Implications and outcomes of cardiac grafts refused by pediatric centers but transplanted by adult centers

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ABSTRACT

Background: According to Organ Procurement Transplant Network policy, hearts from donors age <18 years are offered to pediatric recipients before being offered to adults of the same health status. We aimed to analyze differences in the use of adolescent donor hearts between adult and pediatric candidates and also to analyze the outcomes of pediatric candidates in which an adolescent donor heart was refused and later used in an adult recipient.

Methods: All adolescent donors (age 12–17 years) for 2000 to 2015 were identified using the standard United Network of Organ Sharing dataset and matched against the Potential Transplant Recipient dataset.

Results: Of the 2457 adults who received an adolescent heart, 855 (35%) received it after at least 1 refusal by a pediatric candidate ($n = 844$). Of the 844 pediatric candidates, 643 (76%) subsequently underwent transplantation (designated PCTs) and 201 (24%) never underwent transplantation (designated PCNTs). Among the latter group, 87 patients (43%) died or became too ill for transplantation. These 87 PCNTs refused 256 hearts that were later accepted by adult recipients. Donor quality was the most common reason for refusal. Overall, adult recipients had similar post-transplantation survival compared with PCTs, all pediatric transplants, and all adult transplants ($P > .10$). A breakdown of adolescent heart donors by year shows a trend toward increased use in pediatric candidates.

Conclusions: A significant number of adolescent donor hearts that are refused by pediatric centers result in excellent post-transplantation outcomes in adult recipients. One in 10 pediatric candidates died on the waitlist after refusal of these hearts used by adult recipients. This warrants careful evaluation of the refusal criteria used by pediatric centers. Encouragingly, there now appears to be a trend toward an increased use of adolescent donor hearts by pediatric centers. (*J Thorac Cardiovasc Surg* 2017;154:528–36)

Proportional use of adolescent donor hearts by pediatric recipients over time.

Central Message

Pediatric centers should carefully consider their refusal criteria for adolescent donor hearts, because some of the refused hearts are being used successfully by adult centers.

Perspective

Pediatric transplant centers refuse a significant number of pediatric donor hearts that are successfully used by adult centers. This negatively impacts the outcomes of pediatric candidates for heart transplantation. This situation warrants careful evaluation of refusal criteria by pediatric centers. Encouragingly, there appears to be a recent trend by pediatric centers toward an increased use of these donors.

See Editorial Commentary page 537.

Recently, the number of pediatric heart transplantations performed annually has increased to more than 500; however, at the same time there has been a larger increase in pediatric candidates awaiting a suitable transplant.^{1,2} The size of the active waitlist for pediatric patients increased by >20%

between 2010 and 2014; therefore, the transplantation rate among active pediatric candidates decreased in that period across all pediatric age groups.² The increase in the waitlist is commonly attributed to stagnant donor pool, but in fact only 32% of all available donors and approximately 50% of pediatric donors were used for heart transplantation in 2014.³ To meet the increasing demand, donor selection criteria and special groups of donors need to be

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Abbreviations and Acronyms

OPTN	= Organ Procurement and Transplant Network
PCNT	= pediatric candidate (age ≤ 17 years at listing) who refused adolescent donors and never underwent transplantation
PCT	= pediatric candidate (age ≤ 17 years at listing) who refused adolescent donors before undergoing subsequent transplantation
PTR	= Potential Transplant Recipient
STAR	= Standard Transplant Analysis and Research
UNOS	= United Network of Organ Sharing

examined to improve organ utilization without compromising outcomes. In response to this need, several recent studies have demonstrated the use of extended donor criteria for pediatric heart transplantations that did not adversely affect post-transplantation outcomes.⁴⁻⁶

