insertion. Its clinical utility *in its present form* is twofold: (1) to codify best practices within a single institution, and perhaps alert the clinician or practice when an initial evaluation prior to LVAD insertion is at variance with the model, and (2) to transfer expertise from experienced, successful medical centers to those less experienced. The single-center experience might negatively impact the generality of this model, and the reader is cautioned from blindly extrapolating these results to their clinical service. Until the model has been calibrated and validated on a multi-center data set, the reader would be advised to repeat the analysis with data from their own VAD program to assure consistency before it is employed in clinical practice.

A related limitation is the very definition of what constitutes RV failure, which is a continuum of disease with varying severity, and which has changed over the extended time course of this study, and is also somewhat subjective, hence influenced by institutional bias. This study assumed that the expert decisions represented ground truth, i.e. "more correct" than the model. This would imply that additional, perhaps subconscious, factors[35] may have been overlooked by the model. This applies to both the set of independent variables, and to the definition of optimal outcome. In this regard, it is intriguing to consider the cases in which the model disagreed with the historical clinical decision (See Figure 7.) Those that the

model predicted the need for RVAD but in which the patient did not receive one ($RVAD^{-/+}$) appear to have very similar survival characteristics to $RVAD^{-/-}$. In these cases, it may be concluded that the expert decision was correct, and the model incorrect. Those patients who did receive an RVAD contrary to the model prediction ($RVAD^{+/-}$) faired much more poorly than those RVAD recipients for whom the model and expert agreed ($RVAD^{+/+}$). Early mortality was far more common in this, albeit small, subset of eight patients. However two patients who survived past the critical 90 day period exhibited similar 1 year survival as the RVAD- cohort. It is difficult to explain this disparity without knowledge of the patient history and re-examination of the raw data. This illustrates that clinical judgment cannot be defined in terms of pure mathematics[35]. There are many circumstances in which a bi-ventricular assistance is plainly obvious, such as the presentation of ventricular tachycardia, cardiogenic shock with multi-organ failure or confounding issues such as a ventricular septal defect. Likewise there are circumstances in which an RVAD is clearly unnecessary and does not require a computer to make a decision. The practical utility of a decision support model therefore may be to discriminate the marginal cases: to determine who will recover with a temporary RVAD and who will require chronic support. While this is beyond the scope of the current report, it is clearly the most likely instance where a decision support model can make a clinical impact.

Future improvements to this model will inevitably require additional complexity and sophistication. It would also clearly benefit from enlarging the data set and inclusion of more patients from multiple centers being implanted with the current generation of LVAD technology, which would alleviate many of the deficits caused by the limited patient cohort and single center experience. A prospective study would allow differentiation between various degree of RV failure, the need for short-term versus long-term support, eliminate subjectivity and related institutional bias, and allow focus on more modern LVAD devices, rather than the wide assortment devices spanning from 1996 to 2009.

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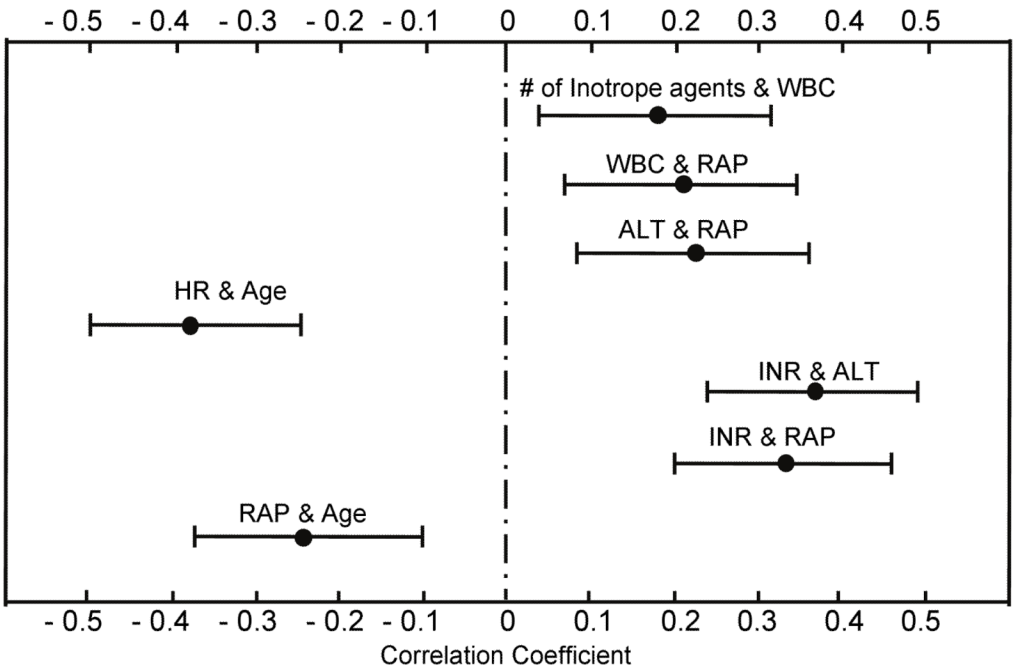

Figure 1.
Significant correlations among the pre-operative variables involved in the decision tree. 95% confidence intervals of correlation coefficients were indicated.

