Relation of Length of Survival After Orthotopic Heart Transplantation to Age of the Donor

Yasuhiro Shudo, MD, PhD, Sabina PW Guenther, MD, Bharathi Lingala, PhD, Hao He, PhD,, William Hiesinger, MD,, John W MacArthur, MD,, Maria E Currie, MD, PhD,, Anson M Lee, MD,, Jack H Boyd, MD, and Y. Joseph Woo, MD*

We aim to evaluate the impact of donor age on the outcomes in orthotropic heart transplantation recipients. The United Network for Organ Sharing database was queried for adult patients (age; ≥60) underwent first-time orthotropic heart transplantation between 1987 and 2019 (n = 18,447). We stratified the cohort by donor age; 1,702 patients (9.2%) received a heart from a donor age of <17 years; 11,307 patients (61.3%) from a donor age of 17 ≥, < 40; 3,525 patients (19.1%) from a donor age of 40 ≥, < 50); and 1,913 patients (10.4%) from a donor age of ≥50. There was a significant difference in the survival likelihood (p < 0.0001) based on donor's age−based categorized cohort, however, the median survival was 10.5 years in the cohort in whom the donor was <17, 10.3 years in whom the donor was 17 ≥, < 40, 9.4 years in whom the donor was 40 ≥, < 50, and 9.0 years in whom the donor was ≥ 50. Additionally, there was no significant difference in the episode of acute rejection (p = 0.19) nor primary graft failure (p = 0.24). In conclusion, this study demonstrated that patients receiving hearts from the donor age of ≥50 years old showed slight inferior survival likelihood, but appeared to be equivalent median survival. **(Am J Cardiol 2020;131:54−59)**

Heart disease is the leading cause of death in the United States. Advanced or medically refractory heart failure represents the end-stage form of heart disease.[1] Many treatment options have been developed for patients with end-stage heart failure, in which orthotropic heart transplantation (OHT) remains the gold standard.[2] Although over 20,000 patients may benefit from OHT per year, only 3,000 will receive a new heart, with a waitlist mortality of 10.7 deaths per 100,000 waitlist-years.[3] In contrast, donor hearts with marginal criteria are often rejected for fear of adverse clinical outcomes. More than 60% of available hearts are still being discarded.[4] Most centers' concern about advanced age was one of the main medical reasons why donors were not allowed to proceed to donation. Unfortunately, we lack guidelines on the evaluation and acceptance of marginal organs, such as an older donor graft. These deficiencies have resulted in variable practice patterns between transplant centers, leading to underutilization of a valuable resource. Therefore, 1 possible solution will be to maximize the use of advanced-aged donors. Thus, attention has focused on the usefulness of advanced-age donor. The outcome of advanced-age donor on the quality of heart grafts has not been studied in detail. To our knowledge, no large multicenter study focusing on advanced-age donor has been performed. Lacking this, we believed the next best option would be to investigate this issue using data from the United Network for Organ Sharing (UNOS) database, which is a multi−institutional physician−overseen registry collecting data on all patients listed for OHT in the United States. Here, we seek to evaluate the impact of donor age on the outcomes in the cohort of recipients by utilizing data from the multi-institutional UNOS database.

Methods

The UNOS registry was used to identified all adult patients who underwent OHT between October 1, 1987 and March 31, 2019 (n = 63,775). Patients were excluded if they were 18 years or younger, did not undergo isolated heart transplantation, or underwent re-heart transplantation. Patients with incomplete data were excluded from the analysis (n = 59,875). Only recipients (age; ≥ 60) were included in this study (n = 18,447, Figure 1). The cohort was stratified as 4 compared groups by donor age: a donor age of < 17; a donor age of 17 ≥ < 40); a donor age of 40 ≥ < 50; and a donor age of ≥ 50.

Information obtained from the database included donor characteristics (age, gender, body mass index [BMI], blood type group), donor past medical history (diabetes mellitus, hypertension, cigarette usage, alcohol usage), donor's left ventricular ejection fraction, recipient baseline characteristics (age, gender, BMI, blood type group), recipient past medical history (diabetes mellitus, hemodialysis), etiology of heart failure, total waitlist time, and preoperative life support (hospitalization, intra-aortic balloon pump [IABP], extra-corporeal membrane oxygenation [ECMO]), history of previous cardiac surgery, and allograft ischemic time.

The primary end point was graft survival, with graft loss being defined as patient death or re-heart transplantation. The secondary end point was transplant related morbidity, such as acute rejection episodes, primary graft dysfunction, cerebrovascular accident, hemodialysis, re-intubation, or

Department of Cardiothoracic Surgery, Stanford University School of Medicine, Palo Alto, California. Manuscript received May 8, 2020; revised manuscript received and accepted June 19, 2020.

