Original Article

Association of Human Leukocyte Antigen Donor–Recipient Matching and Pediatric Heart Transplant Graft Survival

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Background—The effect of donor–recipient human leukocyte antigen (HLA) matching on outcomes remains relatively unexplored in pediatric patients. The objective of this study was to investigate the effects of donor–recipient HLA matching on graft survival in pediatric heart transplantation.

Methods and Results—The UNOS (United Network for Organ Sharing) database was queried for heart transplants occurring between October 31, 1987, and December 31, 2012, in a recipient aged ≤17 years with ≥1 postoperative follow-up visit. Retransplants were excluded. Transplants were divided into 3 donor–recipient matching groups: no HLA matches (HLA-no), 1 or 2 HLA matches (HLA-low), and 3 to 6 HLA matches (HLA-high). Primary outcome was graft loss. Four thousand four hundred seventy-one heart transplants met the study inclusion criteria. High degree of donor–recipient HLA matching occurred infrequently: HLA-high (n=269; 6%) versus HLA-low (n=2683; 60%) versus HLA-no (n=1495; 34%). There were no differences between HLA matching groups in the frequency of coronary vasculopathy (*P*=0.19) or rejection in the first post-transplant year (*P*=0.76). Improved graft survival was associated with a greater degree of HLA donor–recipient matching: HLA-high median survival, 17.1 (95% confidence interval, 14.0–20.2) years; HLA-low median survival, 14.2 (13.1–15.4) years; and HLA-no median survival, 12.1 (10.9–13.3 years) years; *P*<0.01, log-rank test. In Cox-regression analysis, HLA matching was independently associated with decreased graft loss: HLA-low versus HLA-no hazard ratio, 0.86 (95% confidence interval, 0.74–0.99), *P*=0.04; HLA-high versus HLA-no, 0.62 (95% confidence interval, 0.43–0.90), *P*<0.01.

Conclusions—Decreased graft loss in pediatric heart transplantation was associated with a higher degree of donor–recipient HLA matching, although a difference in the frequency of early rejection or development of coronary artery vasculopathy was not seen. ***(Circ Heart Fail. 2014;7:605-611.)***

Key Words: heart transplantation ■ pediatrics

Human leukocyte antigen (HLA) typing of potential donors and recipients is standard of care in pediatric heart transplantation. Advancing knowledge of HLA antibodies has improved the accuracy of virtual crossmatch in sensitized patients,[1] reducing the need for prospective crossmatches and leading to reduced waitlist mortality.[2] These improvements in HLA technology have likely led to improved outcomes in pediatric heart transplantation by optimizing donor selection.[1]

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Despite improved outcomes through the virtual crossmatch, the effect of donor–recipient HLA matching on outcomes remains relatively unexplored in pediatric heart transplantation. Opelz[3] reviewed the impact of HLA compatibility on 150 000 kidney, heart, and liver transplants and found that kidney and heart transplant outcomes were improved with higher degrees of HLA matching. A previous report by Opelz and Wujciak[4] showed that HLA matching of ≥3 loci was

associated with improved outcomes in an exclusively heart transplant cohort. There are other reports that indicate that HLA matching is associated with a decreased risk of rejection in the first post-transplant year, decreased incidence of coronary vasculopathy, and improved graft survival.[5,6]

However, other studies indicate that HLA matching does not improve outcomes in heart transplantation. Tenderich et al[7] performed a single-center retrospective review of 923 adult heart transplants from 1989 to 2005 and found that the degree of HLA donor–recipient matching was not associated with short-term or long-term survival. Similarly, a single-center retrospective study of 243 heart transplants during a 13-year period did not find a relationship between HLA matching and survival, rejection episodes, or post-transplant infections.[8] The latter study included adolescents between 12 and 18 years of age, but no subgroup analysis was performed in this pediatric group.[8]

The only previous report exploring an association between HLA matching and outcomes in an exclusively pediatric

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population found no improvement in survival but was a single-center study reported >20 years ago involving 87 patients.[9] The aim of this study was to investigate possible associations between HLA matching and graft survival in an exclusively pediatric cohort.