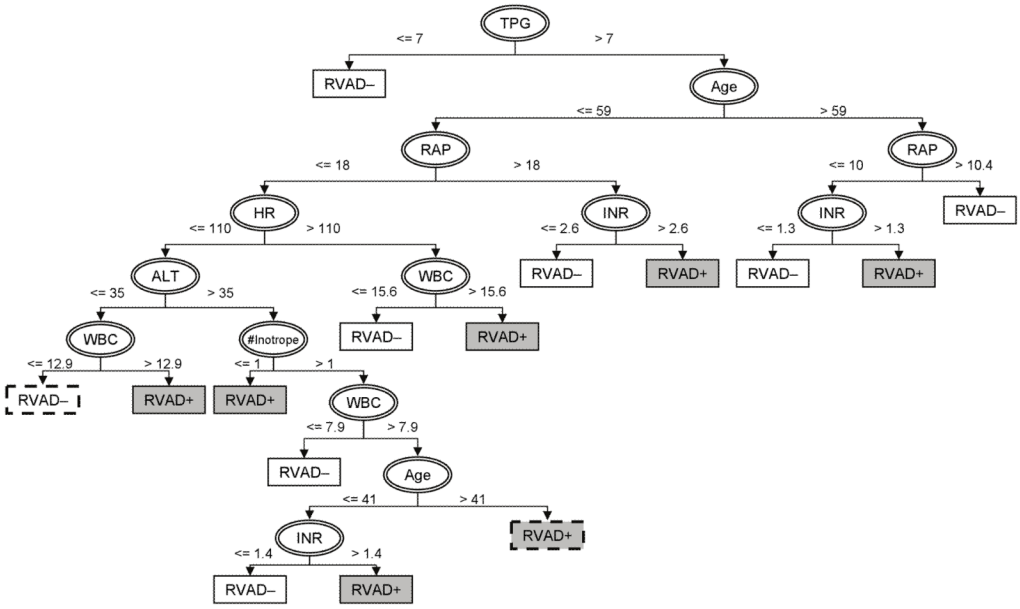

Figure 2.

Decision tree for optimal identification of RVAD support in LVAD patients. Features used for splitting the cohort are indicated by ellipses. Rectangles indicate the predicted outcomes following corresponding branches (white: freedom of RVAD support; gray: necessity of RVAD; dashed borderline: simplified leaves.)

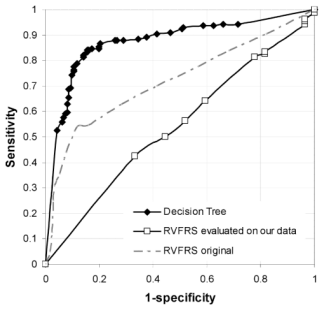

Figure 3.
ROC curve of our decision tree model, RVFRS evaluated on our cohort and RVFRS published in Matthews *et al.*'s study[11].