See page 59 for disclosure information.

*Corresponding Author: Tel: +1 (650) 725-3828; fax: +1 (650) 725-3846.
E-mail address: joswoo@stanford.edu (Y.J. Woo).

0002-9149/© 2020 Elsevier Inc. All rights reserved.
https://doi.org/10.1016/j.amjcard.2020.06.036

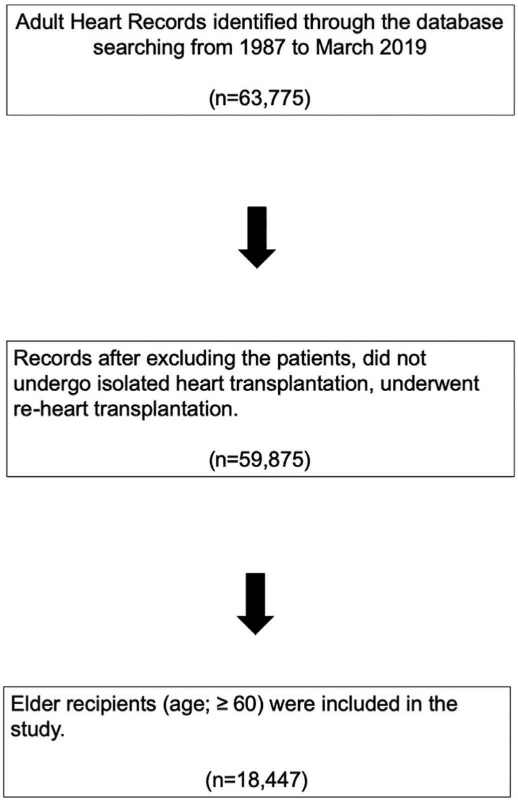

Figure 1. PRISMA flow diagram. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta−analysis.

permanent pacemaker. Studies using this data set have been determined to be exempt from review by the Institutional Review Board of Stanford University School of Medicine.

In the descriptive analyses of the study, continuous variables were presented as mean ± standard deviation. The mean differences between groups were compared by analysis of variance. Chi-square test was used to assess the association between categorical variables. Graft survival curves were constructed using the Kaplan-Meier method, stratified over donor age. Cox proportional hazards regression model was conducted to estimate the effect of donor's age on the 5-year survival of the cohort after risk adjustments of other important factors. For all analyses, p-values <0.05 were considered statistically significant. All analyses were performed using SAS version 9.4 (SAS Institute Inc. NC, USA).

Results

Of 18,447 adult (age ≥ 60) primary heart transplant patients from 1987 to 2019 who met the study inclusion criteria, 1,702 patients (9.2%) received a heart from a donor age of < 17, 11,307 patients (61.3%) received a heart from a donor age of 17 ≥ < 40, 3,525 patients (19.1%) received a heart from a donor age of 40 ≥ < 50, and 1,913 patients (10.4%) received a heart from a donor age of ≥ 50.

Donors' characteristics stratified by donor age are shown in Table 1. The percentage of male donors was high in the donor age of < 17 (74.6%) and donor age of 17 ≥, < 40 (75.3%), and lowest in the donor age of ≥ 50 (53.9%) (p < 0.0001). The mean BMI of the 4 recipient groups were significantly different (p < 0.0001). The percentage of diabetes mellitus was significantly different in the donor age of ≥ 50 (6.0%), the donor age of 40 ≥, < 50 (5.5%), the donor age of 17 ≥, < 40 (2.4%), and the donor age of < 17 (0.5%) (p < 0.0001). The percentage of hypertension was significantly different among the 4 recipient groups (p < 0.0001). The incidence of cigarette and alcohol usage was significantly higher in the groups with donor's age of ≥ 40 (p < 0.0001 for both). Creatinine and total bilirubin were observed to be significantly different (p < 0.0001 for both). The above-mentioned results, higher incidence of diabetes mellitus, and higher percentage of cigarette and alcohol usages, suggest that the cohort in whom donor age was ≥ 40 reflected typical medical characteristics and social habits of the older population, even although the cohort included only accepted donor grafts for heart transplantation. The left ventricular ejection fraction was >60% across all groups.