Adolescents are a particular group of donors being shared between adult and pediatric heart transplantations, but with a preference for pediatric candidates. Organ Procurement and Transplantation Network (OPTN) policy requires that a heart from a donor age <18 years be allocated to a pediatric candidate before being offered to an adult in the same United Network of Organ Sharing (UNOS) status.⁷ This gives pediatric candidates an advantage over adult candidates for pediatric age donors. Although many pediatric age donors are directly offered to an adult in the highest UNOS status because of a lack of pediatric candidates in the same status at the time, there remain a significant number of adolescent grafts that are offered and accepted by adult candidates that were not accepted for pediatric candidates. This presents a unique opportunity to examine the outcomes of some of the eligible donors that were refused by pediatric centers and were later used for transplants. In the present study, we aimed to compare the use of adolescent donor hearts between adult and pediatric heart transplant programs, and to analyze the outcomes of pediatric candidates for whom donor hearts were refused but then used for transplantation into adult recipients, as well as the outcomes in these adult recipients.

METHODS

Data Source, Study Cohort, and Definitions

This is a retrospective analysis of the UNOS database. UNOS is a private, nonprofit organization that administers the OPTN under a federal contract. OPTN is a unified transplant network established by the US Congress under the National Organ Transplant Act of 1982, which requires submission of data on all solid-organ transplants in the United States and is internally audited. UNOS Standard Transplant Analysis and Research (STAR)

files provide data on donors, candidates, transplanted organs, and follow-ups. The UNOS Potential Transplant Recipient (PTR) file provides data on match runs. Each time a deceased donor organ becomes available, a computer program compares donor information with transplantation candidate characteristics stored on the waitlist and creates a list of potential donor-recipient combinations. For each donor organ, computerized matching algorithms are used to produce rank-ordered lists of potential recipients. The matching algorithms used are based on organ allocation policies, transplant center acceptance criteria, and local variances.

Once a deceased donor organ is allocated, the donor Organ Procurement Organization initiates completion of a Potential Recipient Form. Included on the form is a partial rank-ordered listing of potential organ recipients indicated by the match run. For each individual on the list with a higher priority than the actual recipient, a refusal code is entered indicating the reason why the organ was not accepted for transplantation.

All adolescent donors (age 12-17 years) used for heart transplantation between July 2000 and June 2015 were identified from the STAR files. These donors were identified against their respective match runs in the PTR file. Candidates in the match runs for each of the adolescent donors from the PTR file were then identified in the waitlist (STAR) file. Three main groups of candidates were identified for this study: (1) adult candidates (age ≥ 18 years at listing) who accepted adolescent donors (adult recipients) who were previously refused for pediatric candidates; (2) pediatric candidates (age ≤ 17 years at listing) who refused adolescent donors before undergoing transplantation at a later time (PCTs); and (3) pediatric candidates (age ≤ 17 years at listing) who refused adolescent donors and did not undergo transplantation (PCNTs). Overall pediatric and adult heart transplant populations were also used as controls to compare post-transplantation outcomes. No center-specific data were analyzed for this study; thus, "pediatric centers" and "adult centers" refer to centers caring for pediatric and adult candidates, respectively.

The populations were selected with 100% complete data on survival. The key donor and recipient characteristic variables used in the analysis had $<5\%$ data missing. The two variables functional status and PRA had between 27% and 30% missing data. Only available data were analyzed; no imputations were made for missing data. Donor ejection fraction was reported as 1 data point in the dataset and does not account for situations in which multiple echocardiograms were performed in a donor. Comparison of donor ejection fraction between refused and accepted donor hearts is a comparison between the aggregates and not between refusals and acceptance by each pediatric recipient.

Statistical Analysis

Candidate characteristics, donor characteristics, waitlist outcomes, and post-transplantation survival were analyzed. Summary statistics are presented as median (interquartile range) or number (percentage). For baseline characteristics, continuous data were compared using the *t* test and analysis of variance with Tukey's method for normally distributed data and nonparametric tests (Mann-Whitney *U* test for 2 samples and Kruskal-Wallis analysis of variance for multiple samples) for data with a nonnormal distribution. Categorical data were compared using the χ^2 test. Survival curves were estimated using the Kaplan-Meier method; equality of survival curves was tested using a log-rank test. All analyses were performed using SPSS version 21 (IBM, Armonk, NY).