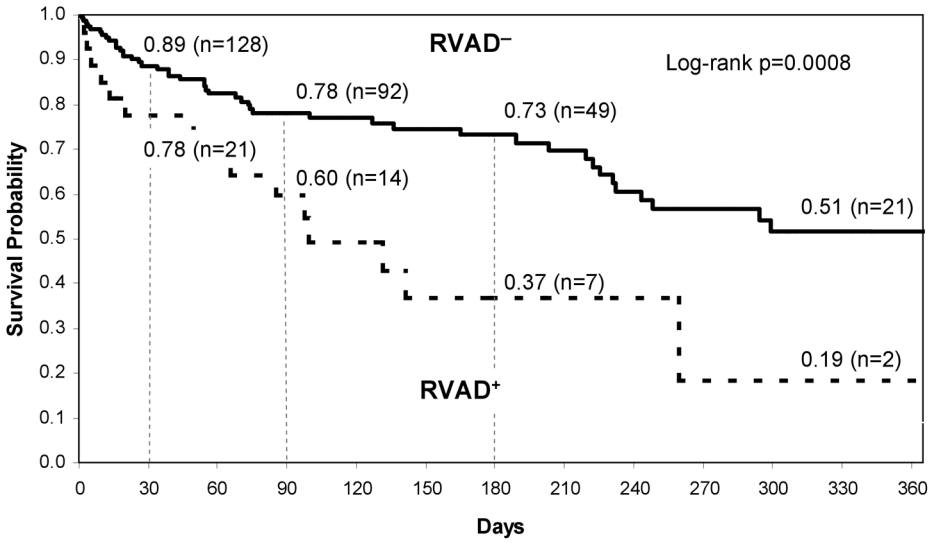

Figure 4.
Kaplan Meier survival curve for retrospective *clinical decision* $RVAD^+$ and $RVAD^-$ patients.

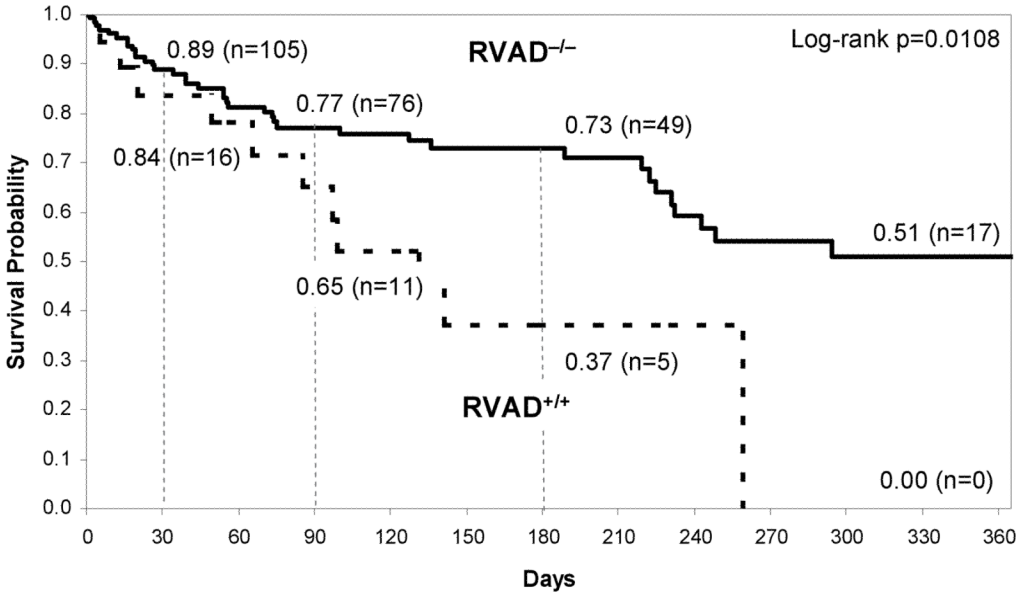

Figure 5.
Kaplan-Meier survival curve for $RVAD^{+/+}$ patients and $RVAD^{-/-}$ patients.

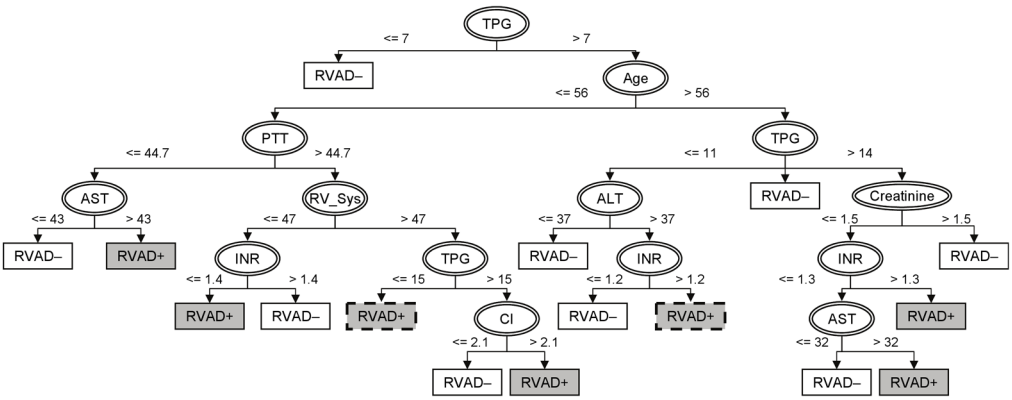

Figure 6.

A variant of the aggregate Decision Tree model with comparative performance to the model shown in Figure 2 (white: freedom of RVAD support; gray: necessity of RVAD; dashed borderline: simplified leaves.)