Methods

A retrospective analysis was performed on data obtained from the United Network for Organ Sharing (UNOS) Standard Transplant Analysis and Research files. The Medical University of South Carolina Institutional Review Board approved the study. Heart transplants performed in the United States between October 1, 1987, and December 31, 2012, were included for analysis. The database was queried for pediatric heart transplants (aged ≤17 years) who underwent heart transplant and had HLA typing of the recipient and donor at the A, B, and DR loci. Transplants were included if there was ≥1 follow-up visit documented. Transplants were excluded if the recipient had a previous heart transplantation. Primary end point for the study was graft loss, which included patient death and retransplantation.

HLA matching was defined as the number of donor HLA antigens that were also present in the recipient. Transplants were divided into 3 groups: no HLA matching (0 of 6 potential matches [HLA-no]), low level of HLA matching (1–2 of 6 potential matches [HLA-low]), and high level of HLA matching (3–6 potential matches [HLA-high]). Patient-specific variables evaluated between groups included the following: recipient supported by inotropic medications, extracorporeal membrane oxygenation, ventricular assist device (VAD), and mechanical ventilation immediately before transplant; cardiac diagnosis (cardiomyopathy, congenital heart disease, or other); recipient race, age, serum creatinine and bilirubin at transplant; ischemic time; donor–recipient weight ratio; crossmatch results; and year of transplant. For VADs, the type of VAD (left VAD, right VAD, and biventricular VAD) is noted. Given the small total number of VADs, for statistical purposes all types of VADs were grouped together. These variables have been previously shown to be associated with graft survival.[10–12]

Secondary end points included the development of coronary vasculopathy throughout the life of the graft and rejection requiring treatment in the first year after transplant. To allow for ≥1 year after transplant for the assessment of rejection or the development of coronary vasculopathy, only transplants before December 31, 2011, were included for analysis of these end points. Rejection in the first transplant year was treated as dichotomous outcome (≥1 episode of rejection versus no episodes).

An additional analysis compared outcomes in patients based on the presence of matching HLA at each individual locus (A, B, DR). Each individual locus was analyzed separately, independent of matching at other locus (no A-locus match versus ≥1 A-locus match; no B-locus match versus ≥1 B-locus match; no DR-locus match versus ≥1 DR-locus match).

To investigate the relationship between the race of donor and donor–recipient racial HLA matching, recipients and donors were classified by the following groups: white, black, Hispanic, Asian, or other. The degree of HLA matching was compared between groups based on recipient race and if there was donor–recipient racial matching.

Statistical Analysis

Data from the UNOS Standard Transplant Analysis and Research files were imported into SPSS, version 21.0 (IBM, Armonk, NY) for analysis. Demographic and patient variable data are reported as medians with intraquartile ranges, or 95% confidence interval, or as percentages, where appropriate. Demographics and patient variables were compared among the 3 groups using Kruskal–Wallis test for continuous variables because data were distributed nonparametrically. Categorical variables were compared between HLA donor–recipient matching groups using the χ^2 test. Cox proportional hazard models were used to assess hazard ratios (HRs) of graft loss between HLA match groups while controlling for age and year of transplant; recipient on extracorporeal membrane oxygenation, VAD, intravenous inotropes, or mechanical ventilation immediately before

transplant; cardiac diagnosis; serum bilirubin and creatinine; donor–recipient weight ratio; and prospective or retrospective crossmatch results. For the purpose of the multivariate Cox-regression analysis, continuous variables of transplant year and age were divided to create categorical variables: early transplant year (1987–1999) versus late transplant year (2000–2012); and infant (<1 year of age), child (1–10 years), and adolescent (11–17 years). Positive and indeterminate retrospective crossmatches were combined into 1 category for multivariate analysis. Recipient race was divided into white and nonwhite. Only data sets with complete data were used in the Cox proportional hazard models, and missing data were not interpolated. HLA-no was the reference group in multivariable analysis.

