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Outcomes of Early Adolescent Donor Hearts in Adult Transplant Recipients

Shivank Madan, MD, MHA,[a] Snehal R. Patel, MD,[a] Peter Vlismas, MD,[b] Omar Saeed, MD,[a] Sandhya Murthy, MD,[a] Stephen Forest, MD,[c] William Jakobleff, MD,[c] Daniel Sims, MD,[a] Jacqueline M. Lamour, MD,[d] Daphne T. Hsu, MD,[d] Julia Shin, MD,[a] Daniel Goldstein, MD,[c] Ulrich P. Jorde, MD[a]

ABSTRACT

OBJECTIVES This study sought to determine outcomes of adult recipients of early adolescent (EA) (10 to 14 years) donor hearts.

BACKGROUND Despite a shortage of donor organs, EA donor hearts (not used for pediatric patients) are seldom used for adults because of theoretical concerns for lack of hormonal activation and changes in left ventricular mass. Nonetheless, the outcomes of adult transplantation using EA donor hearts are not clearly established.

METHODS All adult (≥18 years of age) heart transplant recipients in the United Network for Organ Sharing database between April 1994 and September 2015 were eligible for this analysis. Recipients of EA donor hearts were compared with recipients of donor hearts from the usual adult age group (ages 18 to 55 years). Main outcomes were all-cause mortality and cardiac allograft vasculopathy up to 5 years, and primary graft failure up to 90 days post-transplant. Propensity score analysis was used to identify a cohort of recipients with similar baseline characteristics.

RESULTS Of the 35,054 eligible adult recipients, 1,123 received hearts from EA donors and 33,931 from usual-age adult donors. With the use of propensity score matching, 944 recipients of EA donor hearts were matched to 944 recipients of usual-age adult donor hearts. There was no difference in 30-day, 1-year, 3-year, and 5-year recipient survival or primary graft failure rates in the 2 groups using both Cox hazards ratio and Kaplan-Meier analysis. Of note, adult patients who received EA donor hearts had a trend toward less cardiac allograft vasculopathy (Cox hazard ratio, 0.80; 95% confidence interval: 0.62 to 1.01; $p = 0.07$).

CONCLUSIONS In this largest analysis to date, we found strong evidence that EA donor hearts, not used for pediatric patients, can be safely transplanted in appropriate adult patients and have good outcomes. This finding should help increase the use of EA donor hearts. (J Am Coll Cardiol HF 2017;■:■-■) © 2017 by the American College of Cardiology Foundation.

Although the use of left ventricular (LV) assist devices has increased in recent years, heart transplantation continues to be the gold standard therapy for end-stage heart failure (1). It is estimated that more than 20,000 patients in the United States may benefit from heart transplantation, but only about 2,000 to 2,400 adult heart transplants are performed in the United States every year, largely because of limited donor organ availability (2,3). However, despite a persistent shortage of donor organs for heart transplantation, the donor acceptance rates continue to remain low. There is a need to safely

From the [a]Division of Cardiology, Department of Medicine, Montefiore Medical Center/Albert Einstein College of Medicine, New York, New York; [b]Department of Medicine, Montefiore Medical Center/Albert Einstein College of Medicine, New York, New York; [c]Department of Cardiovascular and Thoracic Surgery, Montefiore Medical Center/Albert Einstein College of Medicine, New York, New York; and the [d]Division of Pediatric Cardiology, Department of Pediatrics, Children's Hospital at Montefiore, Albert Einstein College of Medicine, New York, New York. This work was supported, in part, by Health Resources and Services Administration contract 234-2005-370011C. The content is the responsibility of the authors alone and does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. government. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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ABBREVIATIONS AND ACRONYMS

CAV = cardiac allograft vasculopathy

EA = early adolescent

LV = left ventricular

PGF = primary graft failure

UNOS = United Network Organ Sharing

increase the use of already available donor organs using evidence-based criteria so that heart transplantation can be made available to a greater number of patients (3,4).

Adolescence is defined as a transitional phase of growth and development between childhood and adulthood, occurring between the ages of 10 and 19 years (5). Early adolescence (EA), considered to stretch between 10 and 14 years, is associated with hormonal surge leading to a growth spurt, development of sexual organs, and secondary sexual characteristics (5). Some studies have suggested that the hormonal surge (or activation) of EA is also associated with heart growth, mainly an increase in LV systolic and diastolic wall thickness (6), increase in cardiac contractility (6), and LV mass (7,8).