Recipients' characteristics stratified by donor age are shown in Table 2. The mean age of the 4 recipient groups were 64.78 ± 3.52 years old in the donor age of ≥ 50, 64.38 ± 3.31 years old in the donor age of 40 ≥, < 50, 64.05 ± 3.14 years old in the donor age of 17 ≥, < 40, and 63.59 ± 2.95 years old in the donor age of < 17, respectively (p < 0.0001). The prevalence of male recipients was lowest in the donor age of < 17 group (74.2%), but higher in all other groups with age ≥17.0 (p < 0.0001). The percentage of diabetes mellitus in recipients was significantly greater in the donor age of 17 ≥ < 40 (30.9%), and donor age of 40 ≥, < 50 (30.2%) groups compared with other 2 groups (p = 0.0002).

Regarding preoperative life support, the use of IABP before transplant was not significantly different between groups (p = 0.4281), whereas the percentage of ECMO usage was different (p = 0.0106). Similarly, the rate of hospital admissions before transplant was significantly different between groups (p = 0.0302) and highest in the donor age of ≥ 50 group (15.6%). The above-mentioned results, highest incidence of ECMO and hospital admission before transplant, suggest that the cohort in whom donor age of ≥ 50 was utilized in relatively sicker recipients. The rate of blood type group O was highest in the donor age of ≥ 50 (53.1%) (p < 0.0001), likely reflecting the eagerness of accepting heart organs, presumably because blood type group O recipient needs longer waitlist time.

Overall, 1 year, 3 year, 5 year, and 10 year- survival were 85.8, 79.3, 72.6, and 49.8 % in all adult recipients (age ≥ 60), whereas those were 81.8, 73.7, 66.6, and 45.1 % in recipients whose donor hear was from ≥ 50 years old. There was a significant difference detected in the survival likelihood (p < 0.0001) of patients based on a donor's age−based categorized cohort, however, the median survival was 10.5 years (9.9 to 11.1) in the cohort of donor age of < 17; 10.3 years (10.0 to 10.4) in that of donor age of 17 ≥, < 40; 9.4 years (8.9 to 9.9) in that of donor age of ≥ 40, < 50; and 9.0 years (8.5 to 9.5) in that of donor age of ≥ 50. (Figure 2)

In the posttransplant outcomes, there was no significant difference in the episode of acute myocardial rejection episodes (p = 0.19), defined as necessitating treatment with

Table 1
Donor's characteristics stratified by donor age (years)

Variable	< 17 (n = 1,702)	17 ≥, < 40 (n = 11,307)	40 ≥, < 50 (n = 3,525)	≥ 50 (n = 1,913)	p value
Donors' baseline characteristics					
Age (years)	15.21 ± 1.9 [16 (14, 17)]	27.56 ± 6.71 [27 (22, 33)]	45.37 ± 2.82 [45 (43, 48)]	55.13 ± 3.7 [54 (52, 57)]	<.0001
Male	1,269 (74.6%)	8,514 (75.3%)	2,105 (59.7%)	1,031 (53.9%)	<.0001
Body mass index (kg/m2)	23.63 ± 4.82 [22.8 (20.5, 25.7)]	26.47 ± 5.48 [25.5 (22.8, 29.1)]	27.8 ± 5.82 [26.8 (23.7, 30.8)]	27.68 ± 5.43 [27 (23.9, 30.2)]	<.0001
Left ventricular ejection fraction (%)	61.55 ± 8.49 [60 (55, 66)]	61.21 ± 7.25 [60 (55, 65)]	62.12 ± 6.91 [60 (57, 65)]	62.95 ± 6.94 [63 (60, 66)]	<.0001
Allograft ischemic time (hours)	3.01 ± 1.03 [3 (2.27, 3.65)]	3.07 ± 1.05 [3.05 (2.33, 3.72)]	3.08 ± 1.01 [3.08 (2.35, 3.72)]	3.12 ± 1.07 [3.12 (2.35, 3.8)]	0.0102
Diabetes mellitus	7 (0.5%)	242 (2.4%)	176 (5.5%)	105 (6%)	<.0001
Hypertension	12 (0.9%)	873 (8.8%)	940 (29.7%)	620 (35.5%)	<.0001
Smoker	88 (6.6%)	1,785 (18.1%)	1,215 (38.4%)	611 (35.3%)	<.0001
Alcohol usage	47 (3.5%)	1,654 (16.9%)	826 (26.2%)	396 (22.8%)	<.0001
Preoperative data					
Creatinine (mg/dl)	1.26 ± 1.84 [0.9 (0.7, 1.2)]	1.4 ± 1.45 [1 (0.8, 1.4)]	1.32 ± 1.31 [1 (0.8, 1.3)]	1.25 ± 1.29 [1 (0.7, 1.3)]	<.0001
Total bilirubin (mg/dl)	1.28 ± 1.36 [0.9 (0.6, 1.4)]	1.14 ± 1.56 [0.8 (0.5, 1.3)]	1.01 ± 1.39 [0.7 (0.4, 1.1)]	0.98 ± 1.28 [0.7 (0.4, 1.1)]	<.0001
Blood type					
A	695 (40.8%)	4,257 (37.6%)	1,358 (38.5%)	736 (38.5%)	<.0001
B	215 (12.6%)	1,227 (10.9%)	349 (9.9%)	141 (7.4%)	
AB	51 (3%)	302 (2.7%)	59 (1.7%)	21 (1.1%)	
O	741 (43.5%)	5,521 (48.8%)	1,759 (49.9%)	1,015 (53.1%)	

