Do age and functional dependence affect outcomes of simultaneous heart–kidney transplantation?

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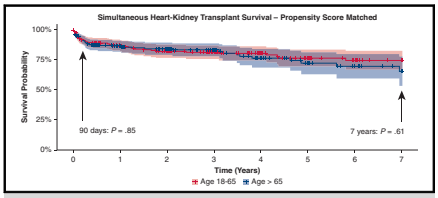
ABSTRACT

Objective: This study assessed characteristics and outcomes of younger (18-65) versus older (>65) recipients of simultaneous heart–kidney (SHK) transplantation with varying functional dependence.

Methods: This study retrospectively analyzed 1398 patients from the United Network for Organ Sharing database who received SHK between 2010 and 2021. Patients who were <18 year old, underwent transplant of additional organs simultaneously, or had previous heart transplant were excluded. The primary end point was all-cause mortality, and secondary end points included adverse events and cause of death. Outcomes were also evaluated by propensity score–matched comparison.

Results: The number of annual SHK transplantation in the United States has significantly increased among both age groups over the past 2 decades ($P < .0001$). After propensity score matching of recipients aged 18 to 65 years (n = 1162) versus age >65 years (n = 236), baseline characteristics were similar and well-balanced between the 2 cohorts. Between matched cohorts, older recipients did not have increased posttransplant mortality compared with younger recipients (90-day survival, $P = .85$; 7-year survival, $P = .61$). Multivariable Cox regression analysis found that age (hazard ratio [HR], 1.039 [0.975-1.106], $P = .2415$) and pretransplant functional status with interaction term for age (some assistance, HR, 0.965 [0.902-1.033], $P = .3079$; total assistance, HR, 0.976 [0.914-1.041], $P = .4610$) were not significant risk factors for 7-year post-SHK transplantation mortality.

Conclusions: Older and more functionally dependent recipients in this study did not have increased post-SHK transplantation mortality. These findings have important implications for organ allocation among elderly patients, as they support the need for thorough assessment of SHK candidates in terms of comorbidities, rather than exclusion solely based on age and functional dependence. (JTCVS Open 2023;15:262-89)



Survival of propensity score–matched heart–kidney transplant recipients age >65 versus 18-65.

CENTRAL MESSAGE

There was insufficient evidence to declare a difference in either short- or long-term survival of simultaneous heart–kidney transplant recipients aged 18 to 65 versus >65, even after propensity matching.

PERSPECTIVE

Recent studies have demonstrated comparable outcomes in older patients after isolated heart transplant, but the effect of age and frailty in simultaneous heart–kidney transplant remains unclear. The results of our propensity-matched UNOS study suggest that noninferior outcomes can be achieved in carefully selected older, more functionally dependent recipients of simultaneous heart–kidney transplant.

See Discussion on page 290.

Kidney failure often develops concurrently with heart failure due to interdependence between the cardiac and renal systems.[1] Although the risk of heart or kidney failure alone increases significantly with age, the risk of developing kidney failure in patients with pre-existing heart failure is even greater in older patients.[2] However, older age has traditionally been viewed as a contraindication to transplantation due to survival and donor availability concerns.[3]

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Abbreviations and Acronyms

CI = confidence interval
eGFR = estimated glomerular filtration rate
HR = hazard ratio
KPS = Karnofsky Performance Score
SHK = simultaneous heart–kidney
UNOS = United Network for Organ Sharing

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Recently, several large-scale studies have demonstrated noninferior outcomes for isolated heart transplantation in carefully selected older recipients, leading several transplant centers to broaden their transplant criteria to include recipients older than 65 years old.[4-6] However, there remain very limited large-scale studies and an overall lack of consensus regarding simultaneous heart–kidney transplantation (SHK) candidacy in older and frailer patient populations, despite the nearly 5-fold increase in SHK transplantations over the last 5 years.[7,8] Many argue that allocating 2 organs to 1 patient may not be justified if these patients have worse posttransplant survival compared with younger, less-frail recipients, but SHK transplant outcomes have not yet been compared in terms of both age and frailty.[9] Moreover, the number of SHK candidates aged 65 years or older will likely increase over time, as more elderly patients have been placed on the heart and kidney transplant waiting lists over the past decade and SHK transplant has become more frequently performed in both young and elderly patients.[9,10]

As there is a huge disparity in number of patients in need of hearts and kidneys compared with organ availability, it is essential to identify which patients would make suitable candidates for SHK and what characteristics would increase the risk of mortality after transplantation. In this study, we investigated the impact of age and functional dependence on patient outcomes in SHK as well as other risk factors contributing to posttransplant mortality.

