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Abnormal nutrition affects waitlist mortality in infants awaiting heart transplant

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BACKGROUND: Although nutritional status affects survival after heart transplant (HTx) in adults and older children, its effect on outcomes in young children is unknown. This study aimed to assess the effect of pre-HTx nutrition on outcomes in this population.

METHODS: Children aged 0 to 2 years old listed for HTx from 1997 to 2011 were identified from the Organ Procurement and Transplantation Network database. Nutritional status was classified according to percentage of ideal body weight at listing and at HTx. Logistic regression analysis evaluated the risk of waitlist mortality. Cox proportional hazard models assessed the effect of nutrition on post-HTx survival.

RESULTS: Of 1,653 children evaluated, 899 (54%) had normal nutrition at listing, 445 (27%) were mildly wasted, 203 (12%) were moderate or severely wasted, and 106 (6%) had an elevated weight-to-height (W:H) ratio. Moderate or severe wasting (adjusted odds ratio, 1.9; 95% confidence interval, 1.3–2.7) and elevated W:H (adjusted odds ratio, 1.7; 95% confidence interval, 1.1–2.6) were independent risk factors for waitlist mortality. HTx was performed in 1,167 patients, and 1,016 (87%) survived to 1-year post-HTx. Nutritional status at listing or at HTx was not associated with increased post-HTx mortality. Nutritional status did not affect the need for early reoperation, dialysis, or the incidences of infection, stroke, or rejection before hospital discharge.

CONCLUSIONS: Moderate or severe wasting and an elevated W:H are independent risk factors for waitlist mortality in patients aged < 2 years but do not affect post-HTx mortality. Optimization of pre-HTx nutritional status constitutes a strategy to reduce waitlist mortality in this age range.

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Nutritional status before heart transplant (HTx) has been shown to affect post-operative outcomes in adults.[1,2] Obesity and wasting have both been associated with decreased post-HTx survival. In the pediatric population, data addressing the effects of nutritional status on HTx outcomes are limited and conclusions vary.[3–6] Rossano et al[5] retrospectively examined the effect of body mass index (BMI) on outcomes in 105 pediatric patients aged older than 2 years who underwent HTx at their center. They concluded that being underweight (defined as BMI < 5th percentile) at the time of HTx was an independent predictor of decreased graft survival compared with patients of normal weight. Subsequently, Kaufman et al[4] reported pre-HTx obesity as a risk factor for post-operative mortality in patients aged 0 to 21 years. In contrast to the Rossano study, wasting did not appear to influence post-HTx survival. A second study performed by Kaufman et al,[3] using the International Society of Heart and Lung Transplantation (ISHLT) HTx registry, demonstrated no difference in post-operative outcomes by nutritional status but specifically excluded patients aged younger than 2 years.

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Each of these studies reached different conclusions, and none adequately addressed the effect of nutritional status on pre-HTx and post-HTx outcomes in infants and young children. Infants undergoing HTx have the highest early post-HTx mortality,[7,8] the reasons for which remain unclear. The potential role of nutritional status in the risk of death in this population is unknown. This study aimed to evaluate the effect of nutritional status on waitlist and early post-HTx mortality in children aged younger than 2 years.

Methods

Data collection

The Organ Procurement and Transplantation Network (OPTN) database was queried for all patients aged younger than 2 years listed for HTx in the United States between 1997 and 2011. This interval was chosen to limit era effect, provide an adequate follow-up interval, and maximize the number of patients included in the study. Weight and length measurements were collected at listing and at the time of HTx for each patient. To minimize inclusion of erroneous data, patients were excluded from analysis if their weight-for-height (W:H) *z*-score was greater than 6 or less than –6, if there was an absolute change of greater than 2 *z*-scores in magnitude between listing and HTx with a waiting time of less than 3 months, or if absolute length decreased by more than 3 cm between listing and HTx. Patients were also excluded from analysis if they underwent a non-orthotopic HTx and if data were incomplete for analysis.