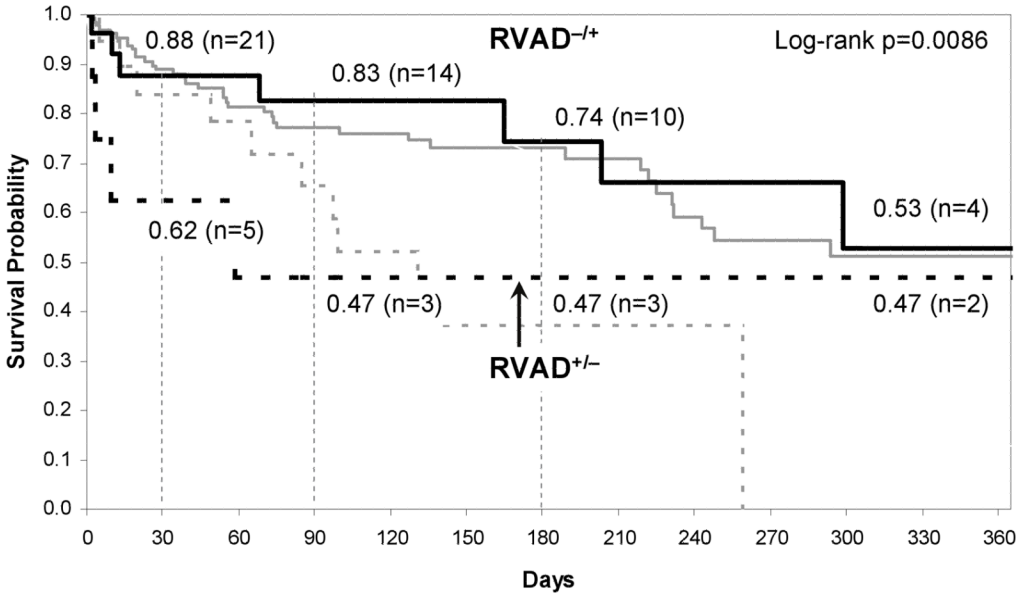

Figure 7.

Kaplan-Meier survival curve for $RVAD^{-/+}$ patients and $RVAD^{+/-}$ patients, superimposed the survival curves of $RVAD^{-/-}$ and $RVAD^{+/+}$ (gray line).

Table 1

Devices utilized in the RVAD⁻ group.

Pulsatile	**121 (77.6%)**
Abiomed AB 5000	6 (3.8%)
Novacor	43 (27.6%)
HeartMate XVE	33 (21.2%)
Thoratec IVAD	6 (3.8%)
Thoratec PVAD	33 (21.2%)
* **Continuous Flow**	**35 (22.4%)**
HeartMate II	15 (9.6%)
JARVIK 2000	2 (1.3%)
Ventrassist	18 (11.5%)
Total	**156**

* lists the number (percentage) of patients with initial continuous-flow LVAD in RVAD⁻ group.

Table 2

Device combination utilized in the $RVAD^{+}$ group.

RVAD Device	LVAD Device	N (%)
ABIOMED BVS 5000	Abiomed AB 5000	2 (7.4%)
ABIOMED BVS 5000	Novacor	1 (3.7%)
Biomedicus	HeartMate XVE	1 (3.7%)
CentriMag	* HeartMate II	3 (11.1%)
CentriMag	Thoratec IVAD	1 (3.7%)
CentriMag	Thoratec PVAD	3 (11.1%)
CentriMag	* Ventrassist	1 (3.7%)
Thoratec PVAD	* HeartMate II	1 (3.7%)
Thoratec PVAD	HeartMate XVE	2 (7.4%)
Thoratec PVAD	Novacor	3 (11.1%)
Thoratec PVAD	Thoratec PVAD	9 (33.3%)
Total		27

* indicates the cases with initial continuous-flow LVAD in $RVAD^{+}$ group (n=5 in total.)

Table 3

Pre-implant characteristics for two groups of patients.

