Early Predictors of Survival to and After Heart Transplantation in Children With Dilated Cardiomyopathy

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Background—The importance of clinical presentation and pretransplantation course on outcome in children with dilated cardiomyopathy listed for heart transplantation is not well defined.

Methods and Results—The impact of age, duration of illness, sex, race, ventricular geometry, and diagnosis of myocarditis on outcome in 261 children with dilated cardiomyopathy enrolled in the Pediatric Cardiomyopathy Registry and Pediatric Heart Transplant Study was studied. End points included listing as United Network for Organ Sharing status 1, death while waiting, and death after transplantation. The median age at the time of diagnosis was 3.4 years, and the mean time from diagnosis to listing was 0.62±1.3 years. Risk factors associated with death while waiting were ventilator use and older age at listing in patients not mechanically ventilated (P=0.0006 and P=0.03, respectively). Shorter duration of illness (P=0.04) was associated with listing as United Network for Organ Sharing status 1. Death after transplantation was associated with myocarditis at presentation (P=0.009), nonwhite race (P<0.0001), and a lower left ventricular end-diastolic dimension z score at presentation (P=0.04). In the myocarditis group, 17% (4 of 23) died of acute rejection after transplantation.

Conclusions—Mechanical ventilator use and older age at listing predicted death while waiting, whereas nonwhite race, smaller left ventricular dimension, and myocarditis were associated with death after transplantation. Although 97% of children with clinically or biopsy-diagnosed myocarditis at presentation survived to transplantation, they had significantly higher posttransplantation mortality compared with children without myocarditis, raising the possibility that preexisting viral infection or inflammation adversely affects graft survival. (Circulation. 2012;126:1079-1086.)

Key Words: cardiomyopathy, dilated □ heart transplantation □ myocarditis □ pediatrics

In children, dilated cardiomyopathy (DCM) is the most common form of cardiomyopathy and the most common indication for heart transplantation.1,2 The annual incidence of DCM is reported to be 0.37 per 100 000 in the United States and 0.57 to 1.13 per 100 000 in Australia.3–5 In children with end-stage heart failure secondary to DCM, heart transplantation is the only therapeutic option currently available. In prior studies from the Pediatric Cardiomyopathy Registry (PCMR), freedom from death or heart transplantation in children with DCM was 61% and 47% at 1 and 5 years, respectively.6–7 Refinements in the management of end-stage DCM in children over the last decade have significantly reduced early mortality, but transplantation remains the definitive treatment.8–11 Death after listing or after heart transplantation remains a significant problem in this group of children, even in the era of mechanical support, and as many as 38% of patients with DCM listed for heart transplantation have significant complications and morbidity while waiting for heart transplantation.12 Outcomes after heart transplantation are favorable in adults13,14 and in children with DCM.2,4,11,15,16 Children with DCM have a 68% to 72% 10-year survival rate after transplantation, higher than that for children transplanted for end-stage congenital heart disease.17,18 Improved surgical and perioperative care has led to an era of improvements in outcomes after transplantation.19

Clinical Perspective on p 1086

Studies of children with DCM requiring heart transplantation have focused on cohorts identified at listing.16,17 The impact of prelisting factors on outcomes both after listing and after transplantation has not been studied. Better outcomes in children with DCM may be possible with better identification and management of preexisting viral infection or inflammation adversely affects graft survival.
hypothesized that important risk factors for worse outcomes after transplantation listing and transplantation might be identified in children with DCM from their prelisting status. To evaluate this hypothesis, we pooled longitudinal data regarding patients with DCM from 2 large pediatric databases, the PCMR and the Pediatric Heart Transplant Study (PHTS) databases, and attempted to define risk factors at presentation and at listing that were associated with worse outcomes after listing in this cohort.

Methods

Patient Population
Patients were identified from a merged data set that included all children enrolled in the PCMR, who were 30 or enrolled in the PHTS. The PCMR is a National Institutes of Health/National Heart, Lung, and Blood Institute–funded registry that enrolled children (<18 years of age at the time of presentation) who were diagnosed with all forms of primary cardiomyopathy from January 1, 1990 (clinical trial registration, http://www.clinicaltrials.gov; unique identifier, NCT00005391). Data collected include echocardiographic measurements and clinical and laboratory information at the time of presentation and at yearly follow-up visits. Patient follow-up in the PCMR is censored at heart transplantation or death.