antirejection medications at least once. There was no significant difference in the episode of primary graft failure (p = 0.24). (Table 3)

Considering the effects of other important factors and controlling for possible confounding, the Cox Proportional Hazards regression model was used to assess the adjusted donor age effects on the 5-year survival probability. In multivariable analyses, after risk adjustments by significant factors, including recipient's age, recipient's BMI, total waitlist time, transplant year, donor's age category, gender match, hospitalization at transplant, and preoperative life support (ECMO, IABP, and inotropes), donor age kept the significant impact for 5-year death risks after OHT (Table 4). In comparison with the donor age of ≥ 50, the 5-year risk of mortality for donor age of ≥ 40, < 50, donor age of 17 ≥, < 40, and donor age of < 17 were

Table 2
Recipient's characteristics stratified by donor age (years)

Variable	< 17 (n = 1,702)	17 ≥, < 40 (n = 11,307)	40 ≥, < 50 (n = 3,525)	≥ 50 (n = 1,913)	p-value
Recipients' preoperative baseline characteristics					
Age (years)	63.59 ± 2.95 [63 (61, 65)]	64.05 ± 3.14 [64 (61, 66)]	64.38 ± 3.31 [64 (62, 67)]	64.78 ± 3.52 [64 (62, 67)]	<.0001
Male	1,263 (74.2%)	9,437 (83.5%)	2,845 (80.7%)	1,525 (79.7%)	<.0001
Body mass index (kg/m2)	24.88 ± 4.19 [24 (22, 27)]	26.44 ± 4.31 [26 (23, 29)]	26.33 ± 4.3 [26 (23, 29)]	26.09 ± 4.25 [26 (23, 29)]	<.0001
Diabetes mellitus	341 (26.6%)	3,027 (30.9%)	950 (30.2%)	462 (26.8%)	0.0002
On hemodialysis	19 (1.4%)	195 (1.9%)	50 (1.6%)	29 (1.6%)	0.2931
Etiology of heart failure					
Non-ischemic cardiomyopathy	584 (34.3%)	3,933 (34.8%)	1,135 (32.2%)	703 (36.7%)	<.0001
Ischemic cardiomyopathy	674 (39.6%)	5,113 (45.2%)	1,657 (47%)	843 (44.1%)	
Restrictive heart disease	21 (1.2%)	227 (2%)	98 (2.8%)	57 (3%)	
Congenital heart disease	7 (0.4%)	38 (0.3%)	21 (0.6%)	4 (0.2%)	
Hypertrophic cardiomyopathy	12 (0.7%)	110 (1%)	38 (1.1%)	13 (0.7%)	
Valvular heart disease	59 (3.5%)	239 (2.1%)	72 (2%)	41 (2.1%)	
Others	345 (20.3%)	1,647 (14.6%)	504 (14.3%)	252 (13.2%)	
Total waitlist time (years)	0.54 ± 0.87 [0.2 (0.1, 0.6)]	0.63 ± 1 [0.3 (0.1, 0.8)]	0.59 ± 0.96 [0.25 (0.1, 0.7)]	0.6 ± 0.98 [0.2 (0.1, 0.7)]	0.0016
Previous cardiac surgery	145 (57.5%)	769 (57.5%)	304 (57.7%)	178 (56.9%)	0.9964
Preoperative life support					
Hospitalization	214 (12.6%)	1,646 (14.6%)	505 (14.3%)	298 (15.6%)	0.0302
IABP	101 (5.9%)	754 (6.7%)	212 (6%)	122 (6.4%)	0.4281
ECMO	0 (0%)	29 (0.3%)	11 (0.3%)	11 (0.6%)	0.0106
Blood type					
A	779 (45.8%)	4,863 (43%)	1,564 (44.4%)	857 (44.8%)	<.0001
B	248 (14.6%)	1,573 (13.9%)	453 (12.9%)	202 (10.6%)	
AB	104 (6.1%)	638 (5.6%)	149 (4.2%)	72 (3.8%)	
O	571 (33.5%)	4233 (37.4%)	1,359 (38.6%)	782 (40.9%)	
Creatinine (mg/dl)	1.31 ± 0.59 [1.2 (1, 1.5)]	1.32 ± 0.5 [1.22 (1, 1.5)]	1.33 ± 0.49 [1.29 (1.03, 1.5)]	1.33 ± 0.49 [1.24 (1, 1.5)]	0.7121
Total bilirubin (mg/dl)	1.16 ± 3.23 [0.7 (0.5, 1.1)]	1.1 ± 2.34 [0.8 (0.5, 1.1)]	1.17 ± 2.71 [0.8 (0.5, 1.2)]	1.22 ± 2.96 [0.8 (0.5, 1.2)]	0.2146