Although the International Society of Heart Transplant guidelines recommend against the routine use of hearts from donors >55 years of age because of reduced myocardial reserve (9), there is a lack of consensus regarding the use of EA donor hearts for adult patients with heart failure. This is largely due to a lack of any robust post-transplant outcomes data and also because of concerns that the absence of hormonal activation (that normally occurs during puberty) could affect cardiac contractility in donor hearts and lead to poor outcomes. Hence, we evaluated the post-transplant outcomes of adult patients who received hearts from EA (ages 10 to 14 years) donors.

METHODS

This was a registry-based analysis using the United Network Organ Sharing (UNOS) database. All transplant services in the country are joined under the nationwide Organ Procurement and Transplant Network, which is managed by UNOS. The U.S. Department of Health and Human Services provides oversight on the activities of both UNOS and the Organ Procurement and Transplant Network. The UNOS database contains patient-level information on key elements for all donors, waitlisted candidates, and transplant recipients, submitted by the Organ Procurement and Transplant Network members. No separate informed consent was required because the data are deidentified and used in compliance with the UNOS data user agreement. The study was deemed exempt by the Institutional Review Board at Montefiore Medical Center.

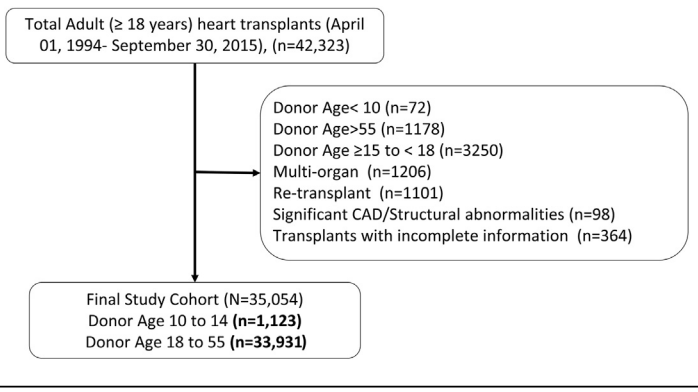
STUDY POPULATION AND DEFINITIONS. All adult (≥18 years of age) recipients who underwent a heart transplant between April 1994 and September 2015 in the United States and registered in UNOS were eligible for this analysis. April 1994 was chosen because this coincided with a major database revision by UNOS to collect additional data variables. Recipients of EA (ages 10 to 14 years) donor hearts were compared with recipients of adult donor hearts in the usual age group (ages 18 to 55 years). The main exclusion criteria were multiorgan transplants, repeat transplants, transplants from donors in the 15 to younger than 18 years age group, donor organs with significant coronary artery disease or any structural abnormalities, and donors with incomplete information (**Figure 1**). Size mismatch by weight was defined as donor weight ≥30% below the recipient weight (9), and size mismatch by height was defined as donor/recipient height ratio <0.90. Sex mismatch was defined as transplant from a female donor to male recipient (10). The current era was arbitrarily defined as January 2005 onward, because this was close to the midpoint of the study period (April 1994 to September 2015).

OUTCOMES. The primary outcome of the study was all-cause mortality. Secondary outcomes included rates of primary graft failure (PGF) and cardiac allograft vasculopathy (CAV). PGF was defined as "death or retransplantation within 90 days of the index cardiac transplant due to graft failure which was not related to infection, rejection or surgical technical issues," similar to other previous UNOS analyses (4,11). CAV diagnosis in UNOS is not standardized and is based on self-reporting by transplant centers at yearly follow-ups. Recipients with missing or unknown CAV status were excluded from the CAV analysis.

STATISTICAL ANALYSIS. All categorical variables were compared using the chi-square analysis and continuous variables were compared using unpaired Student *t* test. Because of differences in the baseline characteristics and sample size of the 2 groups (**Tables 1 and 2**), propensity score analysis was used to identify a cohort of recipients with similar baseline characteristics. Furthermore, in a situation where it is difficult to conduct a randomized clinical trial (EA vs. usual-age adult donor heart allocation), a propensity score methodology can help to reduce the effects of confounding when using observational data (12). The propensity score is a probability of having an exposure (EA vs. usual-age adult donor heart), conditional on a set of baseline characteristics (12). We estimated the propensity scores using a multivariable logistic regression model, with the use of EA donor heart as the dependent variable and all baseline recipient and donor characteristics shown in **Tables 1 and 2** as covariates (except donor LV ejection fraction).