The PHTS is an event-driven registry that has enrolled patients <18 years of age listed for heart transplantation at participating institutions since 1993. The PHTS data set includes outcome after listing, peri-transplantation course, and posttransplantation events such as rejection, infection, graft atherosclerosis, death, malignancy, and need for retransplantation. The registries were merged to allow analysis of data in children with cardiomyopathy from the time of presentation through their posttransplantation course. The merged data set included children transplanted in the United States and Canada. The PHTS registry is currently active. The PCMR is no longer enrolling new patients, but analysis of previously enrolled patients continues. Follow-up for the merged data set was complete through December 31, 2005.

Only children who met the PCMR definition of DCM were included in this analysis. In the PCMR data set, DCM was defined by echocardiographic criteria that included a left ventricular (LV) end-diastolic dimension (EDD) ≥2 SDs for body surface area and an LV percent fractional shortening ≥2 SDs for age. The diagnosis of myocarditis was defined in this study as it has been previously as either the histological evidence of myocarditis (the presence of Dallas criteria) obtained at endomyocardial biopsy or at explantation or clinically by the investigator at the submitting institution if histology was not available.

Risk Factors Studied
We examined several potential diagnoses and prelisting, listing, and transplantation risk factors for the following end points: severity of illness as defined by the need to be listed as United Network for Organ Sharing (UNOS) status 1 (highest-priority UNOS status to receive an organ, a reflection of severity of illness at listing), death after listing while waiting for a heart, and death after heart transplantation. The merged data set included 10 children transplanted in Canada, which does not use UNOS listing criteria. For the variable UNOS status 1 at listing, information was available for 3 children to be coded in the appropriate UNOS status, and the other children were excluded from this portion of the analysis. The potential risk factors for death after listing while waiting for a heart included age at listing, sex, race (white versus nonwhite), diagnosis of myocarditis, time from diagnosis to listing (years), use of mechanical ventilation at the time of listing, and multiple echocardiographic measures of cardiac performance and size, including LV fractional shortening z score and LVEDD z score at presentation. Echocardiographic measurements were expressed as the z score for body surface area to adjust for body size. In this analysis, older age was defined as >10 years and younger age as <1 year; however, in the regression analysis, age was analyzed as a continuous variable. UNOS status 1 versus 2 was also included in the analyses of death while waiting and after transplantation. Age at transplantation, use of mechanical ventilation at the time of transplantation, and time spent waiting for a heart were included in the risk factor analysis for death after transplantation. Transplanted patients with and without the diagnosis of myocarditis were also analyzed.

Data Collection
Institutional Review Board approval was obtained for each registry (PCMR and PHTS) and the merged data set at all study sites. A data-sharing agreement was established between the data coordinating centers (New England Research Institutes, Watertown, MA, and University of Alabama, Birmingham) before the exchange of data.

Statistical Methods
Standard statistical methods for summarizing and displaying data were used. Data are reported as mean and median with standard deviations. Logistic regression was used to determine which variables were associated with listing as UNOS status 1. Kaplan-Meier analysis was used to estimate the time-related probability of death. Time 0 for survival analysis for death while waiting was defined as the date of listing; time 0 for the analysis of death after transplantation was the date of transplantation. The log-rank test was used to compare the survival of designated subgroups. Cox proportional hazard regression was used to identify risk factors for death while waiting and death after transplantation; the results are reported as hazard ratios. We set α at 0.05, and all tests were 2 tailed. Forward selection was used in the multivariable analysis. Comparison of the myocarditis and no myocarditis groups was performed with the unpaired t test for normally distributed data and the Kruskal-Wallis test for skewed data. SAS statistical analysis software (SAS Institute, Cary, NC) was used for all analyses.

Results

PCMR and PHTS Registry Merger
The merged data set included 332 children from 16 participating centers, of whom 261 had a diagnosis of DCM and made up the study cohort (Table 1). The remaining 71 children from the original merged data set (n = 332) were not included in this study because their cardiomyopathy phenotype was not DCM. Of the 261 children, 11% (n = 29) died waiting for a heart. Eighty percent (209 of the 261) went on to heart transplantation, and the remaining 23 children were alive but still waiting at the time of analysis. Of these 209 children transplanted, 40 children (19%) died after heart transplantation.

