Predicting 1-year cardiac transplantation survival using a donor–recipient risk-assessment tool

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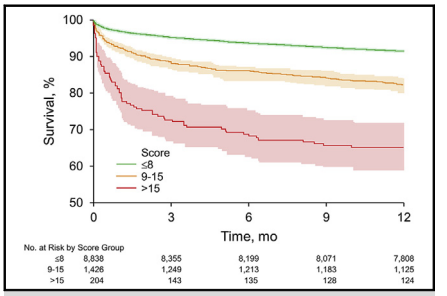
ABSTRACT

Objective: Many donor and recipient factors influence 1-year survival of patients after cardiac transplantation. To date, a statistical model has not been developed to assess the interplay of these factors in predicting outcomes, so we developed a risk-assessment tool to enhance decision-making.

Methods: We analyzed 29 variables that were reported in the United Network for Organ Sharing database for 24,540 cardiac transplantations performed between January 1, 2000, and June 30, 2015. For one half of the patients (the prediction population), a multivariable Cox regression model and the bootstrap resampling method were used to devise a scoring system predicting 1-year survival. The other half (the validation population) were stratified by score into 3 risk categories: high risk, medium risk, and low risk. One-year survival was compared among the 3 groups.

Results: Eleven variables were statistically significant in predicting 1-year survival. One-year survival for patients with risk scores of less than or equal to 8, 9 to 15, and greater than 15 were 91.2%, 81.7%, and 64.6%, respectively ($P < .001$). The C index of the Cox regression model was calculated at 0.62 when using risk score as a continuous predictor.

Conclusions: Donor and recipient risk factors influence patient survival after cardiac transplantation. Long-term outcomes may be optimized with a statistically based risk model to improve donor–recipient matching. (J Thorac Cardiovasc Surg 2018;155:1580-90)



Quantitative risk assessment may enhance the process of donor–recipient pairing.

Central Message

Quantitative risk assessment may enhance the process of donor–recipient pairing.

Perspective

Existing risk-assessment tools in the field of cardiac transplantation fail to account for the interplay between donor and recipient characteristics. We developed a model to predict 1-year posttransplant survival that can aid in the decision-making process.

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In the United States, the Centers for Medicare and Medicaid Services have identified 1-year survival as a key quality metric in the regulatory oversight of cardiac transplantation.[1] Several donor- and recipient-specific risk factors have been identified as important predictors of poor 1-year survival.[2-4] Risk models have been proposed to guide both donor organ selection and listing of recipient candidates.[5-10] However, the existing models have been limited in their ability to capture the interplay between donor and recipient risks when determining whether a given donor–recipient match is likely to result in 1-year survival. We sought to establish a scoring system that would enhance decision-making in determining whether an available donor organ would likely result in a successful 1-year outcome for a given recipient.

METHODS

Data from the Organ Procurement and Transplantation Network/United Network for Organ Sharing registry were used to select patients older than 18 years who underwent isolated cardiac transplantation between January

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Abbreviations and Acronyms
ECMO = extracorporeal membrane oxygenation
LVAD = left ventricular assist device

1, 2000, and June 30, 2015. An additional subset analysis was performed on patients who underwent transplant after 2008 to control for possible confounders due to changes in management (particularly the introduction of continuous-flow left ventricular assist device [LVAD] technology) that may have affected posttransplant outcomes. Those patients were included in the analysis. Risk factors for 1-year mortality were identified from a review of published literature. Variables were excluded from the analysis if data were missing for more than 15% of the overall study population. During analysis, patients with missing data on the specific variable of interest were excluded when the variable was analyzed. Patients were randomly assigned to 1 of 2 groups: 1 group was used for predicting 1-year survival outcome and building the scoring system (the prediction population), and the other group was used for evaluating the scoring system (the validation population). Patients were divided into 2 groups by sorting the patients' record numbers in numerical order and then assigning patients with an odd ranking order to the prediction data set and the ones with an even ranking order to the validation data set.