RESULTS

Cohorts

A total of 3473 adolescent hearts were used during the study period, 1016 (29%) by the pediatric recipients. Of the remaining 2457 adolescent hearts used by adult recipients, 855 were adult recipients, composing 25% of all adolescent donors. These 855 hearts were refused at least

once by 844 pediatric candidates (a total of 2033 refusals). Of the 844 pediatric candidates, 643 (76%) subsequently underwent transplantation (PCTs), and 201 (24%) never underwent transplantation (PCNTs). Among these 201 PCNTs, 87 (43%) died or became too ill to undergo transplantation, composing 10% of all pediatric candidates (PCTs + PCNTs) in the study, and 114 (57%) were delisted for other reasons. The 87 PCNTs who had died or were too ill to undergo transplantation were refused 256 hearts (a total of 319 refusals) that were later accepted by adult recipients (Figure 1). Of all the adolescent donors offered to pediatric candidates, only 36% (1016 of 2788) were accepted, a significantly lower percentage than in adult recipients (57%; 2457 of 4317) ($P < .001$). A breakdown of adolescent heart donors by years show a trend toward increased use in pediatric candidates (Figure 2).

FIGURE 1. Flow diagram showing the derivation of study population.

FIGURE 2. Proportional use of adolescent donors by pediatric recipients over time.

Candidate and Donor Characteristics

Sex and ethnicity distributions were similar across all groups. As expected, the diagnoses differed between the adult recipients and pediatric candidates. Both PCTs ($n = 643$) and PCNTs ($n = 201$) were clinically superior to the adult recipients ($n = 855$) at listing in terms of renal function (median estimated glomerular filtration rate >60 mg/dL in 84% and 78% vs 67%, respectively), ventricular assist device use (10% and 8% vs 15%), and functional status ($>50\%$ in 63% and 69% vs 51%). PCTs were more likely to be sensitized (32% vs 22%), and both PCTs and PCNTs waited longer for heart transplantation compared with adult recipients (88 and 416 days, respectively, vs 69 days) (Table 1). If the 844 pediatric recipients had accepted the first of these adolescent donor offers, then their hypothetical median waitlist time would have been 21 days (interquartile range, 6-79 days).

Donors for PCTs and adult recipients were similar in age and race; however, donors for PCTs were more likely to be female (39% vs 30%), to weigh less (60 vs 66 kg), and to be shorter (165 vs 170 cm). Donors for PCTs also had better left ventricular ejection fraction ($>50\%$: 94% vs 89%; $P = .001$) and renal function (estimated glomerular filtration rate >60 mg/dL: 79% vs 74%) compared with donors for adult recipients (Table 2).

Outcomes

The adult recipient group had a shorter waitlist time compared with the PCT group (69 vs 88 days; $P < .001$). Adult recipients had similar overall post-transplantation survival as PCTs, all pediatric transplants, and all adult transplants (Figure 3). The 256 adult recipients who accepted hearts refused by PCNTs who died while on the waitlist had a 1-year survival of 87% and a 5-year survival of 75%, similar to all pediatric ($P = .112$) and all adult ($P = .720$) post-transplantation survival (Figure 4).

In a group of adult recipients who received adolescent donor hearts ($n = 2457$), we performed a multivariate analysis with factors known to be associated with poor

TABLE 1. Recipient baseline characteristics in the adult recipient, PCT, and PCNT groups

Variable	Adult recipients (n = 855)	PCTs (n = 643)	P value	PCNTs (n = 201)	P value
Age (y), median (IQR)	51 (38-59)	14 (11-16)	<.001	11 (4-17)	.014
Female sex, n (%)	386 (45)	262 (41)	.089	77 (38)	.079
Caucasian race, n (%)	557 (65)	362 (56)	<.001	120 (60)	.071
Diagnosis, n (%)			<.001		<.001
Cardiomyopathy	686 (80)	320 (50)		93 (46)	
Congenital heart disease	48 (5.6)	209 (32.5)		82 (41)	
Retransplantation	41 (4.8)	78 (12)		0 (0)	
Other	80 (9.4)	36 (5.6)		26 (13)	
Functional status <50%, n (%)	314 (49)	172 (37)	<.001	40 (31)	<.001
Ventricular assist device use, n (%)	126 (15)	63 (10)	.004	16 (8)	.011
IV inotrope at listing, n (%)	298 (35)	255 (40)	.057	63 (31)	.345
Duration of waitlist time (d), median (IQR)	69 (21-226)	88 (38-221)	<.001	416 (72-965)	<.001
Sensitized >10%, n (%)	188 (22)	199 (31.5)	<.001	—	—
eGFR (mL/min/1.73 m ²), n (%)					
<90	575 (70)	264 (44)	<.001	105 (59)	.007
<60	270 (33)	74 (12)	<.001	39 (22)	.005