Characteristics of Children With DCM Listed for Transplantation
Demographics of the 261 patients who were listed and the 209 who were transplanted are shown in Table 1. For the children who were listed, the median age at the time of diagnosis was 3.4 years (range, 0–17.9 years), and 43% were diagnosed at <1 year of age (Table 2). A third of the patients listed for transplantation presented after 10 years of age. Thirty percent of all patients listed were ventilator dependent at the time of listing. Data on inotropic support were not available. Of the initial 261 children with DCM, 11% (n = 29) were diagnosed with myocarditis either clinically or by biopsy at presentation.

Risk Factors Associated With Status 1 at Listing
Shorter duration of illness from diagnosis to listing was associated with listing as status 1 (odds ratio, 0.789; 95% confidence interval, 0.631–0.988; P = 0.04). No other factors were found to be associated with listing as status 1.
Death While Waiting for Transplantation

There were 29 deaths before transplant, 3 occurring after 2 years from listing. By 2 years after listing, 11% (n=260) of the patients had died while waiting, 11% (n=260) were still alive waiting, and 79% (n=206) had been transplanted (Figure 1). The primary cause of death was cardiac in nature (primary cardiac failure, sudden death, or multisystem failure) in 16 of the 29 children (55%; Table 3). Neurological events were a common cause of death, occurring in 6 of 29 (21%). Most of the risk factors analyzed did not correlate with death while waiting (Tables 4 and 5). The time on the wait list for children who died while waiting was not significantly shorter than the time from listing to transplantation in those who were transplanted. Mechanical ventilation at listing (P<0.003) was associated with death while waiting by Kaplan-Meier analysis (Figure 2). Mechanical ventilation at listing had a hazard ratio of 4.06 and was strongly associated with death while waiting in the multivariable analysis (P<0.0006). Age was not a risk factor for death while waiting in the univariate analysis (Table 4). A higher proportion of younger patients were ventilated at listing compared with older patients; thus, when mechanical ventilation was included in the analysis, multivariable analysis demonstrated that older age at listing was a risk factor (Table 5). One child with myocarditis died while waiting for heart transplantation. A subgroup analysis in children with DCM without myocarditis (n=232) also showed ventilator use and older age at listing as risk factors for death (P<0.001 and P<0.01, respectively).

Characteristics of Children With DCM Who Survived to Transplantation

Of the 261 patients listed for transplantation, 209 (80%) received heart transplants. The median age at transplantation was 4.4 years. UNOS status 1 at listing did not correlate with death while waiting. The transplanted group had a higher proportion of children who were UNOS status 1 at the time of transplantation compared with the time of listing (86% versus 79%). In the myocarditis group, 23 of 29 were transplanted (1 died waiting, 5 still waiting at analysis). The proportion of children who were status 1 at the time of transplantation was the same in the myocarditis and nonmyocarditis groups. At the time of heart transplantation, 22% of children were ventilator dependent.

Table 3. Primary Causes of Death Among 29 Children With Dilated Cardiomyopathy Who Died After Listing for Cardiac Transplantation

<table>
<thead>
<tr>
<th>Primary Cause of Death</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac failure</td>
<td>12</td>
<td>41</td>
</tr>
<tr>
<td>Neurological or cerebrovascular accident</td>
<td>6</td>
<td>21</td>
</tr>
<tr>
<td>Multiorgan or system failure</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Sudden cardiac death</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Pulmonary hemorrhage</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Other</td>
<td>5</td>
<td>17</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 2. Age Distributions of 261 Children With Dilated Cardiomyopathy

<table>
<thead>
<tr>
<th>Age Group, y</th>
<th>At Diagnosis, n (%)</th>
<th>At Listing, n (%)</th>
<th>At Transplantation, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.5</td>
<td>86 (33)</td>
<td>48 (18)</td>
<td>23 (11)</td>
</tr>
<tr>
<td>0.5–1</td>
<td>26 (10)</td>
<td>32 (12)</td>
<td>32 (15)</td>
</tr>
<tr>
<td>1–10</td>
<td>62 (24)</td>
<td>89 (34)</td>
<td>75 (36)</td>
</tr>
<tr>
<td>&gt;10</td>
<td>87 (33)</td>
<td>92 (35)</td>
<td>79 (38)</td>
</tr>
<tr>
<td>Total</td>
<td>261 (100)</td>
<td>261 (100)</td>
<td>209 (100)</td>
</tr>
</tbody>
</table>