Information on LV ejection fraction was not available for all transplants; hence, LV ejection fraction was not included in the propensity score estimation. After generating propensity scores, matching was performed using a 1:1 matching algorithm (greedy type matching) without replacement, using a caliper width of 0.20 of the standard deviation of the logit of the propensity score. Standardized differences were estimated for all baseline covariates to check for post-match covariate balance and to confirm adequacy of the propensity model. A standardized difference of <10% indicates good balance between groups (13,14). All primary and secondary outcomes were compared using the Cox proportional hazards regression models and Kaplan-Meier analysis. To check the robustness of our findings, we further adjusted Cox models for confounders after propensity matching. Two-sided p values <0.05 were considered significant and were not adjusted for multiple testing. All statistical analyses were done using STATA version 13 software (StataCorp, College Station, Texas).

FIGURE 1 Flowchart for Study Cohort Derivation



CAD = coronary artery disease.

RESULTS

STUDY POPULATION. We identified 35,054 adult heart transplant recipients who met the study inclusion criteria, of whom 1,123 received heart transplants from EA (ages 10 to 14 years) donors and 33,931 received heart transplants from donors in the usual adult age group (ages 18 to 55 years) (Figure 1). Before propensity matching, there were significant differences in the baseline characteristics of the 2 cohorts (Tables 1 and 2). When compared with recipients of hearts from adult donors in the usual-age group, the recipients of EA donor hearts were younger (age 48.4 ± 14.2 years vs. 52.6 ± 11.9 years; $p < 0.001$), were more likely to be female (48.98% vs. 22.76%; $p < 0.001$), had lower body mass index (24.2 ± 4.6 kg/m^2 vs. 26.7 ± 4.7 kg/m^2; $p < 0.001$), and had greater prevalence of size mismatch by weight (10.86% vs. 3.22%; $p < 0.001$) or by height (11.58% vs. 3.67%; $p < 0.001$). They also had a shorter waitlist time (6.0 ± 8.4 months vs. 7.3 ± 11.5 months; $p < 0.001$), lower serum creatinine at transplant (1.2 ± 0.6 mg/dl vs. 1.3 ± 0.9 mg/dl; $p < 0.001$), and were less likely to be on LV assist device-only support (7.12% vs. 18.03%; $p < 0.001$) (Table 1). In terms of donor characteristics, the EA donors were less likely to be on inotropic medications at procurement (9.97% vs. 18.58%; $p < 0.001$) but had a slightly longer ischemic time (3.2 ± 1.1 h vs. 3.1 ± 1.0 h; $p < 0.001$) (Table 2). With the use of propensity score matching, 944 recipients of EA (ages 10 to 14 years) donor hearts were matched to 944 recipients of adult donor hearts in the usual-age group (ages 18 to 55 years). The C statistic for the model was 0.841. After propensity matching, there were no significant differences in the 2 groups, and the standardized differences were <10% for all baseline covariates, indicating good balance between the 2 groups (Tables 3 and 4). After propensity matching, the actual number and mean height of EA donors age 10, 11, 12, 13, and 14 years were n = 28 (151.5 ± 10.4 cm), n = 77 (159.8 ± 9.1 cm), n = 135 (162.2 ± 8.7 cm), n = 272 (166.3 ± 9.7 cm), and n = 432 (169.4 ± 9.1 cm), respectively. On comparing with adults who received usual-age adult donor hearts, adults who received EA donor hearts were shorter in height (168.2 ± 10.4 cm vs. 173.3 ± 10.9 cm; $p < 0.001$) and weighed less (69.4 ± 15.8 kg vs. 74.4 ± 17.6 kg; $p < 0.001$).

ALL-CAUSE MORTALITY AND PRIMARY GRAFT FAILURE. The 30-day, 1-year, 3-year, and 5-year Kaplan-Meier estimates for recipient survival for the overall matched cohort were 94.7%, 88.1%, 81.6%, and 75.1%, respectively. Using Cox models, there were no significant differences in mortality between the adult recipients of EA donor hearts and recipients of usual age group adult donor hearts at 30 days, 1 year, 3 years, or 5 years of follow-up. This was true even after adjusting the Cox models for confounders post-matching (Table 5). Figure 2A shows the Kaplan-Meier estimates of recipient survival in the 2 groups ($p = 0.781$ for log-rank test).