PCT, Pediatric candidate who refused adolescent donors before undergoing subsequent transplantation; PCNT, pediatric candidate who refused adolescent donors and do not undergo subsequent transplantation; IQR, interquartile range; IV, intravenous; eGFR, estimated glomerular filtration rate.

outcomes in adult transplantations. There was no effect of donors refused by pediatric centers (Table E1).

Reasons for Refusal

The 855 donors were refused on 2033 match runs by 844 pediatric candidates. A total of 1045 refusals (51%; accounting for 517 donors) were due primarily to donor quality, and only 86 (4%) were due to recipient illness. The 256

donors were refused on 319 match runs for 87 PCNTs. The most common reason for refusal was donor quality (n = 100 [31%], accounting for 82 donors), followed by no serum for cross-matching (n = 33 [10%]); only 19 refusals (6%; 15 donors) were due to recipient illness. On average, each donor was refused 2 times (range, 1-38 times) by pediatric candidates before being accepted by adults. A subgroup analysis limited to donors who were refused due to donor

TABLE 2. Donor baseline characteristics in the adult recipient and PCT groups

Variable	Adult recipients (n = 855)	PCTs (n = 643)	P value
Age (y), median (IQR)	16 (14-17)	17 (12-21)	<.001
Female sex, n (%)	259 (30)	250 (39)	<.001
Caucasian race, n (%)	555 (65)	396 (62)	.509
Height (cm), median (IQR)	170 (163-177)	165 (152-175)	<.001
Weight (kg), median (IQR)	66 (57-75)	60 (47-72)	<.001
MVA (circumstance of death), n (%)	376 (44)	263 (41)	.257
D-R weight ratio <0.8 or >1.2, n (%)	294 (34)	351 (54)	<.001
CVA (cause of death), n (%)	46 (5.4)	70 (11)	<.001
Any clinical infection, n (%)	409 (48)	299 (46)	.608
eGFR (mL/min/1.73 m ²), n (%)			
<90	562 (66)	389 (61)	.046
<60	224 (26)	134 (21)	.018
Duration of ischemia (h), n (%)			
<4	589 (71)	420 (69)	.474
4-5.9	225 (27)	180 (29)	
>6	12 (1.5)	12 (2.0)	
CPR in donor, n (%)	50 (5.8)	35 (5.4)	.738
LVEF, n (%)			.005
≤50%	93 (11)	37 (6.0)	.001
>50%	727 (89)	578 (94)	
D-R sex mismatch, n (%)	295 (34.5)	272 (42.5)	.002
D-R race mismatch, n (%)	396 (46)	330 (51.3)	.055

PCT, Pediatric candidate who refused adolescent donors before undergoing subsequent transplantation; IQR, interquartile range; MVA, motor vehicle accident; D, donor; R, recipient; CVA, cerebrovascular accident; eGFR, estimated glomerular filtration rate; CPR, cardiopulmonary resuscitation; LVEF, left ventricular ejection fraction.

FIGURE 3. Post-transplantation survival for all adult recipients (adult candidates who accepted adolescent donors that were previously refused by pediatric candidates) compared with (A) PCTs (pediatric candidates who refused adolescent donors and underwent transplantation later) and (B) overall pediatric and adult transplantation.

quality (n = 517) showed similar post-transplantation survival as in PCTs, all adult transplants, and all pediatric transplants (Figure E1).