In additional analysis of matching at each individual HLA locus, demographic and patient variable data were compared between groups using Wilcoxon rank-sum test for continuous variables. For categorical variables, comparisons between groups were performed using the χ^2 test. Cox proportional hazard models were performed in the same manner as previously described. A value of $P<0.05$ was set as statistically significant.

When analyzing race and HLA matching, degree of HLA matching and frequency of donor–recipient racial matching were compared between recipient racial groups using the χ^2 test. Graft survival was compared using log-rank test.

Results

There were 4471 pediatric heart transplants who met the study inclusion criteria. Median recipient age of the study population was 5 (interquartile range, 0–13) years, with 1291 transplants having a recipient age <1 year, 1635 with recipient age from 1 to 10 years, and 1521 transplants with recipient age between 11 and 17 years of age. An underlying diagnosis of cardiomyopathy existed in 2311, 1943 had congenital heart disease, and 193 were reported to have other cardiac diagnoses. Median serum creatinine was 0.5 (interquartile range, 0.4–0.8) mg/dL, and median serum bilirubin was 0.7 (0.4–1.3) mg/dL. Median donor–recipient weight ratio was 1.27 (interquartile range, 1.0–1.7). Median ischemic time was 3.5 (interquartile range, 2.8–4.3) hours. One hundred sixty-four (4%) recipients were on extracorporeal membrane oxygenation at the time of transplant, 702 (16%) were on mechanical ventilation, and 1878 (42%) were on inotropic support. A total of 228 (5%) patients were on VAD at the time of transplant (109 left VADs, 1 right VAD, 3 total artificial heart, 56 biventricular VADs, and 59 not specified.) Median graft survival for the entire cohort was 13.5 (95% confidence interval [CI], 12.7–14.4) years.

A high degree of HLA matching occurred infrequently (HLA-high [n=269; 6%] versus HLA-low [n=2683; 60%] versus HLA-no [n=1495; 34%]). Patient-specific factors did not differ between HLA matching groups (Table 1), except that the HLA-high group was more likely to be on extracorporeal membrane oxygenation at the time of transplant (7% HLA-high versus 4% HLA-low versus 3% HLA-no; $P<0.01$) and more likely to be white (70.3% HLA-high versus 60.5% HLA-low versus 54.6% % HLA-no; $P<0.01$). Median graft survival differed between groups (Figure; $P<0.01$): the HLA-high group had an estimated median survival of 17.1 (95% CI, 14.0–20.2) years, versus HLA-low of 14.2 (95% CI, 13.1–15.4) years and HLA-no of 12.1 (95% CI, 10.9–13.3) years.

Of the 4471 heart transplants with ≥1 follow-up posttransplant visit, 4330 were performed before December 31, 2011, and comprised the group that was assessed for coronary vasculopathy and rejection. The frequency of coronary vasculopathy did not differ between groups: 25% (n=67) for