BMI = body mass index; ECMO = extracorporeal membrane oxygenation; IABP = intra-aortic baloon pump; ICU = intensive care unit.

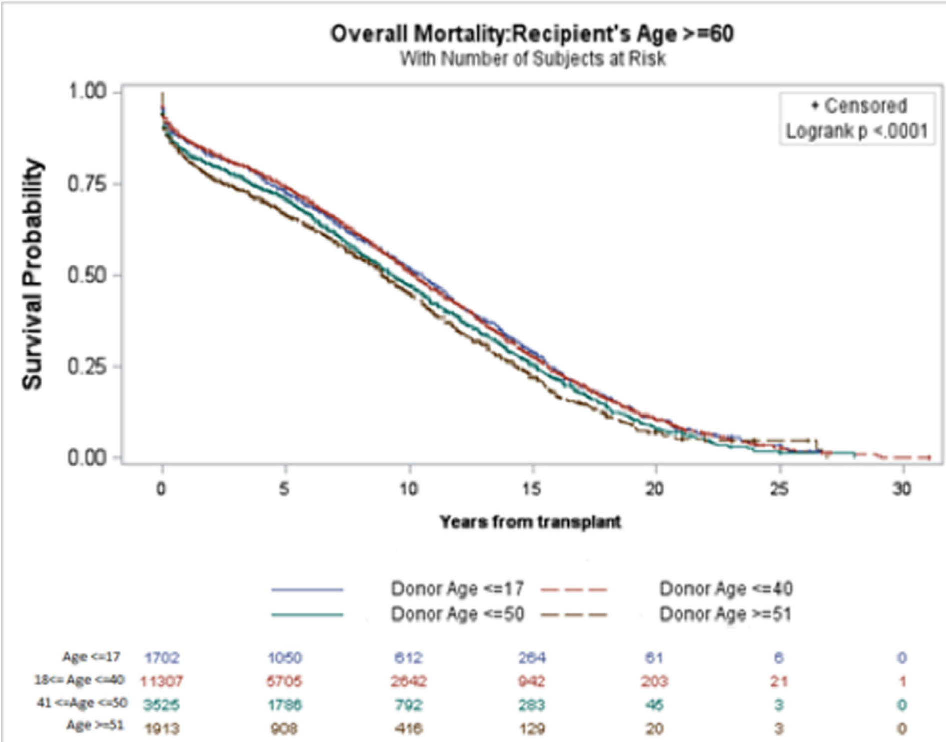

Figure 2. Overall survival Kaplan−Meier estimates stratified according to donor age group. Patients who received a graft from a donor age of < 17 (blue line) versus a donor age of 17 ≥, < 40 (red line) versus a donor age of 40 ≥, < 50 (green line) versus a donor age of ≥ 50 (brown line) ($p < 0.0001$, log−rank test).

Table 3
Outcomes stratified by donor age

Variable	< 17 (n= 1,702)	17 ≥, < 40 (n = 11,307)	40 ≥, < 50 (n = 3,525)	≥ 50 (n = 1,913)	pvalue
Acute rejection	51 (8.3%)	598 (8.4%)	146 (6.8%)	87 (7.7%)	0.1877
Primary graft failure	71 (6.3%)	553 (6.1%)	199 (7.2%)	98 (6.5%)	0.242
Cerebrovascular accident	38 (2.9%)	279 (2.9%)	92 (3%)	63 (3.7%)	0.281
Hemodialysis	87 (6.7%)	985 (10%)	357 (11.4%)	221 (13%)	<0.0001
Re-intubation	0 (0%)	4 (6.2%)	3 (12%)	2 (14.3%)	0.58
Permanent pacemaker	39 (3%)	311 (3.2%)	131 (4.2%)	94 (5.5%)	<0.0001
Death at 30 days post OHT	95 (5.6%)	582 (5.1%)	268 (7.6%)	154 (8.1%)	<.0001
Death at 1year post OHT	217 (12.7%)	1,401 (12.4%)	566 (16.1%)	341 (17.8%)	<.0001
Death at 3 years post OHT	316 (18.6%)	2,034 (18%)	751 (21.3%)	474 (24.8%)	<.0001
Death at 5 years post OHT	431 (25.3%)	2,543 (22.5%)	926 (26.3%)	574 (30%)	<.0001
Death	1,104 (64.9%)	5,508 (48.7%)	1,868 (53%)	1,061 (55.5%)	<.0001