DISCUSSION

The goal of this study was to highlight the nonuse of what appear to be good donor hearts by pediatric centers. When used by adult centers, these hearts resulted in good post-transplantation outcomes. Sadly, 201 of the pediatric candidates who refused these organs never underwent transplantation, and 87 of them died or became too ill to receive a transplant. This situation perhaps presents an opportunity in the wake of an ever-increasing waitlist for pediatric heart transplantation.

Most of the refusals of donor grafts for pediatric candidates were due to donor quality; however, this code is often used because of the indicators included under donor quality codes, such as high-dose vasopressors, cardiac arrest, and cardiopulmonary resuscitation, which historically have been considered associated with poor donor organ quality,

FIGURE 4. Post-transplantation survival for 256 adult transplant recipients from donors turned down by pediatric candidates who later died or were too sick to undergo transplantation, compared with overall pediatric and adult transplantation.

although this is not supported by evidence.⁸ In fact, some literature clearly demonstrates that donor cardiopulmonary resuscitation, inotrope use, and cardiac arrest time have no effect on outcomes.⁹ The present study also demonstrates that donor hearts refused due to donor quality have been associated with acceptable post-transplantation outcomes. Similar findings have been shared by others at both institutional and national levels, confirming that donor hearts refused due to donor quality (multiple times in many cases) can result in comparable post-transplantation outcomes.^{6,10,11}

Another significant finding from this study is that pediatric recipients got donor hearts with better left ventricular ejection fraction compared with the hearts that were refused. This suggests that some of the adolescent donor hearts were likely refused by the pediatric candidates due to a low ejection fraction. In a study from the UNOS database, Rossano et al¹² demonstrated that the use of donor hearts with depressed ventricular function does not affect graft survival, yet the use of these hearts is very infrequent in pediatric heart transplantation (<15% of all transplants).

Pediatric candidates are expected to have less time on the waitlist compared with adult candidates.² PCNTs and, more importantly, PCTs waited significantly longer than the adult recipients. More importantly, if the PCNTs and PCTs would have accepted the first of these adolescent donor offers that were eventually used successfully in adults, their median waitlist time would have been <1 month, compared with their actual waitlist time of 3 months. A rapid increase in cumulative adverse events with increasing time, particularly in the first 90 days on the waitlist, is a well-documented fact.^{13,14} Thus, these types of pediatric candidates have the potential for better waitlist outcomes than were observed in our cohort.

The patients who underwent transplantation analyzed in this study (PCTs and adult recipients) may be considered fundamentally different populations (pediatric and adult). PCTs appeared to be much more stable and better transplant candidates in terms of functional status, ventricular assist device use, and renal dysfunction. In addition, pediatric transplant recipients generally are expected to have better long-term outcomes (median survival, 15 years vs 10 years).^{1,15} Despite these differences, however, our adult recipients had similar post-transplantation outcomes as our PCTs.

PCTs who refused these allegedly poor-quality donors did not appear to have superior outcomes when undergoing transplantation with a presumably better donor heart. If these same PCTs would have used the hearts that they turned down, then the hearts that they eventually accepted would have gone to other transplant candidates. Clearly, the 82 donor hearts that were refused due to donor quality but were used successfully in adults could have allowed for survival in many of the 87 PCNTs who refused these organs. Another difference could be in the perspective of the pediatric and adult programs about what comes next: “a bird in the hand is worth two in the bush” or not. Pediatric programs may believe that subsequent offers will keep coming and likely will be better than the current offer; however, adult programs may view adolescent donors as the best offer that they will get. This underscores the importance of our data and should encourage pediatric programs to carefully reevaluate their refusal of adolescent donors.

Limitations

Patients in this study underwent transplantation over a 15-year period and might have been subjected to various changes in care practices. One of the changes in heart transplant allocation was the broader regional sharing in 2006, which might have influenced the use of these donors. Survival comparisons between the overall pediatric and adult transplant cohorts were performed only to support the idea that the refused donor hearts were associated with similar transplantation outcomes as any other hearts transplanted. However, our cohort comprised unselected patients, and thus our findings should be interpreted only in the appropriate context.