Table 1.   Patient Characteristics and HLA Matching Group

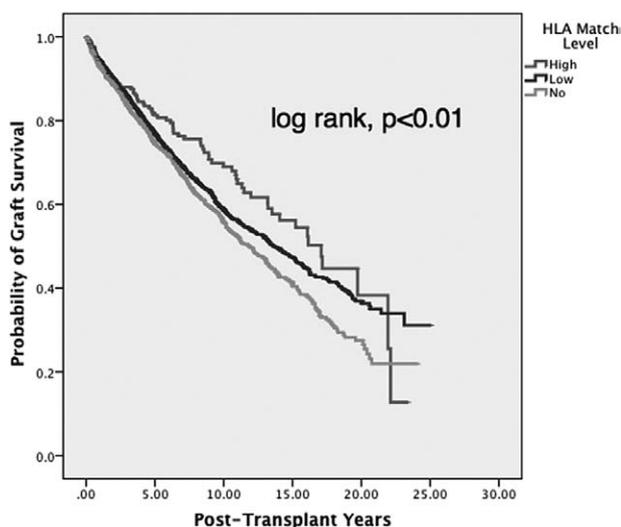|	No HLA Match (n=1592)	Low HLA Match (1–2 Matches, n=2852)	High HLA Match (3–6 Matches, n=287)	P Value
Recipient age, y	5 (0–13)	5 (0–13)	5 (0–13)	0.97
Recipient race, % white	54.6	60.5	70.3	<0.01
Transplant year	2005 (1996–2009)	2005 (1996–2009)	2006 (1996–2010)	0.69
Serum creatinine, mg/dL	0.5 (0.4–0.7)	0.5 (0.4–0.7)	0.5 (0.3–0.7)	0.52
Total bilirubin, mg/dL	0.7 (0.4–1.3)	0.7 (0.4–1.3)	0.7 (0.5–1.3)	0.81
Ischemic time, h	3.5 (2.8–4.3)	3.5 (2.8–4.2)	3.5 (2.8–4.2)	0.81
Donor–recipient weight ratio	1.3 (1.0–1.6)	1.3 (1.0–1.6)	1.3 (1.0–1.6)	0.76
IV inotropes	635 (43%)	1131 (42%)	112 (42%)	0.96
Recipient on ventilator	233 (16%)	422 (16%)	47 (18%)	0.73
VAD support	69 (5%)	136 (5%)	16 (6%)	0.61
Recipient on ECMO	46 (3%)	99 (4%)	19 (7%)	<0.01
Positive or indeterminate crossmatch	96 (7%)	172 (7%)	17 (7%)	0.99
Cardiac diagnosis				
Cardiomyopathy	811 (54%)	1374 (51%)	126 (47%)	0.17
Congenital heart disease	621 (42%)	1189 (44%)	133 (49%)	
Other	63 (4%)	120 (5%)	10 (4%)	

HLA matching group (no, low, and high) had similar characteristics except that HLA-high group was more likely to be on ECMO and white. ECMO indicates extracorporeal membrane oxygenation; HLA, human leukocyte antigen; IV, intravenous; and VAD, ventricular assist device.

HLA-high, 21% for HLA-low (n=558), and 22% (n=335) for HLA-no (P=0.19). The frequency of treated rejection in the first post-transplant year also did not differ between groups: 20% (n=55) for HLA-high, 22% for HLA-low (n=588), and 23% (n=342) for HLA-no (P=0.76). Neither frequency of coronary vasculopathy nor rejection within the first year was associated with HLA matching when the cohort was divided into infants (<1 year of age) and noninfants (≥1 year of age).

Multivariable Cox-regression analysis was performed on all 2852 of 4447 transplants with no missing data. Differences between the transplants with complete data sets and those

Figure. Graft survival by human leukocyte antigen (HLA) matching group. Kaplan–Meier survival curves comparing 3 groups of HLA donor–recipient matches. Higher degree of HLA matching was associated with improved survival (P<0.01, log-rank test).

with incomplete data sets are summarized in Table 2. HLA matching was independently associated with graft survival. Compared with the HLA-no group, HLA-low had an HR of 0.86 (95% CI, 0.74–0.99; P=0.04) for graft loss and HLA-high had an HR of 0.62 (95% CI, 0.43–0.90; P=0.01) for graft loss. When patients with no HLA matching were excluded, HLA-high had an HR of 0.7 (95% CI, 0.5–1.0; P=0.07) for graft loss compared HLA-low. When analyzing infants separately (recipient age <1 year; n=1291), there was no difference in graft survival between HLA-no (14.9 years) versus HLA-low (16.3 years) versus HLA-high (15.7 years) groups; P=0.47. In multivariable Cox-regression analysis of infants, HLA matching class was not associated with graft survival. However, in patients >1 year, associations with graft survival were similar to the entire cohort.