Additional data collected included sex, race, blood type, age at listing, United Network of Organ Sharing status at listing (1A, 1B, or 2), diagnosis (congenital heart disease, cardiomyopathy, or other), waitlist time, the use of extracorporeal membranous oxygenation (ECMO) or ventricular assist device (VAD) support, infections requiring intravenous drug therapy, inotrope use, and ventilator support. Data collected in patients who underwent HTx included serum creatinine at HTx, donor-to-recipient weight ratio, age of donor, surgical method, and hospitalization status at HTx.

Outcome measures

The primary outcomes were (1) waitlist survival to HTx and (2) post-HTx survival to 1 year. Secondary outcomes included post-HTx stroke, the need for dialysis, rejection episodes before hospital discharge, hospital length of stay, reoperation before hospital discharge, the need for additional surgical procedures, and infection before hospital discharge.

Nutritional status stratification

The Waterlow criteria, based on percentage of ideal body weight (%IBW), were used to classify patient nutritional status. These criteria have been previously used to define acute and chronic malnutrition,[9–11] including patients aged younger than 2 years.[4,12–15] According to these criteria, patients were classified at listing and at the time of HTx as having elevated W:H (> 120% IBW), normal nutrition (90%–120% IBW), or wasting (< 90% IBW). The wasting group was further subdivided into mild (80%–90% IBW), moderate (70%–80% IBW), or severe (< 70% IBW). For statistical analysis, the moderate and severe wasting groups were combined due to a small number of patients in the severely wasted cohort.

Statistical methods

Demographics, patient characteristics, and secondary outcomes were compared by nutritional status using chi-square tests for categoric variables, Mantel-Haenszel tests for ordinal variables, and Kruskal-Wallis tests for continuous variables. Risk factors for waitlist mortality were assessed using logistic regression. Variables significantly associated with waitlist mortality on univariate analysis ($p < 0.1$; data not shown) were included in a multivariable logistic regression model. Kaplan-Meier curves of the 1-year post-HTx survival were generated and compared using the log-rank test. Cox proportional hazard models were used to identify factors influencing survival to 1-year post-HTx. Factors associated with 1-year post-HTx survival in the univariate analysis ($p < 0.1$; data not shown) were incorporated into the multivariable Cox regression model. All analyses were performed using SAS 9.3 software (SAS Institute Inc, Cary, NC), with statistical significance set at a p-value of < 0.05 using 2-sided tests.

Results

The study included 1,653 of the 2,239 patients aged 0 to 2 years listed for HTx during the study period. Patient characteristics stratified by nutritional status at listing are reported in Table 1. Patients characterized as having normal nutritional status were more likely to be boys and aged between 1 and 2 years, whereas girls and those aged younger than 1 year were more likely to be wasted or have an elevated W:H. Wasted patients were more likely to have cardiomyopathy, whereas patients with elevated W:H were more likely to have congenital heart disease. Patients with elevated W:H were also more likely to require inotropes, ventilator support, or have an infection requiring intravenous drug therapy within 2 weeks of listing than patients in other nutritional status groups.

Of the patients included in the study, 486 (29%) died on the waitlist; among these, 254 (52%) had normal nutritional status, 114 (24%) were mildly wasted, 75 (15%) were moderate or severely wasted, and 43 (9%) had elevated W:H. Multivariable logistic regression identified nutritional status as an independent risk factor for waitlist death (Table 2). Patients with moderate or severe wasting and those with an elevated W:H had an increased risk of waitlist death compared with patients with normal nutritional status or mild wasting.

HTx was performed in 1,167 patients, and 1,016 (87%) survived at least 1 year. Post-HTx 1-year survival rates were similar between nutritional status groups, whether nutritional status was assessed at listing (Figure 1A) or at the time of HTx (Figure 1B). After controlling for diagnosis, waitlist time, and ventilator or ECMO support, pairwise comparison of the 1-year survival curves by log-rank test and multivariable Cox regression analysis both demonstrated that nutritional status was not associated with increased post-HTx mortality (Table 3). In fact, mild wasting at the time of HTx was associated with improved survival to 1 year compared with other nutritional status groups.

Nutritional status at listing had no effect on any secondary outcomes. In contrast, elevated W:H at HTx