CONCLUSIONS

A substantial number of adolescent donor hearts are refused by pediatric centers that are later used with excellent post-transplantation outcomes in adult recipients. One fourth of the pediatric candidates who refused these hearts were either removed from the waitlist or were still waiting without a transplant. One in 10 of them died or became too ill to undergo transplantation. Encouragingly, there has been a positive change toward an increasing use of

adolescent donors by pediatric age recipients in recent years, and we hope that these data will promote this positive trend.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: pediatric heart transplant, adolescent donors, donor refusal reasons

Discussion

Dr Zafar. Good morning. I would like to thank the program committee for giving us the opportunity to share our work with you today. We do not have any relevant disclosures. This graft represents the number of pediatric heart transplants performed each year from the ISHLT registry. Recently, there

has been an increase in the number of pediatric heart transplants performed each year. However, at the same time, there has been an even greater increase in patients actively listed for pediatric heart transplants. Therefore, the transplant rate among actively listed pediatric candidates has decreased in these years for all age groups. The growth in pediatric heart transplant waitlist is commonly attributed to a stagnant donor pool. In fact, only 32% of all available donors were utilized for heart transplantation in 2014. I believe that to meet the increasing demand, donor selection criteria and special donor groups need to be examined to improve organ utilization.

Adolescents are one particular group of donors that are shared between pediatric and adult candidates. In fact, OPTN policy requires that a heart from a donor less than 18 years old be offered to a pediatric candidate before being offered to an adult in the same UNOS status, which gives pediatric candidates preference. This gives us a unique opportunity to examine the outcomes of some of the eligible donors that were refused by pediatric candidates and were later utilized for transplant. Therefore, the objective of this study was to compare the utilization of adolescent donor hearts between adult and pediatric heart transplantation programs and to analyze the outcome of pediatric candidates for whom adolescent donor hearts were refused. Also, to analyze the outcome of the adult recipients who accepted these refused hearts. For the purpose of this study, the UNOS database was reviewed from July 2000 to June 2015. Heart transplants performed using adolescent donors were identified. Adolescent donors were then matched against the potential transplant recipient file to identify all the match runs on these donors. This is the graft representing utilization of cardiac donors by adult and pediatric recipients. Adolescent aged donors are more likely to be utilized by adult recipients. Of all the adolescent donors who were transplanted to adult recipients, 35% were first offered to 844 pediatric candidates.

When we looked at the waitlist outcome of these 844 pediatric candidates, one quarter of them never got transplanted. In fact, 1 in 10 died or became too sick for a transplant on the waitlist. This is how we came to this study group for our analysis. The first group was adult candidates who accepted adolescent donors, which were previously refused by pediatric candidates. These were 855 adult recipients. The second group was pediatric candidates who

refused adolescent donors and were transplanted later. These were 642 pediatric recipients. The final group was pediatric candidates who refused adolescent donors and were never transplanted. These were 201 pediatric candidates. When we compared the recipient characteristics among these 3 groups, pediatric candidates had better functional status and renal function compared to adult candidates. Pediatric candidates were more likely to be sensitized and more likely to wait longer on the waitlist.

When we compared the donor characteristics between the transplanted adult and pediatric recipients, pediatric candidates who were refused these adolescent donors later received donors that had better renal function and left ventricular ejection fraction compared to donors that were refused. Despite these differences in donor and recipient characteristics, which favored pediatric candidates, adult recipients had similar survival to pediatric recipients and they actually had similar survival to all adult and all pediatric heart transplants. Now, the 256 adults who received hearts that were refused by PCNT group had similar survival to all adult and all pediatric heart transplants. When we looked at the proportional use of adolescent donors by adult and pediatric recipients over the years, there is a clear trend toward better utilization of these donors by pediatric centers.

There are some limitations to our study. It was a retrospective review. Patients in this study were transplanted over a 15-year period and might have been subjected to changes in practice over time.