UNOS indicates United Network for Organ Sharing; LVEF, left ventricular ejection fraction; LVFS, left ventricular fractional shortening; and LVEDD, left ventricular end-diastolic dimension.
Table 4. Univariate Risk Factors for Death Among Children With Dilated Cardiomyopathy

<table>
<thead>
<tr>
<th>Potential Risk Factor</th>
<th>Univariate P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death while waiting for transplantation (29 deaths in 261 children)</td>
<td></td>
</tr>
<tr>
<td>White race</td>
<td>0.12</td>
</tr>
<tr>
<td>Male sex</td>
<td>0.73</td>
</tr>
<tr>
<td>On ventilator at listing</td>
<td>0.003</td>
</tr>
<tr>
<td>Older age at listing*</td>
<td>0.30</td>
</tr>
<tr>
<td>UNOS status 1 at transplantation</td>
<td>0.10</td>
</tr>
<tr>
<td>Time from diagnosis to listing</td>
<td>0.45</td>
</tr>
<tr>
<td>LVFS z score at presentation</td>
<td>0.52</td>
</tr>
<tr>
<td>LVEDD z score at presentation</td>
<td>0.89</td>
</tr>
<tr>
<td>Death after transplantation (40 deaths in 209 children)</td>
<td></td>
</tr>
<tr>
<td>Nonwhite race</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male sex</td>
<td>0.94</td>
</tr>
<tr>
<td>On ventilator at transplantation</td>
<td>0.97</td>
</tr>
<tr>
<td>Older age at transplantation</td>
<td>0.05</td>
</tr>
<tr>
<td>UNOS status 1 at transplantation</td>
<td>0.48</td>
</tr>
<tr>
<td>Myocarditis at diagnosis</td>
<td>0.02</td>
</tr>
<tr>
<td>Time from diagnosis to listing</td>
<td>0.83</td>
</tr>
<tr>
<td>Time from listing to transplantation</td>
<td>0.47</td>
</tr>
<tr>
<td>LVFS z score at presentation</td>
<td>0.07</td>
</tr>
<tr>
<td>LVEDD z score at presentation (lower)</td>
<td>0.10</td>
</tr>
</tbody>
</table>

UNOS indicates United Network for Organ Sharing; LVFS, left ventricular fractional shortening; and LVEDD, left ventricular end-diastolic dimension.

*Mechanical ventilation removed from analysis.

Causes of Death After Transplantation

Among the 209 children who underwent heart transplantation, 40 died; 1-year survival was 92%, 5-year survival was 80%, and 10-year survival was 72% (Figure 3A). The most common cause of death after transplantation was the development of graft vasculopathy and/or myocardial infarction in 11 patients (28% of deaths). Sudden cardiac death occurred in 4 children (10% of deaths), likely related to either vasculopathy or acute rejection.17 Rejection was the cause of death in 10 patients (9 acute, 1 hyperacute rejection; 25% of deaths). There were 2 deaths from early graft failure and 1 from hyperacute rejection.

Risk Factors for Death After Transplantation

The results of the univariate and multivariable analyses of death after transplantation are shown in Tables 4 and 5, respectively. Older age at transplantation was associated with death after transplantation (P=0.05) by univariate analysis but not multivariable analysis (Figure 3B). Nonwhite race was significantly associated with worse survival in both the univariate and multivariable analyses (P<0.0001; Figure 3C). A diagnosis of myocarditis was associated with worse survival in the univariate and multivariable analyses (P=0.02 and P=0.009, respectively; Figure 4A). A lower LVEDD z score was also associated with worse posttransplantation survival by multivariable analysis (P=0.04).

Myocarditis and Outcomes

Survival at 1 and 3 years after transplantation was 83% and 65% in children with myocarditis compared with 93% and 88% in the group without myocarditis (P=0.01; Figure 4A). The median age at transplantation was 11.4 years in the children with myocarditis at presentation and 3.6 years in the children who did not have myocarditis at transplantation (P=0.03; Table 6). LV fractional shortening z score was not significantly worse in the myocarditis group. The LVEDD z score was similar between the 2 groups. Smaller LVEDD z score was a risk factor for death in the nonmyocarditis subgroup (P=0.02). Because of small numbers, the LVEDD z score could not be analyzed in the myocarditis subgroup.

