Predicting survival among high-risk pediatric cardiac transplant recipients: An analysis of the United Network for Organ Sharing database

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✍ Supplemental material is available online.

Objective: Studies of high-risk pediatric cardiac transplant recipients are lacking. The purpose of this study is to evaluate early posttransplant survival in high-risk pediatric patients.

Methods: The United Network for Organ Sharing (UNOS) provided de-identified patient-level data. The study population included 3502 recipients aged less than 21 years who underwent transplantation from January 1, 1995, through December 31, 2005. Recipients were stratified on the basis of the presence or absence of high-risk criteria: pulmonary vascular resistance index greater than 6 Wood units/m^2 (n = 285, 8.1%), creatinine clearance less than 40 mL/min (308, 8.8%), hepatitis C positivity (33, 0.9%), donor/recipient weight ratio less than 0.7 (80, 2.3%), panel reactive antibody greater than 40% (235, 6.7%), retransplantation (235, 6.7%), and age less than 1 year old (840, 24.0%).

Results: Overall, 1575 (45.0%) patients met at least one high-risk criterion. Higher numbers of high-risk criteria in a patient were correlated with increased 30-day mortality (0 high-risk criteria: 5.2%; 1 criterion: 7.9%; 2 criteria: 12.9%; and 3 or more criteria: 25.0%; $P < .0001$) and poor long-term survival ($P < .0001$). Among patients with high-risk criteria, a simplified scoring scale accurately predicts both 30-day and contingent 1-year mortality ($P < .0001$).

Conclusions: Individually, the effect of high-risk criteria on posttransplant survival varied; however, increasing numbers of criteria in a patient resulted in a cumulative increase in mortality. A scoring scale allows for the prediction of approximate mortality rates after transplantation. These findings suggest that recipient criteria for transplantation should focus on the number of high-risk criteria as well as clinical status, rather than the presence or absence of a single risk factor.

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Optimal allocation of the limited—and decreasing[1]—supply of pediatric donor hearts requires accurate pretransplant assessment of survival and data-derived selection of criteria indicating high risk. Unfortunately, criteria for transplant eligibility remain largely the result of consensus opinion.

In the adult population, continued improvements in posttransplant outcomes (as well as the ongoing shortage of donor organs) have prompted attempts to expand the pools of both donors and recipients. Results from the use of such "alternate-list" strategies have been variable. Some authors have reported results equivalent to those in standard criteria recipients,[2] whereas others have had less success.[3] In some cases, specific traditional high-risk criteria (HRC) have failed to consistently predict poor posttransplant outcome (older age,[4-6] recipient hepatitis C positivity[7]), whereas others clearly increase posttransplant mortality (elevated pulmonary vascular resistance [PVR][8]).

The applicability of any of these data to pediatric recipients is unclear. Although less well studied in children, some results suggest that pediatric HRC recipients have acceptable outcomes and that our criteria remain too strict.[9,10] Evidence-based estimates of posttransplant survival in a pediatric population would allow for better stratification of potential recipients and optimization of transplant selection criteria.

This report uses data from the United Network for Organ Sharing (UNOS) database to assess posttransplant outcomes in patients meeting traditional HRC. Our goals were (1) to estimate the impact of HRC on posttransplant outcomes and (2) to develop a simplified scoring system to predict short-term posttransplant survival.

Methods

Data Collection

UNOS provided de-identified patient level data from the Thoracic Registry (data source #021606-4). Use of these data is consistent with the regulations of our university's institutional review board. Records with incomplete data were excluded from analyses requiring those data points.

Study Population

The study population consists of 3502 transplants performed on patients less than 21 years of age between January 1, 1995, and December 31, 2005. Recipients were stratified on the basis of the presence or absence of traditional HRC: PVR index greater than 6 Wood units/m^2 (n = 285, 8.1%), creatinine clearance (CrCl) less than 40 mL/min (308, 8.8%), hepatitis C positivity (33, 0.9%), donor/recipient weight ratio less than 0.7 (80, 2.3%), panel reactive antibody greater than 40% (235, 6.7%), retransplantation (235, 6.7%), and age less than 1 year old (840, 24.0%). These criteria were established before data analysis and are based on internal criteria for transplantation at our institution, as well as a review of published reports.[11] Congenital heart disease (CHD) was not considered as one of the HRC because previous work had suggested that it is *complex* rather than *any* CHD which indicated elevated risk,[9] and the UNOS database does not contain detailed data regarding the CHD diagnosis that would enable such stratification. In addition, patients were grouped by the number of HRC present: one (n = 1189, 34.0%), two (n = 334, 9.5%), and three or more (n = 52, 1.5%) Overall, 1575 (45.0%) patients met at least one HRC.