METHODS

A retrospective review of deidentified data from the United Network for Organ Sharing (UNOS) thoracic registry identified 1659 total patients who received simultaneous heart kidney transplantation between January 1, 2010, and March 1, 2021 (Figure 1). The institutional review board of Columbia University approved the study protocol (approval number AAAU2877; January 6, 2023) and publication of data. Patient written consent for the publication of the study data was waived by institutional review board, given research of existing data/records. Of these patients, 1398 were adults (≥18 year old) who did not have additional simultaneous liver transplant or history of previous heart transplant. These adult recipients were then stratified by age: younger, aged 18 to 65 years (n = 1162, 83.1%), and older, aged > 65 (n = 236, 16.9%). Distribution of ages in each cohort is displayed in Figure E1.

Several analyses in this study used the functional status at transplant variable in the UNOS dataset, which reported Karnofsky Performance Score (KPS).[11] In brief, KPS increases by 10 points from 0 to 100 as patient independence improves and symptoms resolve. Functional dependence in each patient was categorized based on a KPS of 80 to 100 ("Good," no assistance), 50 to 70 ("Moderate," some assistance), and 10 to 40 ("Poor," total assistance). Among the 2 age groups combined, there was missing data for 81 patients (5.8%) for KPS score at transplant.

Transplant center identifiers were obtained from the UNOS dataset and quantified as a continuous variable based on their respective total number of SHK transplant surgeries performed during the study period.

Serum creatinine level measured immediately before transplant was provided in the UNOS dataset and used in the 2021 Chronic Kidney Disease Epidemiology Collaboration CKD-EPI equation below to calculate patients' pretransplant estimated glomerular filtration rate (eGFR).[12] The equation uses 3 variables: sex, age, and serum, creatinine.

$$\mathrm{eGFR_{Cr}} = 142 \times \min\left(S_{Cr}/\kappa, 1\right)^{\alpha} \times \max\left(S_{Cr}/\kappa, 1\right)^{-1.200} \times 0.9938^{\mathrm{Age}} \times 1.012\ [\text{if female}]$$

where S_{Cr} is serum creatinine in mg/dL, κ is 0.7 for female and 0.9 for male patients, α is –0.241 for female and –0.302 for male patients, "min" indicates the minimum of S_{Cr}/κ or 1, and "max" indicates the maximum of S_{Cr}/κ or 1.

Clinical characteristics and outcomes were compared between groups. The primary outcome of interest was all-cause mortality. Secondary outcomes of interest included adverse posttransplant events and causes of mortality.

Statistical Methods

The "tableone," "survival," "survminer," "ggplot2," "ggsurvplot," "ggsurvfit," "gtsummary," "condSURV," "party," "dplyr," "MatchIt," "lubridate," "tidyverse," and "tidycmprsk" packages of R statistical software (version 4.2.1; R Foundation) were used for all statistical analyses and illustrations. Trend analysis *P* value was obtained from a generalized regression using Wald χ^2 test. Continuous variables are expressed as median [interquartile range]. Categoric variables are presented as proportions with absolute numbers. Differences between groups were measured using the χ^2 test for categorical variables and Mann–Whitney *U* test for continuous variables. Kaplan–Meier curves were created to compare survival between subgroups and assessed differences in survival using log rank tests. Information on follow-up time and number of subjects missing follow-up data is displayed in Table E1. Propensity score matching was used to balance variables between younger and older cohorts: the pretransplant variables indicated in Table 1 were entered into a logistic regression model for which the dependent variable was age group. Percentages of patients with missing values for each variable are listed in Table E2. All patients who did not have missing values on the matching variables were subjected to propensity score matching using the sequential nearest neighbor, caliper-constrained matching technique. A greedy matching algorithm matched the older cohort (n = 209) to the younger cohort (n = 209). The caliper used in the matching algorithm equals to 0.2. Standardized mean difference <0.2 was considered acceptable for propensity score matching.[13] Characteristics of matched versus unmatched subjects in each age group are displayed in Tables E3 and E4, and distribution of covariate balance in this propensity matching model is shown in Figure E2.