Death resulting from acute rejection was more common in the myocarditis group compared with the nonmyocarditis group (P=0.003; Figure 4B).

Discussion

Identification of risk factors for worse outcome after listing is an important step toward optimizing the management of children with DCM. The merged data set available from the PCMR and PHTS offers a unique opportunity to follow up patients from the time of diagnosis through the posttransplantation period. In our study, mortality on the heart transplantation wait list was 11%. None of the variables measured at the time of diagnosis of DCM...
was associated with death while waiting for heart transplantation except mechanical ventilation and older age, which have previously been described as risk factors. Death after transplantation was associated with 3 factors: nonwhite race, a small LV dimension, and a diagnosis of myocarditis at the time of presentation.

Other studies have identified older age and black race as risk factors for worse survival after transplantation. In our study, older age was a predictor for death after transplantation in univariate but not multivariable analysis. Older age, particularly adolescence, is a known predictor for death after transplantation in children. This finding has been attributed to adolescent defiance, nonadherence to treatment, and risk-taking behavior. Worse outcome in this age group is not limited to heart transplantation patients; it is also seen in other solid-organ transplantation patients and with other chronic diseases such as diabetes mellitus. Black race is a common finding in many transplantation outcome studies. Higher mortality and morbidity in blacks compared with individuals of other races have been attributed largely to lower socioeconomic status, lower level of education, and limited access to health care but may also be attributed to genetic differences in drug metabolism and immunity. Although the black population may have genetic as opposed to demographic causes or social characteris-

Figure 3. A, Kaplan-Meier posttransplantation survival curve for children with dilated cardiomyopathy (n=209). B, Kaplan-Meier posttransplantation curves for children <1, 1 to 10, and >10 years of age at transplantation. C, Kaplan-Meier posttransplantation survival curves for nonwhite (Non-W) vs white children. Error bars represent 70% confidence limits.
myocarditis and demonstrated similar survival outcomes between the 2 groups.\textsuperscript{21} Subgroup analysis of each of these 2 methods of diagnosis for myocarditis separately was not feasible because of small numbers and the retrospective nature of the study design. In a PHTS analysis of children with DCM, myocarditis identified at transplantation was not a risk factor for death after transplantation.\textsuperscript{18} Differences between that study and the present study may best be addressed with a prospective study of children with biopsy-proven myocarditis to resolve this discrepancy.

Our finding that the diagnosis of myocarditis was associated with worse survival after transplantation raises the possibility that infectious or immune mechanisms persist that may affect outcome. The finding that acute rejection was a common cause of death in the myocarditis group supports this hypothesis. Possible explanations include ongoing subclinical viral infection, a change in immune or heterologous memory, viral reactivation after transplantation, or ongoing autoimmunity. In animal studies, persistent viral infection at the time of heart transplantation increases the tempo and likelihood of acute rejection and precludes the induction of allograft tolerance.\textsuperscript{29,30} Heterologous immunity and acquired immune memory shape immune responses on the basis of infections encountered. Because heterologous immunity has been shown to be associated with increased acute rejection, it has potential to increase the need for immunosuppression to avoid allograft rejection. Viral myocarditis has been shown to relapse occasionally after transplantation.\textsuperscript{31} Parvovirus B19 has been associated with death in children after heart transplantation and may contribute to cardiac transplantation rejection.\textsuperscript{32,33} In this respect, myocardial damage may be directly mediated by the virus itself, as in the case of Coxsackie B3 viral myocarditis.\textsuperscript{34,35} In heart transplantation patients, viral genome detection by polymerase chain reaction in endomyocardial biopsies from children after transplantation has been associated with acute rejection, transplant vasculopathy, and graft loss.\textsuperscript{36,37} On the other hand, the immune response and subsequent autoimmunity may be important in the pathogenesis of myocardial dysfunction. Nonspecific markers of inflammation such as C-reactive protein have been associated with worse outcome in myocarditis.\textsuperscript{38} Persistent viral immunity also may have a role in the pathogenesis of myocarditis. In support of this hypothesis, several reports describe favorable outcomes in children with biopsy-proven myocarditis in DCM who improved with either immunomodulation (immune globulin)\textsuperscript{39,40} or immunosuppression.\textsuperscript{41–44} Unfortunately, in our study, no information was available on the presence of active virus at transplantation or viral polymerase chain reaction testing of endomyocardial biopsies.