OHT = orthotopic heart transplant.

decreased 13%, 26%, and 28% respectively. On average, an increase in donor age by 1 year increased the 5-year risk of mortality by 2.5 %; an increase in total waitlist time by 1 year increased the 5-year risk of mortality by 5.0 %. The 5-year risk of mortality for recipients who required ECMO support before transplant was nearly 3 times that of those who did not require ECMO, whereas preoperative inotrope usage decreased the 5-year risk of mortality by 13%. This finding may reflect the typical phenomenon prevalent in the previous allocation system that inotrope inotropes were routinely used to give more priority to the recipient on the waitlist, regardless the recipient's sickness.

Discussion

This is a comprehensive study to investigate the impact of donor age on the outcome in elder heart transplant recipients (age; ≥ 60) using the UNOS database. We stratified the cohort by disjoint categories of donor age: age of < 17; age of 17 ≥, < 40; age of 40 ≥, < 50; and age of ≥ 50. The most important finding of this study is that patients receiving hearts from donor age of ≥ 50 showed slight inferior survival likelihood, but at least almost equivalent median survival.

Historically, many treatment options have been developed for patients with end-stage heart failure, in which OHT remains the gold standard.[2] However, approximately

Table 4
Survival effects of donor age in cox models

Parameter	Hazard ratio	95% CI lower limit	95% CI upper limit	p-value
Recipient's age - per 1 year increase	1.025	1.015	1.035	<.0001
Recipient's BMI - per 1 unit increase	1.02	1.013	1.028	<.0001
Total waitlist time - per 1 year increase	1.048	1.018	1.079	0.0016
Transplant year - per 1 year later	0.971	0.967	0.975	<.0001
Donor's age category				
Advanced-age donor	ref			
Very young donor	0.716	0.63	0.814	<.0001
Young donor	0.74	0.674	0.812	<.0001
Middle-age donor	0.871	0.784	0.967	0.0095
Gender match				
Male donor to Male recipient	ref			
Female donor to Female recipient	0.969	0.872	1.077	0.5583
Male donor to Female recipient	1.174	1.05	1.312	0.0048
Female donor to Male recipient	1.112	1.032	1.199	0.0056
Hospitalization at transplant				
Hospitalized in ICU	1.193	1.103	1.291	<.0001
Hospitalized	1.157	1.056	1.268	0.0018
Preoperative life support				
Inotropes usage	0.87	0.812	0.933	<.0001
IABP usage	1.198	1.06	1.354	0.0038
ECMO usage	3.149	2.084	4.757	<.0001

BMI = body mass index; ECMO = extracorporeal membrance oxygenation; IABP = intra-aortic balloon pump; ICU = intensive care unit.

10% of all candidates on the waiting list for solid-organ transplantation die each year without receiving an organ.[3] To surmount the organ shortage challenge, we have previously proposed alternative approaches to maximize organ allocation by utilizing marginally acceptable organs,[5,6] harvesting donor hearts from distant locations,[7] accepting longer cold ischemic times,[8] utilizing obese donor hearts,[9] and applying a domino heart transplantation as a uniquely efficacious surgical strategy.[10] Although the mean donor age for heart transplant has increased from 31 years old in 1992 to 35 years old in 2013,[11] only 3% of donor graft was from advanced-aged donor > 60 years. Therefore, 1 possible solution could be to maximize the use of advanced-aged donor graft.