Clinical parameters before transplantation were analyzed to determine contributing factors for posttransplant mortality using univariable Cox models for 7-year mortality and univariable logistic regression for posttransplant dialysis. For multivariable analyses, variables with a *P*-value of 0.10 or less on univariable analysis (Table E5) and other variables that were highly clinically relevant were included in a final multivariable

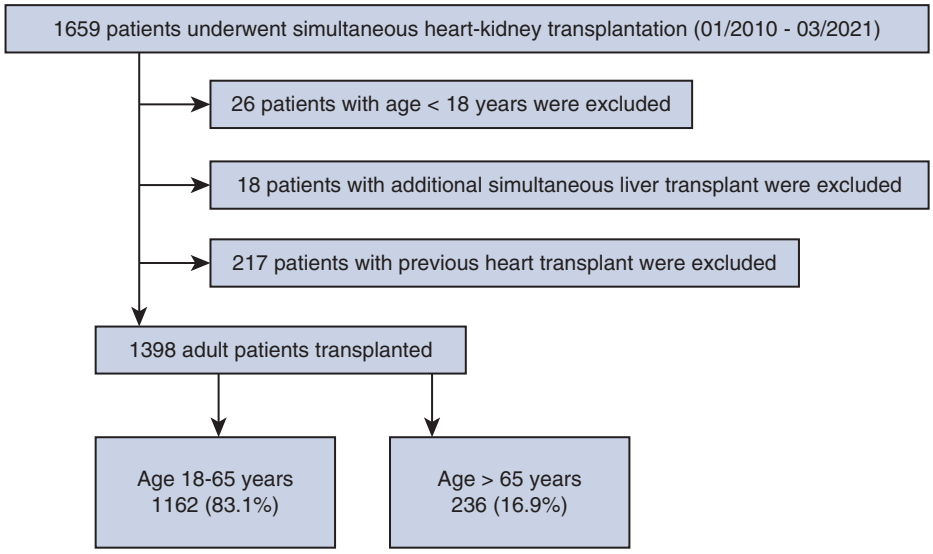


FIGURE 1. Cohort derivation.

model. The proportional hazard assumption evaluated by the Schoenfeld residuals plot and not violated. No collinearity was found given all variance inflation factors <2. Interaction terms for age with functional status at transplant were used in the multivariable Cox model to examine the effect of age in each KPS category. A restricted cubic spline model with 4 knots was used to examine nonlinear correlations between age and long-term mortality. Results are presented as hazard ratio (HR) or odds ratio with corresponding 95% confidence interval (CI).

Within a 6-year follow-up time of our unadjusted study cohort, using the UNOS thoracic follow-up dataset, we constructed a nonparametric cumulative incidence curve for patients on long-term dialysis accounting for recurrent events of long-term dialysis and the competing risk of death. Another similar cumulative incidence curve was constructed for the unadjusted cohort stratified by age group (18-65 years vs >65 years). The cumulative incidence function and its 95% CI was calculated for each year of follow-up time. Fine–Gray regression was used to determine whether differences in cumulative incidence of long-term dialysis between age groups were due to the competing risk of death.[14]