The clinical implications of the finding that DCM caused by myocarditis is a risk factor for worse survival after transplantation suggest the need for improved pretransplantation and posttransplantation interventions in children. Standardizing the assessment of chronic viral infection and inflammation of the myocardium has long been a goal of the pediatric cardiology community and appears to be pertinent in the assessment for transplantation eligibility.\textsuperscript{45} Treatment also needs to be standard-
ized because as many as 5% of patients with DCM receive immunomodulatory therapy without objective evidence of myocarditis.9 Posttransplantation immunosuppression protocols varied among the centers in our study. Therefore, it was not possible to determine the impact of the type and intensity of immunosuppression or the use of induction regimens (including the routine use of intravenous immune globulin) on the outcome of patients with myocarditis.

Limitations of the Study Design

Pediatric DCM is a diverse collection of diseases with both acquired and genetic causes. As a result, registry-based studies like ours have limitations in that heterogeneity may obscure causal relationships. This study was limited by its retrospective nature; despite the merger of 2 registries, there was a relatively modest number of patients. Subgroup analysis such as that for myocarditis results in even smaller numbers in each group, which makes robust statistical statements challenging. Data were limited to what was available and included in the databases before the merger in 2005. Data were also limited to the number of variables collected in the registries, without the possibility of additional collection. Despite these limitations, the information is valuable in predicting outcome and counseling families. These limitations remain a reality of research into rare diseases such as pediatric cardiomyopathy and further emphasize the need for larger and more detailed continued data collection efforts by registries. In addition, although diagnostic evaluations and treatment strategies were similar at the data collection sites, standardized protocols were not used within the study group. Multiple physicians initiated, manipulated, and terminated therapy for individual patients in different ways. This limitation can be overcome only with a prospective randomized study design, which would be challenging because of the low incidence of children presenting with severe heart failure and myocarditis.

Conclusions

Mechanical ventilation and older age at listing in patients not mechanically ventilated were risk factors for death while waiting for heart transplantation, factors that allow risk stratification of patients at the time of listing. Outcomes of children with DCM after transplantation are affected by nonwhite race and older age. Myocarditis is associated with a higher mortality after transplantation and suggests a persisting infectious or immune mechanism.

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Disclosures

None.

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Ventricular remodeling and survival are more favorable for myocarditis than for idiopathic dilated cardiomyopathy in childhood: an outcomes study from the Pediatric Cardiomyopathy Registry. *Circ Heart Fail*. 2010;3:689–697.


CLINICAL PERSPECTIVE

Factors that affect outcome in pediatric heart diseases such as dilated cardiomyopathy are often difficult to define because of the rarity of disease. To study the potential importance of factors at presentation and at listing for heart transplantation in children with dilated cardiomyopathy on outcome, we analyzed data from 2 large pediatric registries: the Pediatric Cardiomyopathy Registry and the Pediatric Heart Transplant Study. In the merged data set, there were 261 children with dilated cardiomyopathy. Among the factors studied were age, duration of illness, sex, race, ventricular geometry, and the clinical or histological diagnosis of myocarditis at presentation. We found that death while waiting was associated with ventilator use and older age at listing. A shorter duration of illness was associated with a more urgent listing status (United Network for Organ Sharing status 1). Death after transplantation was associated black race and lower left ventricular end-diastolic dimension z score at presentation. We also found that death after transplantation was associated with the diagnosis of myocarditis at presentation (P<0.009). Death while waiting was not associated with the diagnosis of myocarditis, and 97% of children with myocarditis survived to transplantation. Furthermore, the most common cause of death after transplantation in the myocarditis group was acute rejection (17%). This is the first study to show that children with dilated cardiomyopathy and myocarditis have significantly higher posttransplantation mortality with children without myocarditis. This finding suggests that preexisting viral infection or inflammation could adversely affect heart allograft survival and has implications for the management of these children before and after heart transplantation in the future.
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