Additional analysis of graft survival was performed between matching at each individual HLA locus. Transplants that had 1 or 2 matches at the A locus (n=1772) had a longer estimated median graft survival, in univariate analysis, of 15.2 (95% CI, 13.5–16.9) years versus transplants that had no match (n=2675), 12.9 years (11.9–13.9 years; P<0.01, log-rank test). In multivariable Cox-regression analysis, matching at the A locus had an HR of 0.88 (0.76–1.02; P=0.11) for graft loss compared with no matching (Table 3). In univariate analysis, matching at the B locus did not lead to statistically significant longer median graft survival. However, in multivariable Cox-regression analysis, matching at the B locus was independently associated with lower HR of graft loss compared with no match group (HR, 0.80; 95% CI, 0.67–0.97; P=0.03). Matching at the DR locus was associated with longer estimated median graft survival in univariate analysis, 15.1 (95% CI, 13.7–16.7) years for transplants with 1 match versus 13.0 (12.0–14.0) years for transplants with no match (P<0.01), but

Table 2. Comparison of Transplants With Missing Data Versus Complete Data for Multivariate Analysis

	Missing Data (n=1595)	Compete Data (n=2852)	P Value
Recipient age, y	6 (0–13)	5 (0–13)	<0.01
Recipient race, % white	61.6	57.7	<0.01
Transplant year	2003 (1998–2006)	2006 (2000–2009)	<0.01
Serum creatinine, mg/dL	0.5 (0.4–0.8)	0.5 (0.4–0.7)	0.25
Total bilirubin, mg/dL	0.7 (0.4–1.2)	0.7 (0.4–1.3)	0.54
Ischemic time, h	3.6 (2.7–4.5)	3.5 (2.8–4.2)	0.58
Donor–recipient weight ratio	1.3 (1.1–1.6)	1.3 (1.0–1.6)	0.01
IV Inotropes	447 (28%)	1431 (50%)	<0.01
Recipient on ventilator	237 (15%)	465 (16%)	0.21
VAD support	50 (3%)	171 (6%)	<0.01
Recipient on ECMO	38 (2.4%)	126 (4.4%)	<0.01
Positive or indeterminate crossmatch	67 (6%)	218 (8%)	0.07
Cardiac diagnosis			
Cardiomyopathy	779 (49%)	1532 (54%)	<0.01
Congenital heart disease	748 (47%)	1195 (62%)	
Other	68 (4%)	125 (4%)	
HLA match level			
No match	560 (35%)	935 (33%)	
Low match (1–2 matches)	938 (59%)	1745 (61%)	0.27
High match (3–6 matches)	97 (6%)	172 (6%)	

Patients not included in multivariable analysis because of missing data points were less likely to be on ECMO, VAD, or IV inotropes, more likely to have congenital heart disease, white, and tended to be younger. ECMO indicates extracorporeal membrane oxygenation; HLA, human leukocyte antigen; IV, intravenous; and VAD, ventricular assist device.

in Cox-regression analysis this association was no longer significant (Table 3).

The race of the entire transplant recipient cohort was 59.1% white, 19.7% black, 15.5% Hispanic, 3.1% Asian, and 2.6% other. Donor race was white in 59.1% of transplants, 19.7% black, 15.5% Hispanic, 3.1% Asian, and 2.5% other. Two donors did not have their race recorded. White recipients received the same race donor 64.3% of the time versus 22.2% for blacks, 26.5% for Hispanics, 0.7% for Asians, and 0.9% for other (P<0.01). Transplants with donor–recipient racial matching were more likely to be in HLA-high group (8.4% versus 4.0%; P<0.01). Blacks and Asians were the most likely to have no HLA matches (42.2% and 41.3%, respectively) versus white and Hispanic recipients (31.1% and 32.2%, respectively; P<0.01). Median graft survival was lowest for blacks (7.8 years; 95% CI, 6.8–8.8 years), whereas whites, Hispanics, and Asians had similar median graft survival (15.1, 17.1, and 15.6 years, respectively); the shorter graft survival for blacks met statistical significance (P<0.01, log-rank test).