Cox regression models were used to identify the significant univariate and multivariable predictors of 1-year mortality for the original prediction population. The proportional hazard assumption of the Cox regression model was tested for each predictive variable by testing the significance of the interaction terms between the variable and follow-up time in the Cox regression model predicting 1-year mortality. The bootstrap method was used to resample the prediction population 100 times with replacement, and the number of patients in each resampled data set was set to be the same number as the sample size of the original prediction population. For each resampled population, a multivariable model was selected among the significant predictors from univariate analysis with the stepwise selection method. Finally, only the variables that were entered into the multivariable model at least 70 times were included in the scoring system. The mean coefficients of all the multivariable models from the resamples were calculated and used to derive the prediction score. The predictor with the smallest coefficient was identified, and with its score set to 1, all the other predictors were assigned a score value equal to the quotient of their linear coefficients divided by the smallest coefficient. A score was then calculated for each patient in the validation population according to the scoring system generated previously. To generate low-risk (survival rate about 90%), intermediate-risk (survival rate about 80%), and high-risk (survival rate <70%) groupings, patients' scores were divided into 3 groups ($\leq$8, 9-15, and >15) based on the 1-year survival rate of patients with each score. The Kaplan–Meier method was used to generate survival curves and calculate 1-year survival statistics for the 3 groups. The C index was calculated to measure the discrimination of the scores, and the calibration plot was drawn to show the agreement between the observed and predicted survival rates by grouping patients by every 10th percentile of the predicted risk of 1-year mortality. Descriptive statistics for categorical variables were summarized as frequency and percentage; continuous variables were summarized as mean (standard deviation) or median (range) as appropriate. All statistical tests were 2-sided, with an α level of .05 for statistical significance. Statistical analysis was performed with SAS version 9.4 software (SAS Institute Inc, Cary, NC).

RESULTS

A total of 24,540 patients older than 18 years underwent isolated cardiac transplantation between January 1, 2000, and June 30, 2015. This population was randomly divided into a prediction data set (n = 12,270) and a validation data set (n = 12,270). Baseline and operative data were summarized for the 2 groups (Table 1). One-year survival for the prediction population was 88.2% (95% confidence interval, 87.6%-88.8%). After the exclusion of risk factors for which more than 15% of the data were missing for the study population, a total of 29 variables were selected for analysis, and no variable was missing more than 7% of the data. Donor-specific risk factors included distance from the transplant center, ischemic time, cause of death, left ventricular ejection fraction, hypertension, and clinical infection. Recipient-specific risk factors included dialysis, extracorporeal membrane oxygenation (ECMO), durable LVAD support, intra-aortic balloon pump, use of inotropes at listing, cause of heart failure, cerebrovascular disease, total bilirubin level, days on the waiting list, and number of previous transplants. Age, sex, ethnicity, presence of diabetes mellitus, and creatinine level were evaluated in both groups. Ethnic mismatch, sex mismatch, and donor-to-recipient height-weight ratio were studied as risk factors with a combined potential to influence 1-year survival. These variables were incorporated into a univariate Cox proportional hazards regression model (Table 2) and multivariable Cox proportional hazards regression model (Table 3).

The bootstrap method was used to create resamples and identify variables that were entered into the multivariable model more than 70% of the time. According to these results, the following risk factors were included in the scoring system: waiting time, recipient creatinine level greater than 2.0 mg/dL or condition requiring dialysis, LVAD, ECMO, recipient age, recipient total bilirubin of at least 3.0 mg/dL, donor age, ischemic time, and female donor or sex mismatch (Table 4). The multivariable model containing these factors had a C index of 0.64.

Risk scores were calculated for 10,468 patients in the validation population in which all variables of interest were available. Calculated risk scores ranged from 0 to 32 (mean [standard deviation], 5.1 [3.9]) (Figure 1). Groupings were then assigned according to the following cutoffs: low risk (score $\leq$8), medium risk (score, 9-15), and high risk (score >15). Survival curves for the 3 risk groupings are shown in Figure 2: Low-risk patients had a 91.2% 1-year survival, medium-risk patients had an 81.7% 1-year survival, and high-risk patients had a 64.6% 1-year survival ($P < .001$). For the subset of patients who underwent transplant after 2008, the results were similar, with 1-year survival rates of 92.3%, 84.6%, and 72.1% for low-, medium-, and high-risk patients, respectively ($P < .001$) (Figure 3).

High-risk scores were most frequently related to end-organ function, age (of donor and recipient), and LVAD use (Figure 4). Although ECMO use was a heavily weighted risk factor in the scoring system, it contributed to only a small percentage of the overall high-risk group. Recipient