Generally, the perception is that heart grafts from advanced-aged donors are of inferior quality, as compared with younger donors. The impact of donor age on the quality of heart grafts has been studied previously, however, the reported results are conflicting. The majority of large multicenter retrospective studies have found an inverse relation between increased donor age and recipient survival.[12] The International Society of Heart and Lung Transplantation report identified donor age as a predictor of early graft failure in 2015, indicating the average donor age was 42.0 years old in the cohort of early graft failure.[11] There is another study showing that increased donor age of >40 affect mortality and transplant-related cardiac allograft vasculopathy.[13] In contrast, there was a study indicating comparable 30-day and actuarial survival with old donors (age ≥ 50), as compared with younger donors (age < 40).[14] Here, our data demonstrated that survival likelihood was impacted by the donor's age group, which is consistent with several large multicenter retrospective studies,[11−13] however, importantly, this study revealed that the median survival appeared to be equivalent regardless of donor age group especially in the recipient age of ≥ 60, which was not found in previous reports, including previous UNOS study.[13] This finding is supported by the previous study indicating donor-recipient age difference did not negatively impact posttransplant outcome.[15]

In our analysis, we showed that the cohort of donor age of ≥ 50 had a highest percentage of hypertension and diabetes mellitus in a step-wise manner from a younger to older donor group. This is consistent with the typical medical conditions of the general older population. In addition, the cohort of donor age of 40 ≥, < 50 had a highest incidence of cigarette and alcohol usages. This is likely to be translated into the typical social habits in the general population. Moreover, the donor age of < 17 group showed a lowest BMI, which can be explained by the prevalence of obesity in general population.[16] Our data also identified that the cohort receiving hears from donor age of ≥ 50 showed a higher incidence of hospitalization and pre-transplant ECMO usage before transplant, suggesting that recipients receiving grafts from donor age of ≥ 50 might be relatively sicker than those receiving younger donor grafts. Together with higher percentage of blood type group O recipients in the donor age of ≥ 50 group, this can likely be explained by the eagerness and urgency for organ acceptance due to the severity of clinical status in this recipient population, despite potential concerns for donor age of ≥ 50.

One may have a concern about acute rejection episode, since previous studies with patients and animal models of kidney transplantation reported a stronger immune response in recipients with older donors, thereby inducing a higher incidence of acute rejection episode.[17] There is also a general assumption that older donor hearts will elicit a more marked immune response in young recipients.[18] However, our data have shown a similar incidence of acute rejection episode, regardless the donor age group.

Lastly, the concept of an alternative list for elder patients, and the potential usage of marginal donor grafts for the alternative list has been raised in the last few years ("aged-for-aged" concept). Looking forward, the definition of elder patients as well as appropriate age matching may be of interest for further study. It may also be greatly beneficial to examine geographic patterns by evaluating the rates of donor heart usage and the graft outcomes in different UNOS regions.

This study has limitations consistent with retrospective analyses and the use of a national multicenter database. Specifically, the UNOS database has some considerable uncollected data for the important factors during some specific time periods.[19] Nevertheless, the UNOS and Organ Procurement and Transplantation Network registry has provided a large sample size to assess the impact of the donor age on outcomes after heart transplantation in the current era. Next, the potential selection bias may be related to beliefs among physicians that advanced age is a prohibitive risk factor for OHT. Only donors whose hearts were accepted for transplantation were included. Selecting a suitable donor is a complicated process. Clinicians need to consider multiple factors, weighing recipient urgency against donor characteristics, allograft ischemic time, recipient sensitization, and donor or recipient size mismatch. For example, coronary angiography is routinely considered in donors older than 45 years of age. In addition, more information is needed to identify the impact of such practice. Moreover, there are donor selector nuances which enable to make a transplant process successful however, unfortunately these are rarely recorded. As this study addressed only mortality, further data are needed on the impact of the donor age on the morbidity of recipients.

In conclusion, in the cohort of heart transplant recipient (age of ≥ 60), the equivalent median survival reported at follow-up is encouraging with respect to the utilization of hearts from donor age of ≥ 60.

Disclosures

The authors declare that they have no known competing financial interests or personal relations that could have appeared to influence the work reported in this report.

Author Contributions

Yasuhiro Shudo, MD, PhD- Conceptualization, Writing - Original Draft, Project administration. Sabina PW Guenther, MD- Writing - Review & Editing. Bharathi Lingala, PhD- Methodology, Data Curation, Formal analysis. Hao He, PhD- Methodology, Formal analysis. William Hiesinger, MD- Validation. John W MacArthur, MD- Validation, Resources. Maria E Currie, MD, PhD - Validation. Anson M Lee, MD- Validation. Jack H Boyd, MD- Validation. Y. Joseph Woo, MD- Supervision.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2020.06.036.

