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# Interaction of older donor age and survival after weight-matched pediatric heart transplantation

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**KEYWORD:**
pediatric heart transplant;
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adolescent age donors;
age mismatch

**BACKGROUND:** Donors are matched for weight in pediatric heart transplantation (PHT), yet age differences are not considered in this decision. In this study we attempt to identify the effect of age differences in weight-matched patients and the effect these differences have on post-transplant survival.

**METHODS:** The United Network of Organ Sharing (UNOS) database was queried for the period from October 1987 to March 2014 for all pediatric heart transplant patients. Transplants with donor-to-recipient (D-R) weight ratios of 0.8 to 1.5 were identified (weight-matched). D-R age differences were categorized as: donors 5 years younger than recipients (D<R−5); donors within 5 years of recipients (D=R±5); and donors 5 years older than recipients (D>R+5).

**RESULTS:** A total of 4,408 patients were identified as weight-matched transplants. Of these transplants, 681 were D>R+5, 3,596 were D=R±5 and 131 were D<R−5. D>R+5 transplants were found to be associated with decreased post-transplant survival compared with D=R±5 ($p = 0.002$). Rates of acute rejection were similar among all groups but post-transplant coronary allograft vasculopathy (CAV) was more prevalent in D>R+5 than D=R±5 patients (28% and 18%, respectively; $p < 0.001$). Increasing age difference by each year was associated with decreasing median post-transplant survival time ($p < 0.001$; hazard ratio 1.018, range 1.011 to 1.025). The overall negative association with mortality was due to the adolescent cohort (11 to 17 years), specifically D>R+5 transplants, utilizing organs from donors >25 of age.

**CONCLUSION:** In PHT, increasing D-R age difference decreases survival; however, this effect is driven by recipients 11 to 17 years old and donors >25 years old. Allocation of younger donor organs to adolescent recipients should be a priority.

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Heart transplantation is the treatment of choice for end-stage heart failure, and pediatric heart transplantation (PHT) is growing: 577 were performed in 2013, the largest number reported in a 1-year period.[1] There is a scarcity of pediatric donor organs and considerable mortality associated with the heart transplant waitlist.[2,3] This shortage has led to transplants that utilize so-called "marginal organs" from donors who are significantly larger, smaller or older, or with longer ischemic times, etc. Some donor characteristics, such as donor-to-recipient (D-R) weight ratio, have been well

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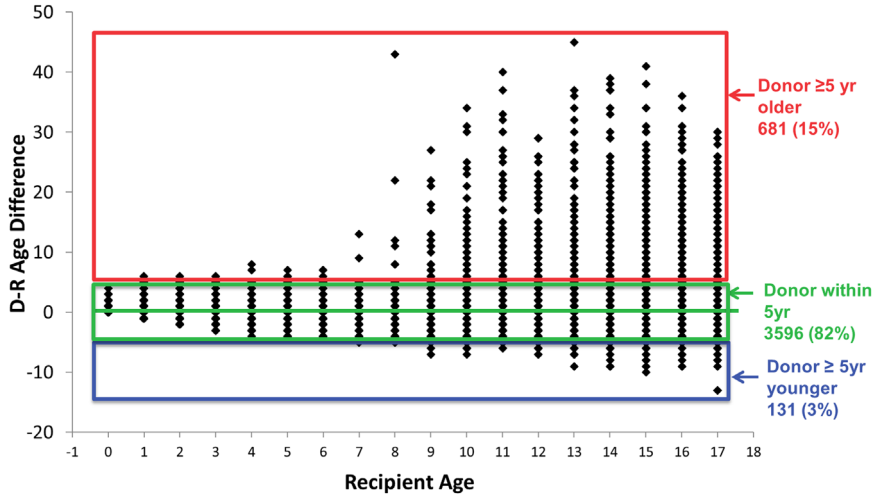


**Figure 1** Distribution of donor-recipient (D-R) age difference by recipient age. A dot at a given recipient age and D-R difference may represent more than donor-recipient pair. The majority of cases involving donors >5 years older than recipients took place in the adolescent population, whereas the majority of cases overall involved donors within 5 years of the recipient.

studied,[4–6] whereas the effect of D-R age difference has largely been ignored.