Discussion

This represents the first report to specifically investigate the association between HLA donor–recipient matching using a multi-institutional database in pediatric heart transplant patients. We found an association between improved survival and a higher degree of donor–recipient HLA matching. The reason for improved graft survival with increased HLA matching in pediatric heart transplantation is an area that needs further study. Early reports in adult heart transplantation reported that HLA matching decreased the frequency of rejection and the incidence of steroid-resistant rejection.[13] More recent studies have found that HLA matching is associated with a lower incidence of rejection within the first year for adult heart transplant recipients.[5,6] However, the present study did not find a difference in the rate of rejection in the first year related to degree of HLA matching. The fact that HLA matching was not associated with improved graft survival in infants indicates a possible immunologic cause for the improved graft survival. As a result of an immature and developing immune system, infants are more likely to develop graft tolerance and less likely to mount a strong immunologic response to the transplanted graft.[14] However, determining the exact mechanism of how donor–recipient matching leads to improved outcomes is important because

Table 3. Graft Survival Multivariable Analysis by Human Leukocyte Antigen Locus

	Hazard Ratio for Graft Loss (95% CI)	P Value
A locus		
≥1 match versus no match	0.88 (0.76–1.02)	0.11
B locus		
≥1 match versus no match	0.80 (0.67–0.97)	0.03
DR locus		
≥1 match versus no match	0.91 (0.78–1.1)	0.19

Matching at A and B loci was associated with better graft survival in multivariable Cox-regression analysis. CI indicates confidence interval.

it could lead to targeted therapies after transplant in patients with low degree or no HLA matching. This is most likely to be accomplished by linking multiple pediatric heart transplantation databases.

HLA matching has been associated with improved outcomes in adult heart transplantation. However, the impact of HLA matching on graft survival seems to be stronger in the adult population compared with our results of a complete pediatric population.[4,6] Possible explanations to why there is a difference between age groups include differences in the development of the immune system as well as the influence of other factors such as medical adherence. In the infant population, HLA matching was not associated with graft survival likely because of the infant's immature immune system and the development of graft tolerance. Also, the relatively high rate of medical nonadherence seen in adolescents is known to lead to increased risk of graft loss and therefore will decrease the impact of HLA matching on graft survival.[15]

The importance of matching at different HLA loci has been extensively researched in pediatric kidney transplantation. HLA-DR matching has been associated with improved graft survival and lower incidence of lymphoma.[16–18] HLA-DR matching has been suggested to improve outcomes in adult heart transplant recipients.[6] The present study suggests that matching at the B locus is independently associated with improved survival; however, the HR (95% CI) that approached 1, while matching at the A and DR loci, was associated with improved graft survival in univariate analysis. These results suggest that the number of total matches should be given more influence than matching at an individual locus. Our study included typing of HLA-A, B, and DR loci because these loci were routinely typed during the entirety of our study. Typing of the HLA-DQ and C loci is now routine. Therefore, over time, more data will be available to analyze the effects of matching at these loci in pediatric heart transplantation.

We did not find an association between HLA matching and the development of coronary vasculopathy. This is in contrast to findings in adult heart transplantation in which a higher degree of HLA matching has been reported to be associated with lower incidence of transplant coronary vasculopathy.[6] Coronary vasculopathy is a time-dependent process, with steadily increasing incidence as time from transplantation increases. In our analysis, the HLA matching groups had similar years of transplant and therefore similar time to develop coronary vasculopathy as well as similar recipient age, a known risk factor for coronary vasculopathy.[19,20] Our findings were consistent with another report on pediatric heart transplantation from a multi-institutional database that did not find a link between HLA matching and coronary vasculopathy.[20] In kidney transplantation, HLA matching, specifically at the B locus, has been associated with decreased rates of post-transplant lymphoproliferative disease.[21] The exact mechanism that leads to the improved graft survival through HLA matching in the pediatric heart transplant population could not be determined with the available database. Elucidating the protective mechanism of HLA matching on graft survival should be the subject of further investigations because this knowledge could help guide diagnostic and therapeutic interventions in patients with a high degree of HLA mismatching.