PGF leading to death or retransplant occurred in 35 (1.89%) recipients up to 90 days of follow-up. Recipients of EA donor hearts were not at increased risk of developing PGF, when compared with recipients of adult donor hearts in the usual age group using Cox proportional hazards regression analysis (Table 5). Figure 2B shows the Kaplan-Meier estimates of PGF

TABLE 1 Baseline Recipient Characteristics Before Matching

	Early Adolescent Donor Heart (Ages 10–14 yrs; n = 1,123)	Adult Donor Heart (Ages 18–55 yrs; n = 33,931)	p Value	SD, %
Age at transplant, yrs	48.4 ± 14.2	52.6 ± 11.9	<0.001	31.90
Age category				
<50 yrs	482 (42.92)	10,885 (32.08)	<0.001	23.00
50–59 yrs	366 (32.59)	12,153 (35.82)		
≥60 yrs	275 (24.49)	10,893 (32.10)		
Female	550 (48.98)	7,721 (22.76)	<0.001	56.80
Black race	194 (17.28)	5,578 (16.44)	0.457	2.20
Sex mismatch (female donor to male recipient)	120 (10.69)	5,765 (16.99)	<0.001	18.30
Size mismatch by weight (donor weight <70% of recipient)	122 (10.86)	1,091 (3.22)	<0.001	30.20
Size mismatch by height (donor/recipient height ratio <0.90)	130 (11.58)	1,246 (3.67)	<0.001	30.10
Donor/recipient height ratio	0.98 ± 0.08	1.00 ± 0.06	<0.001	31.70
Etiology of heart failure (ischemic)	257 (22.89)	11,836 (34.88)	<0.001	26.70
History of any previous cardiac surgery	126 (11.22)	7,242 (21.34)	<0.001	27.70
Total waitlist time, months	6.0 ± 8.4	7.3 ± 11.5	<0.001	12.60
UNOS status 1A or old status 1 at transplant	519 (46.22)	17,957 (52.92)	<0.001	13.40
Recipient creatinine at transplant, mg/dl	1.2 ± 0.6	1.3 ± 0.9	<0.001	15.40
Recipient creatinine at transplant >1.5 mg/dl	228 (20.30)	8,125 (23.95)	0.005	8.80
Recipient blood type O	401 (35.71)	13,168 (38.81)	0.036	6.40
Recipient BMI at transplant, kg/m^2	24.2 ± 4.6	26.7 ± 4.7	<0.001	54.90
Recipient BMI >30 kg/m^2 at transplant	134 (11.93)	7,991 (23.55)	<0.001	30.80
History of blood transfusion since listing	166 (14.78)	6,723 (19.81)	<0.001	13.30
Current era (2005 onward)	337 (30.01)	17,743 (52.29)	<0.001	46.50
Life support with inotropes	545 (48.53)	15,331 (45.18)	0.027	6.70
LVAD only life support at transplant	80 (7.12)	6,119 (18.03)	<0.001	33.30
LVAD and RVAD support at transplant	18 (1.60)	616 (1.82)	0.599	1.60

Values are mean ± standard deviation or n (%).
BMI = body mass index; LVAD = left ventricular assist device; RVAD = right ventricular assist device; SD = standardized difference; UNOS = United Network Organ Sharing.

in the 2 groups up to 90 days follow-up (p = 0.405 for log-rank test).

CARDIAC ALLOGRAFT VASCULOPATHY. In the matched cohort, information on CAV was available for 1,722 transplant recipients (n = 865 in the EA donor group and n = 857 in the usual age adult donor group). Baseline covariates in the 2 subgroups were similar (Online Table 1). In the overall cohort, 25.8% of recipients developed CAV at 5 years of follow-up using Kaplan-Meier estimates. Recipients of hearts from EA donors had a trend toward reduced CAV (hazard ratio: 0.80 [95% confidence interval: 0.62 to 1.01]; p = 0.071), when compared with recipients of hearts from adult donors in the usual age group up to 5 years of follow-up. This trend was present even

TABLE 2 Baseline Donor Characteristics Before Matching

	Early Adolescent Donor Heart (Ages 10–14 yrs; n = 1,123)	Adult Donor Heart (Ages 18–55 yrs; n = 33,931)	p Value	SD, %
Female	342 (30.45)	9,977 (29.40)	0.447	2.30
Donor creatinine >1.5 mg/dl	107 (9.53)	5,740 (16.92)	<0.001	21.90
History of donor smoking	23 (2.05)	9,169 (27.02)	<0.001	75.80
CMV mismatch (D+/R−)	133 (11.84)	5,571 (16.42)	<0.001	13.20
Blood infection donor	49 (4.36)	2,220 (6.54)	0.003	9.60
LVEF, % (n = 25,672)	62 ± 10	62 ± 7	0.1963	4.70
Inotropic medications at procurement	112 (9.97)	6,303 (18.58)	<0.001	24.80
Ischemic time, h	3.2 ± 1.1	3.1 ± 1.0	<0.001	10.00
Donor cause of death (head trauma)	808 (71.95)	19,604 (57.78)	<0.001	30.00

Values are n (%) or mean ± SD.
CMV = cytomegalovirus; LVEF = left ventricular ejection fraction; SD = standardized difference.