RESULTS

Figure 2 shows trends in annual numbers of SHK transplants performed over the past 3 decades, stratified by age group. Number of SHK transplants performed each year has significantly increased in both age groups during this time period ($P < .0001$). In the unadjusted analyses, there were marked differences in patient characteristics between younger (age 18-65, n = 1162) and older (age > 65, n = 236) cohorts (Table E6). Older SHK transplant recipients were more likely to be male, White, receive surgery at greater-volume transplant centers, have implantable defibrillator or intra-aortic balloon pump at time of listing, and have history of cigarette use, malignancy, or previous nontransplant cardiac surgery. They also more often received heart and kidney from an older donor with a history of heavy alcohol use. Younger SHK transplant recipients were more likely to be on inotropes or any type of life support at time of listing, wait longer before receiving donor organs, receive dialysis either in the past or between listing and transplant, have greater creatinine and lower eGFR levels, or be on a ventilator between listing and transplant. After propensity score-matching, these characteristics were no longer significantly different between the 2 age groups (Table 1).

In unadjusted analyses, older patients stratified by functional status at transplant did not have decreased 90-day ($P = .49$) or long-term ($P = .68$) posttransplant survival compared with younger patients stratified by functional status (Figure 3, *A*). Pairwise comparisons are shown in Figure E3, and additional survival analysis comparing age 18 to 65 versus 66 to 69 versus ≥70 is displayed in Figure E4. Analysis of propensity score–matched younger versus older cohorts did not demonstrate differences in 90-day (91.0% vs 90.5%, $P = .85$) or long-term (75.0% vs 65.9%, $P = .61$) posttransplant survival either (Figure 3, *B*).

Posttransplant adverse events in propensity score–matched cohorts are summarized in Table 2, with corresponding unadjusted analysis displayed in Table E7. After propensity score matching, older SHK transplant recipients had similar length of hospital stay (21 vs 19 days, $P = .226$) and similar rates of cardiac graft failure (20.0% vs 19.6%, $P = 1.000$), acute heart rejection requiring treatment (6.8% vs 5.3%, $P = .644$), stroke (3.4% vs 3.8%, $P = 1.000$), pacemaker (1.5% vs 2.4%, $P = .747$), and dialysis (26.8% vs 29.2%, $P = .671$) immediately after transplant compared with younger SHK transplant recipients. Further comparison of pretransplant dialysis versus acute posttransplant dialysis in younger and older cohorts are compared in Table E8, along with pretransplant characteristics that

TABLE 1. Comparison of baseline characteristics among propensity score–matched SHK transplant recipients aged 18-65 y (n = 209) and aged >65 y (n = 209)