1. Hunt SA, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, Jessup M, Konstam MA, Mancini DM, Michl K, Oates JA, Rahko PS, Silver MA, Stevenson LW, Yancy CW, Antman EM, Jr Smith SC, Adams CD, Anderson JL, Faxon DP, Fuster V, Halperin JL, Hiratzka LF, Jacobs AK, Nishimura R, Ornato JP, Page RL, Riegel B. American College of Cardiology. American Heart Association Task Force on Practice Guidelines. American College of Chest Physicians. International Society for Heart and Lung Transplantation. Heart Rhythm Society. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). *Circulation* 2005;112(12):e154–e235.
2. Joyce DL, Li Z, Edwards LB, Kobashigawa JA, Daly RC. Predicting 1-year cardiac transplantation survival using a donor-recipient risk-assessment tool. *J Thorac Cardiovasc Surg* 2018;155(4):1580–1590.
3. U.S. Department of Health and Human Services. Organ procurement and transplantation network. Available at: https://optn.transplant.hrsa.gov. Accessed August 1, 2017.
4. Khush KK, Menza R, Nguyen J, Zaroff JG, Goldstein BA. Donor predictors of allograft use and recipient outcomes after heart transplantation. *Circ Heart Fail* 2013;6:300–309.
5. Kaczorowski DJ, Woo YJ. Aortic valve repair by sinotubular junctional remodeling to eliminate aortic regurgitation in donor cardiac allograft. *J Thorac Cardiovasc Surg* 2012;144:722–724.
6. Okamura H Woo YJ. Ex vivo allograft mitral valve leaflet repair prior to orthotopic heart trasnaplantation. *J Card Surg* 2014;29(3):424–426.
7. Currie ME, Shudo Y, Woo YJ. Successful outcome following orthotopic heart transplantation with a donor half way across the country. *Transplant Proc* 2018;50(10):4062–4063.
8. Shudo Y, Wang H, Woo YJ. A modified technique for orthotopic heart transplantation to minimize warm ischaemic time. *Eur J Cardiothorac Surg* 2018;53:1089–1090.
9. Shudo Y, Cohen JE, Lingala B, He H, Woo YJ. Impact of donor obesity on outcomes after orthotopic heart transplantation. *J Am Heart Assoc* 2018;7(23):e010253. 4.
10. Shudo Y, Ma M, Boyd JH, Woo YJ. Current status of domino heart transplantation. *J Card Surg* 2017;32(3):229–232.
11. Khush KK, Cherikh WS, Chambers DC, Harhay MO, Jr Hayes D, Hsich E, Meiser B, Potena L, Robinson A, Rossano JW, Sadavarte A, Singh TP, Zuckermann A, Stehlik J, International Society for Heart and Lung Transplantation. The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: Thirty-sixth adult heart transplantation report − 2019; focus theme: donor and recipient size match. *J Heart Lung Transplant* 2019;38(10):1056–1066.
12. Jawitz OK, Raman V, Klapper J, Hartwig M, Patel CB, Milano C. Donor and recipient age matching in heart transplantation: analysis of the UNOS Registry. *Transpl Int* 2019;32(11):1194–1202.
13. Sorabella R, Guglielmetti L, Kantor A, Castillero E, Takayama H, Christian Schulze P, Mancini D, Naka Y, George I. Cardiac donor risk factors predictive of short-term heart transplant recipient mortality: an analysis of the United Network For Organ Sharing Database. *Transplant proc* 2015;47:2944–2951.
14. Prieto D, Correia P, Baptista M, Antunes MJ. Outcomes after heart transplantation from older donor age: expanding the donor pool. *Eur J Cardiothorac Surg* 2015;47:672–678.
15. Ram E, Lavee J, Kogan A, Kassif Y, Elian D, Freimark D, Peled Y. Does donor-recipient age difference matter in outcome of heart transplantation? *Clin Transplant* 2019;33(7):e13593.
16. Milaniak I, Wierzbicki K, Sadowski J. Post−transplantation body mass index in heart transplant recipients: determinants and consequences. *Transplant Proc* 2014;46:2844–2847.
17. Dayoub JC, Cortese F, Anzic A, Grum T, de Magalhaes JP. The effects of donor age on organ transplants: a review and implications for aging research. *Exp Gerontol* 2018;110:230–240.
18. Young A, Kim SJ, Speechley MR, Huang A, Knoll GA, Ramesh Prasad GV, Treleaven D, Diamant M, Garg AX. Donor nephrectomy outcomes research (DONOR) Network. Accepting kidneys from old living donors: impact on transplant recipient outcomes. *Am J Transplant* 2011;11:743–750.
19. Shudo Y, Wang H, Lingala B, He H, Kim FY, Hiesinger W, Lee AM, Boyd JH, Currie M, Woo YJ. Evaluation of risk factors for heart-lung transplant recipient outcome: an analysis of the United Network for Organ Sharing Database. *Circulation* 2019;140(15):1261–1272.