TABLE 3 Baseline Recipient Characteristics After Matching

	Early Adolescent Donor Heart (Ages 10-14 yrs; n = 944)	Adult Donor Heart (Ages 18-55 yrs; n = 944)	p Value	SD, %
Age at transplant, yrs	48.9 ± 13.8	48.2 ± 14.0	0.232	5.50
Age category				
<50 yrs	392 (41.53)	411 (43.54)	0.643	2.90
50-59 yrs	318 (33.69)	302 (31.99)		
≥60 yrs	234 (24.79)	231 (24.47)		
Female	429 (45.44)	437 (46.29)	0.712	1.70
Black race	158 (16.74)	156 (16.53)	0.902	0.60
Sex mismatch (female donor to male recipient)	110 (11.65)	122 (12.92)	0.400	3.90
Size mismatch by weight (donor weight <70% of recipient)	78 (8.26)	86 (9.11)	0.513	3.00
Size mismatch by height (donor/recipient height ratio <0.90)	80 (8.47)	82 (8.69)	0.869	0.80
Donor/recipient height ratio	0.99 ± 0.07	0.99 ± 0.07	0.677	1.90
Etiology of heart failure (ischemic)	223 (23.62)	222 (23.52)	0.957	0.20
History of any previous cardiac surgery	119 (12.61)	123 (13.03)	0.783	1.30
Total waitlist time, months	6.0 ± 8.5	6.2 ± 10.3	0.700	1.80
UNOS status 1A or old status 1 at transplant	437 (46.29)	442 (46.82)	0.818	1.10
Recipient creatinine at transplant	1.2 ± 0.6	1.2 ± 0.7	0.960	0.20
Recipient creatinine at transplant >1.5 mg/dl	161 (17.06)	147 (15.57)	0.383	4.00
Recipient blood type O	339 (35.91)	352 (37.29)	0.535	2.90
Recipient BMI at transplant, kg/m^2	24.4 ± 4.6	24.4 ± 4.6	0.887	0.70
Recipient BMI >30 kg/m^2 at transplant	124 (13.14)	131 (13.88)	0.637	2.20
History of blood transfusion since listing	151 (16.00)	161 (17.06)	0.535	2.90
Current era (2005 onward)	326 (34.53)	338 (35.81)	0.563	2.70
Life support with inotropes	458 (48.52)	445 (47.14)	0.549	2.80
LVAD life support only at transplant	75 (7.94)	95 (10.06)	0.108	7.40
LVAD and RVAD support at transplant	18 (1.91)	18 (1.91)	1.000	0.00

Values are mean ± SD or n (%).
Abbreviations as in Table 1.

after adjusting for confounders including recipient age, sex mismatch, donor recipient height ratio, ischemic etiology, total waitlist time, UNOS status 1a or old 1 at transplant, LV assist device at transplant, graft ischemic time, and donor cause of death (head trauma vs. others) (hazard ratio: 0.80 [95% confidence interval: 0.62 to 1.02]; p = 0.076). Kaplan-Meier analysis also showed a decrease in CAV in recipients of EA donor hearts (p = 0.041 for log-rank test) (Figure 2C).

USE OF EA DONOR HEARTS. In a separate analysis, we found 6,000 EA donors (ages 10 to 14 years) with outcomes information registered in the UNOS database from October 1987 to September 2015. Of these, 2,919 were transplanted. For the remaining 3,081

TABLE 4 Baseline Donor Characteristics After Matching

	Early Adolescent Donor Heart (Ages 10-14 yrs; n = 944)	Adult Donor Heart (Ages 18-55 yrs; n = 944)	p Value	SD, %
Female	297 (31.46)	302 (31.99)	0.805	1.10
Donor creatinine >1.5 mg/dl	92 (9.75)	91 (9.64)	0.938	0.40
History of donor smoking	21 (2.22)	24 (2.54)	0.651	2.10
CMV mismatch (D+/R−)	120 (12.71)	122 (12.92)	0.890	0.60
Blood infection donor	44 (4.66)	48 (5.08)	0.669	2.00
LVEF (%)	62 ± 10 (n = 504)	62 ± 8 (n = 654)	0.494	4.00
Inotropic medications at procurement	109 (11.55)	115 (12.18)	0.669	2.00
Ischemic time, h	3.21 ± 1.10	3.24 ± 1.01	0.584	2.50
Donor cause of death (head trauma)	674 (71.40)	682 (72.25)	0.682	1.90

Values are n (%) or mean ± SD.
Abbreviations as in Table 2.