Characteristic	Age 18-65 y (n = 209)	Age >65 y (n = 209)	*P* value	SMD
Propensity score–matched characteristics				
Male sex, n (%)	179 (85.6)	178 (85.2)	1.000	0.0136
BMI			.828	
Underweight	1 (0.5)	1 (0.5)		0.0000
Normal	62 (29.7)	70 (33.5)		0.0812
Overweight	102 (48.8)	97 (46.4)		0.0479
Obese	44 (21.1)	41 (19.6)		0.0366
IABP at listing, n (%)	24 (11.5)	28 (13.4)	.657	0.0570
Inotropes at listing, n (%)	61 (29.2)	62 (29.7)	1.000	0.0105
Diabetes, n (%)	103 (49.3)	96 (45.9)	.577	0.0672
Implantable defibrillator at listing, n (%)	169 (80.9)	168 (80.4)	1.000	0.0121
Previous cardiac surgery at listing, n (%)	98 (46.9)	94 (45.0)	.768	0.0384
Life support at listing, n (%)	114 (54.5)	119 (56.9)	.694	0.0482
Ethnicity, n (%)			.587	
White	144 (68.9)	134 (64.1)		0.1005
Black	45 (21.5)	54 (25.8)		0.0994
Hispanic	14 (6.7)	12 (5.7)		0.0418
Other	6 (2.9)	9 (4.3)		0.0718
Functional status at transplant, n (%)			.477	
Good	16 (7.7)	10 (4.8)		0.1366
Moderate	54 (25.8)	55 (26.3)		0.0107
Poor	139 (66.5)	144 (68.9)		0.0513
ECMO at transplant, n (%)	3 (1.4)	4 (1.9)	1.000	0.0355
Dialysis between listing and transplant, n (%)	65 (31.1)	57 (27.3)	.451	0.0868
Infection requiring IV drug therapy, n (%)	27 (12.9)	27 (12.9)	1.000	0.0000
Any previous non-heart transplant, n (%)	3 (1.4)	2 (1.0)	1.000	0.0500
Total bilirubin	0.70 [0.50, 1.10]	0.80 [0.50, 1.20]	.176	0.0769
Transplant center volume	30.00 [17.00, 48.00]	25.00 [17.00, 48.00]	.695	0.0165
Donor age	35.00 [26.00, 44.00]	33.00 [25.00, 44.00]	.988	0.0078
Ischemic time	3.20 [2.50, 3.70]	3.10 [2.40, 3.60]	.604	0.0210
eGFR at transplant	26.99 [16.57, 40.74]	30.84 [21.35, 40.75]	.068	0.0545
Unmatched characteristics in propensity-matched cohorts				
Cigarette use, n (%)	87 (41.6)	93 (44.5)	.621	–
Cerebrovascular disease, n (%)	18 (8.7)	20 (9.6)	.865	–
Any history of malignancy, n (%)	18 (8.6)	29 (13.9)	.122	–
Functional status at listing, n (%)			.492	–
Good	13 (6.0)	20 (9.3)		–
Moderate	68 (31.6)	69 (32.1)		–
Poor	127 (59.1)	122 (56.7)		–
Medical condition, n (%)			.716	–
Hospitalized (not in ICU)	39 (18.7)	41 (19.6)		–
In ICU	91 (43.5)	97 (46.4)		–
Not hospitalized	79 (37.8)	71 (34.0)		–
Any history of dialysis, n (%)	80 (38.3)	63 (30.1)	.099	–
IABP at transplant, n (%)	28 (13.4)	40 (19.1)	.145	–
Inotropes at transplant, n (%)	93 (44.5)	95 (45.5)	.922	–
Ventricular assist device at transplant, n (%)	66 (31.6)	62 (29.7)	.750	–
Life support at transplant, n (%)	168 (80.4)	162 (77.5)	.549	–
Days on waitlist	74.00 [25.00, 248.00]	55.00 [16.00, 181.00]	.077	–
Cardiac output at transplant	4.60 [3.80, 5.92]	4.66 [3.84, 5.90]	.826	–
Donor–recipient sex mismatch, n (%)	56 (26.8)	49 (23.4)	.499	–
Donor diabetes, n (%)	7 (3.4)	5 (2.4)	.763	–
Donor history of heavy alcohol use, n (%)	48 (23.4)	58 (28.4)	.296	–

(Continued)

TABLE 1. Continued

Characteristic	Age 18-65 y (n = 209)	Age >65 y (n = 209)	*P* value	SMD
Donor history of cigarette use, n (%)	36 (17.5)	25 (12.3)	.178	–
Donor history of hypertension, n (%)	32 (15.5)	36 (17.3)	.707	–
Donor clinical infection, n (%)	166 (79.4)	158 (77.1)	.645	–
Donor BMI	27.18 [23.71, 30.99]	26.51 [23.50, 30.24]	.327	–
Donor creatinine	0.90 [0.70, 1.20]	0.90 [0.71, 1.16]	.983	–
Donor LV ejection fraction	60.00 [58.00, 65.00]	60.00 [60.00, 65.00]	.929	–

Values are n (%) or median [interquartile range]. *SMD*, Standardized mean difference; *BMI*, body mass index; *IABP*, intra-aortic balloon pump; *ECMO*, extracorporeal membrane oxygenation; *IV*, intraventricular; *eGFR*, estimated glomerular filtration rate; *ICU*, intensive care unit; *LV*, left ventricular. *Statistically significant value ($P < .05$).

increased risk of being placed on dialysis immediately after transplant in Table E9. Regarding SHK transplant recipients' need for long-term dialysis within 6 years of follow-up, cumulative incidence curve of recipients on long-term dialysis with death as a competing variable showed significantly greater incidence ($P = .02$) of long-term dialysis among those aged 18 to 65 years (10%; 95% CI, 8.3%-12%) compared with those aged >65 years (5.6%; 95% CI, 2.6%-10%) in the unadjusted study population (Figure E5). Among SHK recipients who died after transplant, there were no differences in cause of death between younger and older patients at both 90-day and most recent follow-up (Table E10).