Data Analysis

Data were analyzed by SAS 9.13 for Windows software (SAS Institute, Inc, Cary, NC). The primary outcomes were 30-day and contingent (on 30-day survival) 1-year mortality; other outcomes included long-term survival (time to death) and in-hospital complications. All variables analyzed are available in Table E1; only significant variables are reported. Continuous variables are reported as means ± standard deviation and were compared by the Student t test (with Bonferroni correction). Ordinal variables were compared by the χ^2 test. All P values are 2-sided. Multivariate regression (stepwise, $P < .05$) was also performed. Kaplan–Meier analysis and Cox proportional hazards regression (stepwise, $P < .05$) were used for time-to-event analysis;

patients without accurate follow-up times were excluded from these analyses. Risk, odds (OR), and hazard ratios are reported with 95% confidence intervals (95% CI) in parentheses. Simplified predictive scores were developed for both 30-day and contingent 1-year mortality. Data from both multivariate and univariate analysis were used to assign points on the basis of the presence of specific comorbidities. The predictive value of the scores was assessed by the χ^2 test and logistic regression.

Results

Baseline demographics are given in Table 1 with a comparison of HRC versus normal-risk recipients; patients in the HRC group required higher levels of support and critical medical care before transplantation.

Early and Late Mortality

Thirty-day (9.2% vs 5.2%; $P < .0001$) and contingent 1-year mortality (10.2% vs 7.7%; $P < .0229$) were higher in patients with HRC than in those without. Within the HRC group, indicators of clinical support (hospitalization, mechanical ventilation) were the most significant predictors of 30-day and contingent 1-year mortality (Table 2). Patients undergoing retransplantation and those with elevated panel reactive antibody or PVR index did not have an increased risk of early mortality (Table 2), whereas those with renal failure did (OR 3.01, 95% CI 2.05–4.43). Small sample sizes limited the analysis of hepatitis C positivity (n = 33, OR 1.72, 95% CI 0.65–4.52) and low donor/recipient weight ratio (n = 80, OR 1.77, 95% CI 0.94–3.36). Later year of transplantation was associated with increased survival at 30 days ($P = .0069$). In multivariate analysis, similar factors were important in predicting poor short-term outcomes (Table 3).

In-hospital Complications

Early survival was drastically reduced in HRC patients having postoperative complications. Patients requiring dialysis had significantly higher 30-day (28.0% vs 5.2%) (OR 7.10, 95% CI 5.13–9.81) and contingent 1-year mortality (38.4% vs 7.2%) (OR 8.04, 95% CI 5.52–11.71). Less severe increases in 30-day (10.7% vs 5.4%) (OR 2.10, 95% CI 1.59–2.79) and contingent 1-year mortality (17.4% vs 6.3%) (OR 3.14, 95% CI 2.38–4.16) occurred in patients with postoperative infections.

Multivariate predictors of the need for postoperative dialysis in HRC patients included preoperative CrCl less than 40 mL/min (OR 4.03, 95% CI 2.54–6.42), redo transplantation (OR 2.32, 95% CI 1.28–4.18), and the need for mechanical ventilation (OR 2.54, 95% CI 1.57–4.09); age less than 1 year was protective (OR 0.56, 95% CI 0.34–0.94). Infections occurred with greater frequency in patients with poor pretransplant clinical status as indicated by CrCl less than 40 mL/min (OR 1.44, 95% CI 1.02–2.03), the need for mechanical ventilation (OR 2.47, 95% CI 1.74–3.50), intensive care support (OR 1.59, 95% CI 1.11–2.26), as well