TABLE 5 Cox HR for Mortality and PGF in Adult Recipients of Early Adolescent Donor Hearts (Ages 10–14 Years) Compared With Recipients of Usual-Age Group Adult Donor Hearts (Ages 18–55 Years) in the Propensity-Matched Cohort

	Cox HR (95% CI); p Value	Cox HR (95% CI); p Value*	Cox HR (95% CI); p Value†
30-day mortality	1.11 (0.75–1.65); 0.602	1.11 (0.75–1.65); 0.603	1.11 (0.74–1.65); 0.599
1-yr mortality	0.90 (0.69–1.18); 0.454	0.90 (0.69–1.18); 0.453	0.90 (0.68–1.17); 0.419
3-yr mortality	0.89 (0.72–1.10); 0.282	0.89 (0.72–1.10); 0.282	0.88 (0.71–1.09); 0.239
5-yr mortality	1.03 (0.85–1.24); 0.781	1.03 (0.85–1.24); 0.782	1.02 (0.84–1.23); 0.851
PGF up to 90 days	0.75 (0.39–1.47); 0.407	0.75 (0.38–1.47); 0.406	–

*Adjusted for propensity score. †Adjusted for recipient age, sex mismatch, donor recipient height ratio, ischemic etiology, total waitlist time, UNOS status 1a or old 1 at transplant, LVAD at transplant, graft ischemic time, and donor cause of death.

CI = confidence interval; HR = hazard ratio; PGF = primary graft failure; other abbreviations as in Table 1.

donor hearts, the hearts were not transplanted for the following reasons: consent was not requested (n = 167), consent was not obtained (n = 213), organ was not recovered (n = 1,549), organ was recovered but not for transplant (n = 1,108), and organ was recovered for transplant but was not transplanted (n = 44). Hence, almost 3,000 EA donor hearts were not accepted for transplantation during the entire study period. This may seem to be a small figure, but it is greater than the number of adult heart transplants performed in the United States annually (~2,400 transplants) (3).

DISCUSSION

In this largest analysis to date, we evaluated the post-transplant outcomes in adult recipients of EA (ages 10 to 14 years) donor hearts using a multicenter national registry. Our principal findings are, first, that adults who received hearts from EA donors had similar rates of PGF leading to death or retransplant up to 90 days of follow-up when compared with adults who received hearts from donors in the usual adult age group (18 to 55 years). Second, 30-day, 1-year, 3-year, and 5-year mortality did not differ between groups. Finally, we observed a trend towards lower rates of CAV up to 5 years of follow-up in recipients of EA donor hearts. Particularly after taking into account that nearly 3,000 EA donor hearts (or one-half of all those available) were not accepted for transplantation, we believe these are important findings that should help to increase the utilization rates of EA donor hearts not used for pediatric patients.

According to the current UNOS guidelines, a heart from a pediatric donor is first allocated to a pediatric heart candidate by status and geographic location. However, if for any reason there is no suitable high-urgency status pediatric recipient available, then this pediatric donor heart is offered to an adult patient listed as UNOS status 1A within the region before being offered to pediatric recipients with lower urgency status (15).

A previous small, single-center study that involved 37 adult recipients of hearts from younger donors in the 10 to 15 years age group found that such donor hearts can have acceptable outcomes in appropriately selected adults (16). In a propensity-matched cohort (of 944 matched pairs), we found that adults who received hearts from EA donors had similar post-transplant survival when compared with adults who received hearts from donors in the usual age group, up to 5 years of follow-up. Currently, only 1 in 3 donor hearts are accepted for transplantation because the acceptance criteria for donor hearts remains poorly studied and standardized (3). There are wide discrepancies in the donor acceptance criteria of transplant centers across the United States, which may lead to nonuse of many potentially acceptable donor organs (3). Our study provides important post-transplant outcomes data and shows that appropriately selected adults who receive donor hearts from young adolescents (ages 10 to 14 years) have good short- and intermediate-term survival. These results should help adult transplant programs to make informed decisions about accepting or rejecting EA donor heart offers for adult patients.