Risk factors for 7-year mortality post-SHK transplantation were identified in multivariable Cox regression analysis (Table 3). Of note, there was no difference in survival attributed to age as a continuous variable (HR, 1.039; 95% CI, 0.975-1.106; $P = .2415$), functional status requiring "some assistance" (HR 0.965; 95% CI, 0.902-1.033; $P = .3079$) with interaction term for age, or functional status requiring "total assistance" (HR, 0.976; 95% CI, 0.914-1.041; $P = .4610$) with interaction term for age. Previous malignancy, extracorporeal membrane oxygenationat transplant, transplant era postallocation policy change, lower transplant center volume, total bilirubin at transplant, and donor age were found to be significant risk factors for 7-year post-SHK transplant mortality. Restricted cubic spline regression model also showed a nonlinear V-shaped relationship between age and HR of long-term mortality, with age 62 associated with highest risk of post-SHK transplant mortality (Figure E6).

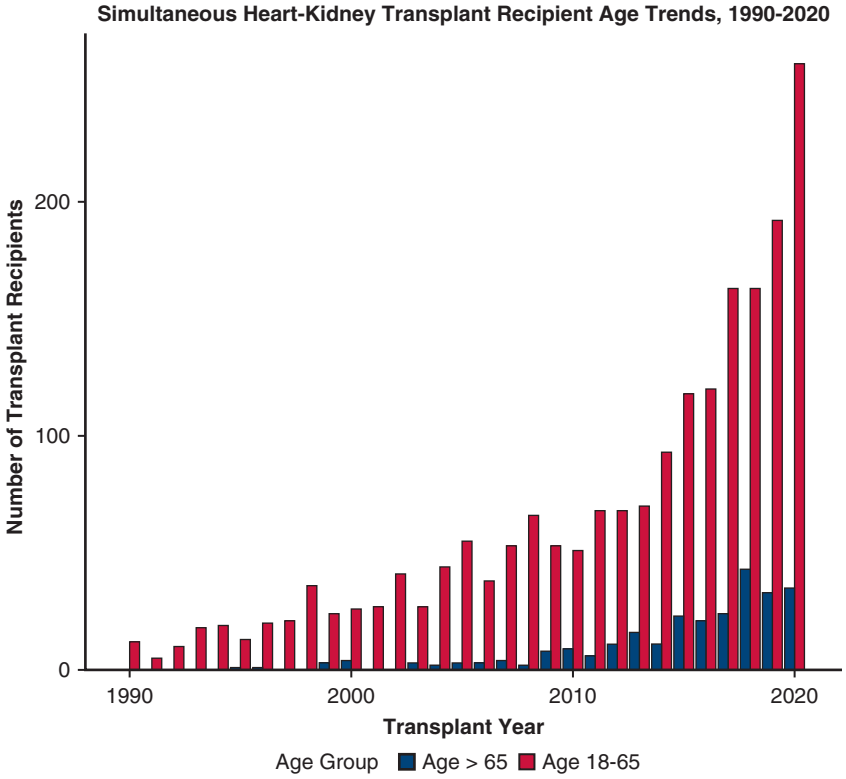
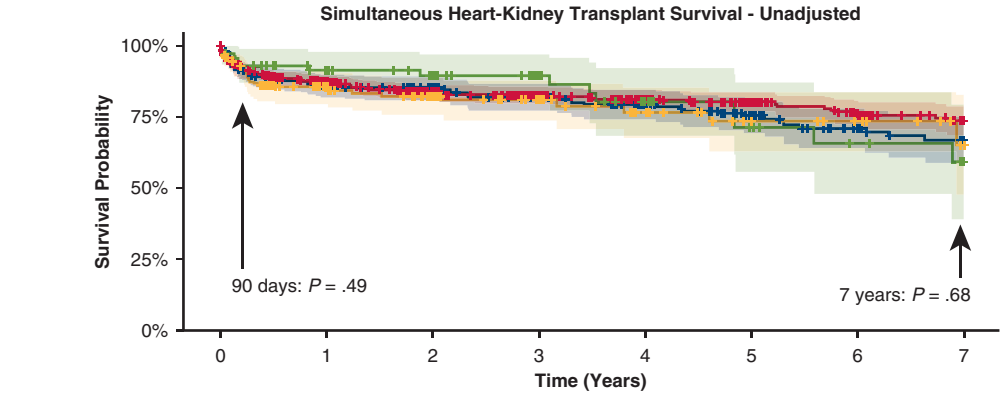