One of the changes in the heart transplant allocation was the broader region sharing in 2006, which might have had an effect on the utilization of these donors. In conclusion, a substantial number of adolescent donor hearts are refused by pediatric centers that are later utilized with excellent post-transplant outcomes in adult recipients. One fourth of the pediatric candidates that were refused these hearts never got transplanted, and 1 in 10 died or became ineligible for transplant due to a decline in condition. However, increasingly, there has been a positive change toward more utilization of adolescent donors by pediatric recipients in recent years, and we hope these data will promote this trend. Thank you.

Dr M. McMullan (*Seattle, Wash*). I'd like to thank the WTSa for the privilege of discussing this paper in such a wonderful location. Dr Zafar and his colleagues are to be congratulated on performing such an insightful and timely analysis. I enjoyed reading the manuscript and listening to the well-organized presentation. The topic of cardiac graft allocation is important for 2 reasons. First, a sizeable subset of donated organs are ideally suited for adult and pediatric patients, groups that often have very different forms of underlying heart disease, mechanical support options, and medical comorbidities. Second, the new pediatric heart

status 1A and 1B requirements go in effect in a matter of days, and broad changes to adult heart allocation system had been proposed by the OPTN UNOS Thoracic Organ Transplantation Committee that may significantly impact pediatric patients awaiting heart transplantation. The primary finding from your study confirms what some of the busier pediatric centers have suspected for years, namely that grafts are frequently better, of better quality than they are given credit, and that even less than ideal organs are generally better than those they will replace. Your findings are based on solid clinical data. Although I agree with your message and in some ways feel that you are letting the transplant community in on a little secret shared by a number of pediatric centers, one might imagine that our adult transplant colleagues will be less enthusiastic about this analysis. It appears, after all, that we may simply be shifting waitlist mortality rates between the 2 populations.

I have 3 questions for you. First, during the study period, 10% of all pediatric candidates who did not utilize a subsequently transplanted organ either died or became too sick for transplantation. Do you have similar outcome data for adults in whom an organ was declined but was ultimately transplanted into another recipient during the study period?

Dr Zafar. We did not analyze the adult recipient data. That would be a different analysis, and I agree with you that it would be very interesting to see what happens; however, I would respond to one of your comments that the proportion of adolescent donors utilized by adult recipients in general is so small that the effect of pediatric centers utilizing more adolescent donors would not be noticeable on the adult side.

Dr McMullan. Second, based on the findings of your study, are there specific donor organ exclusion criteria that you would advise pediatric transplant centers to reconsider?

Dr Zafar. I would say that there are. One thing that we have noted from this analysis and then in a different analysis that we just presented at the ISHLT this year is that there is an overuse of donor refusal code for donor quality and the indicators for that code, particularly use of high-dose vasopressors, donors that had low EF, were significantly overused and these donors that we analyze here, the majority of the refusals were for donor quality, so one thing I would carefully say is that we should look at our use of donor quality and put in procedures where if we are using donor quality refusal, it should be reviewed by several members of the team.

Dr McMullan. Finally, the proposed changes to the heart allocation system are based on historical organ utilization benchmarks and a mandate to improve overall organ allocation. Can you comment on what impact, if any, increased graft utilization for pediatric recipients may have on potential adult recipients if these changes are implemented?

Dr Zafar. It would definitely have a positive impact on pediatric utilization, but in general, the purpose of this analysis was not to go down adult versus pediatric utilization but to highlight the number of donors that were refused, the amount of good-quality donors that were refused by pediatric centers in general. As you said in your first comment, a lot of these pediatric centers are coming to realize that the quality of donors that we refuse is far better than we understand.

Dr McMullan. Congratulations on the paper; it is an important topic, and doing this analysis is highly valuable to the transplant community. The question I have for you relates around the donor refusal codes, because I think that's where the real meat of this paper is. Why are these organs being turned down? The donor refusal codes we currently have are fairly coarse. Organ quality doesn't really mean anything. It means something to somebody on the phone but when you go back and review it, it doesn't mean anything for these CDC and high-risk donors or there are other factors that contributed to that. We did this same analysis in our own center and found that we were able to substantially increase our donor utilization. What are you doing to change it in your center, or what would you recommend to other centers?