One of the major concerns that adult transplant centers may have about hearts from EA donors is that a lack of pubertal hormonal activation could affect post-transplant cardiac contractility. This largely stems from earlier animal model studies that showed that cardiac contractility is affected by changes in hormones in both pre- and post-pubertal males and females (17). Later studies showed an increase in both LV systolic and diastolic wall thickness with puberty (6). Although this may be true, Simone et al. (18) studied 766 human subjects and found that the influence of body growth on development of LV mass decreases after early infancy and becomes a function of hemodynamic load and sex. Similarly, the Muscatine study, which was a 5-year longitudinal

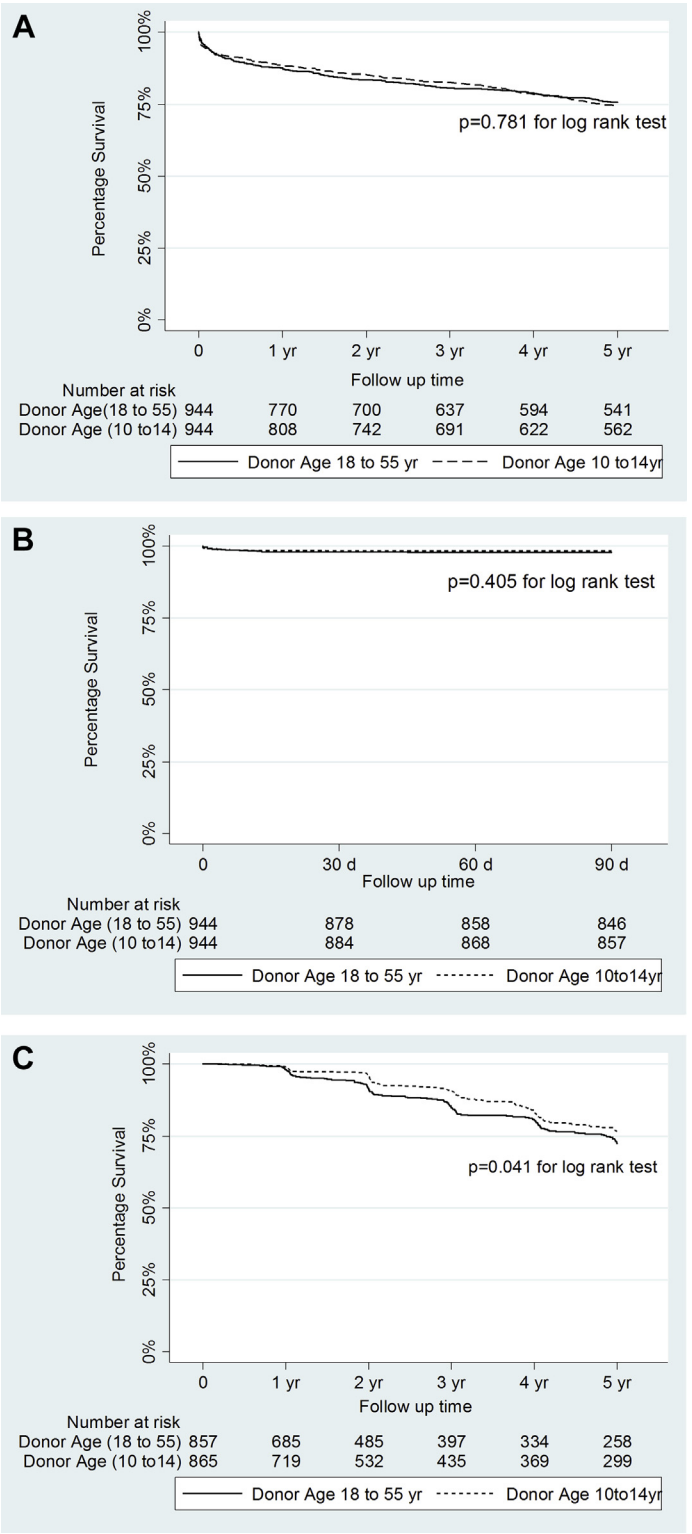
follow-up of 123 subjects (that completed baseline assessments) from pre-puberty or early puberty to post-puberty (n = 61 boys, mean age 10.8 years; and n = 62 girls, mean age 10.3 years), found that there was an increase in LV mass for both boys and girls. However, in addition to changes in fat-free body weight, this increase in LV mass was also dependent on cardiac workload and sex (7). Hence, changes in heart size or contractility (if it occurs) during puberty is likely dependent on a combination of factors: hormonal changes of puberty, somatic growth, and changes in cardiac workload. Examining early post-transplant cardiac contractility, we did not find any significant differences in the rates of PGF in the 2 groups (EA donor hearts vs. usual-age adult donor hearts). Similar to other previous analyses, we used a hard definition of PGF leading to death or retransplant (not related to infection, rejection, or surgical technical issues) (4,11).