HLA matching is currently not a factor in heart transplant donor allocation. Authors of previous reports have argued that HLA matching should be considered in cardiac donor allocation because of improved outcomes.[6] HLA matching has been used in organ allocation in kidney transplantation.[22] However, after decreasing the importance of HLA matching in Canada and the United Kingdom, reports have indicated decreased waitlist times.[22,23] Although pediatric heart transplant waitlist mortality has decreased during the past 20 years, it still remains elevated at 13%.[24] Other considerations in donor allocation, such a donor–recipient size, ischemic time, surgical complexity, and rising rates of HLA sensitization in listed patients, make addition of HLA matching to donor allocation algorithms difficult. Based on the kidney transplant data, addition of HLA matching could possibly lead to increased waitlist mortality.[22,23] Therefore, before any consideration of HLA matching in pediatric heart transplant donor allocation, effects of waitlist time and mortality must be evaluated.

The higher degree of HLA matching seen when donors and recipients were of the same race is not surprising because HLA haplotypes are often conserved within racial groups.[25] Donor–recipient race matching has been associated with increased graft survival in all races in pediatric heart transplantation.[26] The graft survival associated with donor–recipient race matching is likely because of the increasing degree of HLA matching when the race of donor and recipient is the same.

The reason that blacks and Asians were more likely to have no HLA matches compared with whites and Hispanics is because of an interaction between race of donors and shared haplotypes between races. Whites and Hispanics made up the largest 2 racial categories of donors, 79.5% of donors when combined. Also, HLA haplotypes that are commonly found in white and Hispanics in the United States are frequently seen in other racial groups.[25] However, this is not true for Asians and blacks; common HLA haplotypes in these populations are rarely found in other populations.[25] Therefore, less donors of the same race and less chance of having an HLA match from another race lead to Asians and blacks being more likely to receive a heart without HLA matching. Blacks being more likely to have no HLA matches and the fact the HLA-no group had the shortest graft survival provide a possible reason that previously reported graft survival is worse for blacks even after controlling for socioeconomic status.[12]

Limitations

The influence on HLA matching in donor evaluation by transplant centers is not known; therefore, the distribution of HLA matching may not represent actual random chance but be influenced by decision making processes not accounted for. There was no set definition of transplant coronary vasculopathy or rejection within the first year, and therefore reporting of this information was solely left to the discrimination of the reporting institution. The methods and frequency of surveillance for transplant coronary vasculopathy are not known and could have varied greatly between institutions influencing the

reporting of coronary vasculopathy. The database is dependent on accurate reporting from participating institutions. The type of rejection, cellular versus antibody-mediated versus mixed, was not reported in the database and therefore limited the authors' ability to discern associations between HLA matching and frequency of specific types of rejection, such as antibody-mediated rejection. A lack of consistent late reporting of rejection in the database prevented the authors from assessing associations between HLA matching and late rejection.

Conclusions

A greater degree of HLA donor–recipient matching (≥3 matches) occurs relatively infrequently in pediatric heart transplants but is associated with improved graft survival. This information can help the transplant team identify patients who are at higher risk for graft loss. Additional studies into the pathogenesis of the association of HLA matching with improved graft survival will help the transplant team tailor therapeutics to transplant with low or no HLA matching.

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CLINICAL PERSPECTIVE

Human leukocyte antigen (HLA) typing of donors and recipients at the A, B, and DR loci is standard practice in pediatric heart transplantation. There are many possible HLA antigens at each locus, making it unlikely that the donor and recipient will be perfect matches. We used the multi-institutional UNOS (United Network for Organ Sharing) database to investigate the possible association between HLA matching and graft survival in pediatric heart transplantation. A high level of matching (3–6 matches of 6 possible matches) occurs in only ≈6% of pediatric heart transplants, whereas a low level of matching (1–2 matches) occurs in ≈60% of transplants. Higher levels of HLA matching are associated with improved graft survival, and estimated median graft survival for high level of matching was 17.1 years versus 14.2 years for low level of matching and 12.1 years for transplants with no matching. When performing multivariable Cox-regression analysis, increased level of HLA matching was independently associated with increased graft survival. There was no individual HLA locus that carried the greatest impact on survival. This information can be used to identify pediatric heart transplant recipients at increased chance of graft loss.

Association of Human Leukocyte Antigen Donor–Recipient Matching and Pediatric Heart Transplant Graft Survival

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