It is generally believed that, for the youngest children, D-R weight matching prevents extreme differences in age, but in older children and adolescents large differences (>5 years) in age are not uncommon. In adults, a D-R weight ratio of 0.8 to 1.2 is the generally accepted criterion.[4] In the pediatric population, larger hearts are more acceptable,[5,6] and different D-R weight ratio criteria are used among centers. Studies to date have not shown D-R weight ratio to be a significant factor in determining survival, except when extremely low ratios are used (i.e., <0.6).[7] Nonetheless, weight matching remains standard practice.

According to the 2008 Registry of the International Society for Heart and Lung Transplantation (ISHLT) Pediatric Report, donor age >30 years was found to be a risk factor for mortality within 1 year of transplant.[8] Chin et al showed donor age >40 years to be a risk factor for 1-year mortality in PHT.[9] The 2014 ISHLT Pediatric Report identified D-R age difference and donor age to be continuous risk factors for 10- and 15-year mortality, respectively.[10] The goal of this study was to investigate the effect of D-R age difference on survival among weight-matched PHT recipients in various age groups.

## Methods

### Study design and patient population

This was a respective analysis of data reported to the United Network for Organ Sharing/Organ Procurement and Transplantation Network registry for pediatric patients who underwent primary heart transplantation from October 1987 to March 2014. Transplants with a D-R weight ratio of 0.8 to 1.5 were identified as weight matched. D-R age differences were categorized into 3 groups: donors >5 years older than recipient (D>R+5); donors within 5 years of recipient (D=R±5); and donors >5 years younger than recipient (D<R−5).

### Statistical analysis

Continuous data were compared using the *t*-test and analysis of variance, with Tukey's method for normally distributed data. Non-parametric tests (Mann–Whitney *U*-test for 2 samples and Kruskal–Wallis analysis of variance for multiple samples) were used for data without a normal distribution. The chi-square test was used to compare categorical data. Survival curves were estimated using the Kaplan–Meier method, and survival curves were compared between groups using a log-rank test. Multivariate analyses were performed using Cox proportional hazards model and a stepwise selection technique to identify independent predictors of post-transplant mortality. D-R age difference was tested as both a continuous and categorical variable in different models. Donor age subgroup analysis was performed in increments of 5 years and long-term survival was compared. Analyses were performed using IBM SPSS Statistics version 21 (IBM Corp., Armonk, NY) software.

## Results

A total of 4,408 PHTs were identified as weight matched. D>R+5 was observed in 15% ($n$ = 681), D=R±5 in 82% ($n$ = 3,596) and D<R−5 in 3% ($n$ = 131) of the cohort (Figure 1).

Median donor age for the D>R+5, D=R±5 and D<R−5 groups was 27 years, 4 years and 8 years, respectively. The total number of transplants with D>R+5 was stable between transplant eras: 225 for the current era (2007 to 2014); 228 for the middle era (2000 to 2006); and 228 for the early era (1989 to 1999). However, the overall percentage of D>R+5 transplants decreased, down to 13% from 18% and 17% in the middle and early eras, respectively ($p$ < 0.001). D>R+5 transplants were less likely to have a female donor compared with D=R±5 or D<R−5 transplants (37% vs 46% vs 50%; $p$ < 0.001). Those with D>R+5 were also less likely to have congenital heart disease compared to those with D=R±5 or D<R−5 (18% vs 44% vs 49%; $p$ < 0.001). Ventricular assist device (VAD) support was more common among D>R+5 than D=R±5 or D<R−5 (18% vs 12% vs 5%; $p$ < 0.001)