	RVAD⁻ (n=156) mean (±std)	RVAD⁺ (n=27) mean (±std)	p-value
Demographics			
Age (yrs)	53.3 (±12.7)	49.9 (±10.5)	† 0.04
female (%)	14%	37%	† 0.01
Pulsatile-flow LVAD (%)	78%	81%	0.80
Body mass index (kg/m^2) – mean	28.2 (±6.1)	27.8 (±5.4)	0.99
Weight (kg) – 15nn	89.3 (±21.7)	76.0 (±17.3)	0.06
Ischemic etiology (%)	54%	56%	0.99
Hemodynamics			
Cadiac index (liter/min/m^2) – 20nn	2.3 (±0.8)	2.3 (±0.8)	0.80
Cardiac output (liter/min) – 10nn	4.3 (±1.0)	4.3 (±1.4)	0.22
Pulmonary capillary wedge pressure (mmHg) –10nn	26.6(±8.4)	24.2(±8.9)	0.42
Transpulmonary gradient (mmHg) – 10nn	11.3 (±6.0)	13.4 (±3.9)	0.10
Pulmonary vascular resistance (wood units) – mean	2.2 (±2.6)	3.6 (±1.7)	0.35
Mean pulmonary artery pressure (mmHg) – 7nn	38.1 (±9.4)	37.8 (±10.8)	0.86
Pulmonary arterial systolic pressure (mmHg) – 10nn	55.6 (±14.6)	56.8 (±16.8)	0.81
Pulmonary arterial diastolic pressure (mmHg) –10nn	27.4 (±8.2)	26.8 (±9.8)	0.75
Right atrial pressure (mmHg) – 10nn	12.1 (±6.2)	9.9 (±6.1)	0.26
Right ventricular diastolic pressure (mmHg) – 10nn	10 (±6.3)	11 (±7.0)	0.70
Right ventricular systolic pressure (mmHg) – 5nn	54.4 (±15.8)	56.4 (±14.2)	0.67
Pulmonary arterial oxygen saturation (%) – 15nn	51.8 (±12.7)	53.7 (±13.8)	0.53
Heart rate (beat/min) – 15nn	93.0 (±25.1)	81.3 (±28.5)	0.18
Intra aortic balloon pump (%) – mean	76%	74%	0.81
Laboratory tests			
Creatinine (mg/dL) – 15nn	1.5 (±0.7)	1.4 (±0.7)	0.23
Blood urea nitrogen (mg/dL) – 15nn	32.0 (±20.5)	28.6 (±18.9)	0.37
Aspartate aminotransferase (IU/L) – 7nn	83.7 (±162.8)	60.7 (±50.6)	0.47
Alanine asminotransferase (IU/L) – 15nn	92.8 (±174.1)	53.5 (±36.3)	0.76
Total bilirubin (mg/dL) – 15nn	1.2 (±0.9)	1.4 (±1.6)	0.75
Hematocrit (%) – 15nn	33 (±7.0)	35 (±7.4)	0.34
White blood cell count (10^9/L) – 10nn	9.4 (±3.9)	11.8 (±7.3)	0.16
Platelet count (10^9/L) – 20nn	207.7 (±78.8)	187.7 (±94.0)	0.23
International normalized ratio – 15nn	1.3 (±0.4)	1.5 (±0.7)	0.48
Hemoglobin (g/dL) – 20nn	13.8 (±10.4)	14.6 (±10.1)	0.30
Albumin (g/dL) – 5nn	3.3 (±0.6)	3.4 (±0.8)	0.46
Prothrombin time (sec) – mean	56.6 (±28.7)	58.3 (±29.6)	0.92
Sodium (MEQ/L) – median	134.2 (±5.8)	133.5 (±5.8)	0.58

* Imputing methods indicated following dash line.

nn: nearest neighbor.

Table 4

Pre-operative variables significantly correlated with late-RVAD support.

Pre-operative variables	Late-RVAD support		
	Correlation	95% CI	Significant Probability
Gender	0.21	(0.07, 0.35)	0.004
WBC	0.18	(0.04, 0.32)	0.012
Weight	−0.16	(−0.29, −0.01)	0.004

Table 5

The expected performance of aggregate model. Predictive outcomes are suggested by the model; clinical decisions are made by the experts in hospital.

(a) Performance evaluated on the complete cohort (n=183.)

		CLINICAL DECISION	
		RVAD+	**RVAD−**
PREDICTION	RVAD+	$RVAD^{+/+}$ (True Positive) Sensitivity: 85%	$RVAD^{-/+}$ (False Positive) False Positive Rate: 17%
	RVAD−	$RVAD^{+/-}$ (False Negative) False Negative Rate: 15%	$RVAD^{-/-}$ (True Negative) Specificity: 83%

(b) Performance evaluated on the sub-group with initial continuous-flow LVAD (n=40.)

		CLINICAL DECISION	
		RVAD+	**RVAD−**
PREDICTION	RVAD+	$RVAD^{+/+}$ (True Positive) Sensitivity: 80%	$RVAD^{-/+}$ (False Positive) False Positive Rate: 20%
	RVAD−	$RVAD^{+/-}$ (False Negative) False Negative Rate: 14%	$RVAD^{-/-}$ (True Negative) Specificity: 86%