In our study, of the 1,722 transplant recipients who had follow-up information on CAV, 25.8% developed CAV at 5 years of follow-up. Using both Cox models and Kaplan-Meier analysis, we found that adults who received hearts from EA donors had a trend toward less CAV. This is consistent with previous studies showing that older donor age may confer a greater risk of developing CAV (19). Because CAV is still a major limiting factor in the long-term success of heart transplantation, these results should be encouraging.

As expected, we found that adults who received hearts from young EA donors were shorter in height and weighed less when compared with adults who received hearts from usual-age adult donors. Finally, although the adult female recipients account for 22% to 25% of the total number of heart transplants in the United States annually (20), almost one-half of the adult recipients of EA hearts in our study cohort were women. This is expected because women tend to have a smaller body habitus and thus would be more likely to be an appropriate size match for the young EA donor hearts.

STUDY LIMITATIONS. This study should be interpreted in the context of several important limitations, mainly caused by its registry-based retrospective analytical design. First, we could not analyze whether hearts from EA donors changed in size post-transplant. Future research with serial post-transplant follow-up imaging may be required to answer this. Second, although we could not directly assess post-transplant contractility of EA donor hearts, we did not find any increased risk of PGF leading to death or retransplant in adults who received unused hearts from EA donors.

FIGURE 2 Kaplan-Meier Curves



Kaplan-Meier curves for freedom from **(A)** recipient mortality, **(B)** primary graft failure, and **(C)** cardiac allograft vasculopathy.

We may have underestimated the graft failure rates in our study, because PGF leading to extensive inotropic support or temporary mechanical circulatory support in the peritransplant period is not captured by UNOS and could not be included in this analysis. Third, UNOS does not have information on CAV for all recipients because this is based on self-reporting by transplant centers. Transplant recipients with missing or unknown CAV statuses were excluded from the CAV analysis, and it is unknown how this may have affected the results of the CAV analysis. Fourth, because it is difficult to establish a threshold of safety or equivalence margin for a given donor heart, we refrained from using the noninferiority hypothesis testing and used the 2-tailed hypothesis testing instead for our analysis. Finally, there may be variability in the age of onset of puberty, depending on sex, racial, genetic, and environmental factors. We were unable to determine if this variation could have affected the results of our study. Despite these limitations, this study provides important outcomes data for a donor-recipient group that has not been thoroughly evaluated in any of the prior studies.

CONCLUSIONS

This study shows that EA donor hearts that are not used for pediatric recipients can be safely transplanted in appropriately selected adults without any increased risk for short- or intermediate-term mortality or PGF. In fact, adult recipients of EA donor hearts may be less likely to develop CAV. These findings should help to increase the utilization rates of EA donor hearts and thus increase the number of heart transplants performed.

ADDRESS FOR CORRESPONDENCE: Dr. Shivank A. Madan, Division of Cardiology, Montefiore Medical Center, Albert Einstein College of Medicine, 111 East 210th Street, Bronx, New York 10467. E-mail: smadan@montefiore.org.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: In our study, we found that early adolescent donor hearts not used for pediatric patients can be safely used in appropriately selected adults and have good outcomes in terms of recipient survival and primary graft failure. In fact, recipients of early adolescent donor hearts may be at a less risk of developing cardiac allograft vasculopathy. This study provides robust outcomes data that should help adult transplant programs in making informed decisions regarding accepting or rejecting early adolescent donor hearts for adult heart failure patients.

TRANSLATIONAL OUTLOOK: Despite a shortage of donor organs, the donor acceptance rates continue to remain low. There is a need to safely increase the utilization rates of already available donor organs using evidence-based criteria, so that heart transplantation can be made available to a greater number of patients. Future research is required to address the wide discrepancies in donor acceptance criteria and stop wastage of many potentially acceptable donor organs.

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KEY WORDS donor, donor age, early adolescent, heart, transplant

APPENDIX For a supplemental table, please see the online version of this article.