Dr Zafar. More recently, if you look at the UNOS database, there have been comments added after you code for donor quality. There have been comments about whether the patient was on high vasopressors, but again, that data were so scarce that we weren't able to analyze that. From whatever data were available, we found that close to 51% of the refusal reasons were donor quality from the pediatric centers. Also, that represents close to more than 500 donors that were not utilized by pediatric candidates. I think what we have been trying to do is that if you use the donor quality as your refusal reason, it must be evaluated by at least 3 physicians on the team, and a cardiothoracic surgeon must be part of that decision. Again, I would say that more precise definition of donor refusal quality codes is what would give us better understanding of this problem.

Dr D. Ravkin (*Loma Linda, Calif*). Thank you for the nice talk. I have 2 questions. The first is did you have any outcome data on the hearts that were refused in the pediatric population that were then transplanted into the adult population?

Dr Zafar. I'm sorry, what ...

Dr Ravkin. Do you have outcome data as how those hearts fared after they were refused in the pediatric population but transplanted in the adult population?

Dr Zafar. Yes, the hearts that were refused and later utilized by adults had similar outcomes to pediatric candidates that were later transplanted and actually to all adult transplants in general.

Dr Ravkin. Yes, that's what I expected. I recently reviewed the UNOS data for adult hearts that were refused,

and 20% of them were refused exclusively for poor ventricular function. There have been numerous studies, both in the pediatric population and in the adult population, which showed these hearts can be transplanted with equivalent outcomes as hearts with normal ventricular function. It's probably related to the pathophysiology of brain dead and it just doesn't seem to be catching on. I mean, we keep, in the adult population, in distinction to what the data you showed, the number of transplants with those hearts in the last 15 years. In fact, the utilization of hearts has gone down, and 20% of these hearts most likely could be safely used. It's kind of an unfair question, but do you have any idea why these studies don't have an impact on the utilization of these hearts which most likely can be used?

Dr Zafar. I would completely agree with you. There is a nice paper from the pediatric side as well looking at these ventricular functions from Rossano et al. There are a significant number of hearts that are utilized in pediatric transplants that have poor left ventricular ejection fraction and they do just as well post-transplant. I don't have a good answer to your question. I guess it will take time for people to realize that and probably get over to utilize these donors, and that we are already seeing signs of improvement in utilization.

Dr Ronald Woods. Great work. Quick question. In the absence of being able to understand what this rejection for quality is, there are certain things that are unique to pediatric transplants, and I'm wondering if you can parcel out that data. For example, how many were refused because of the size and mismatch? We tend to be very inclusive when we list people, but toward the end, we can change the way we can resize it. The second thing is how many of these were for congenital heart disease, because you have high presensitization. If that's the case, PVR is high, and that's a unique challenge for the congenital population. That heart may be perfectly reasonable for an adult with cardiomyopathy, so without being able to say what the reason of rejection for quality is, there's a little cloudiness in the data.

Dr Zafar. We definitely included that in our manuscript. You should be able to read that once that comes out. As I said earlier, the majority of these were donor quality refusal codes, which is separate from donor size. You're right, the patients that never get transplanted, there was a significant number of patients that were refused for not having serum for crossmatch, so you're right, but you will see that data when the manuscript comes out.

FIGURE E1. Kaplan–Meier survival comparison of 517 adolescent recipients using donors refused for quality with waitlisted pediatric candidates who refused adolescent donors and underwent transplantation later (PCTs), all adult transplants, and all pediatric transplants.

TABLE E1. Multivariate predictors of overall mortality (Cox proportional hazard model) for all adult recipients of an adolescent donor heart (n = 2457)

Covariate	P value	HR (95% CI)
Ventilator support at transplant	<.001	2.295 (1.546-3.406)
Pretransplantation diabetes	.002	1.310 (1.105-1.552)
Congenital heart disease	.016	1.500 (1.080-2.085)
Black race	.034	1.224 (1.015-1.475)
Chronic steroid use at transplantation	.036	1.248 (1.015-1.534)
Recipient age (y)	.328	1.003 (0.997-1.009)
Transplantation using a previously refused donor	.953	1.005 (0.860-1.173)

HR, Hazard ratio; CI, confidence interval.