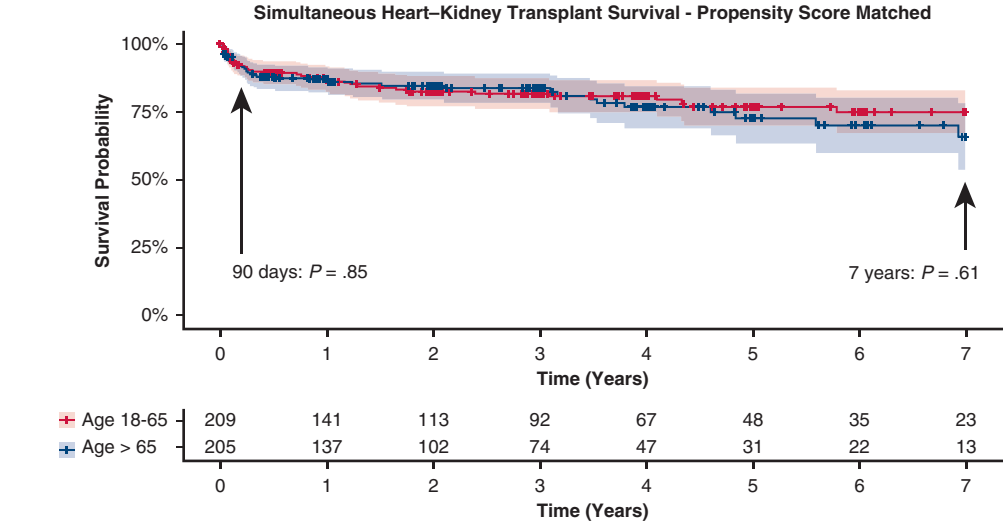
FIGURE 2. Trends in annual simultaneous heart–kidney transplantation, 1990 to 2020. Wald χ^2 test, $P < .0001$.



Unadjusted, KPS at Transplant		
Group	90-Day Survival	7-Year Survival
Age 18-65 (Good/Moderate)	90.8% [87.5, 94.1]	66.9% [58.9, 74.9]
Age 18-65 (Poor)	91.8% [89.8, 93.8]	73.8% [68.6, 78.9]
Age > 65 (Good/Moderate)	93.0% [87.1, 98.9]	59.3% [39.1, 79.5]
Age > 65 (Poor)	89.7% [84.8, 94.6]	65.2% [47.5, 82.9]

Values are probability [95% CI]

A



Propensity Score Matched		
Group	90-Day Survival	7-Year Survival
Age 18-65	91.0% [87.0, 95.0]	75.0% [67.1, 82.8]
Age > 65	90.5% [86.4, 94.6]	65.9% [53.5, 78.3]

Values are probability [95% CI]

B

FIGURE 3. Kaplan-Meier survival analysis with 95% confidence interval and *P*-values. A, Survival of unadjusted recipient cohorts age >65 years with KPS 50 to 100 (*green*) versus age >65 years with KPS 10 to 40 (*yellow*) versus age 18 to 65 years with KPS 50 to 100 (*blue*) versus age 18 to 65 years with KPS 10 to 40 (*red*) at 90 days' and 7 years' posttransplant. B, Survival of propensity score–matched patients age >65 years (*green*) versus age 18 to 65 years (*red*) at 90 days' and 7 years' posttransplant. *G/M*, Good/moderate; *P*, poor; *KPS*, Karnofsky Performance Score; 95% *CI*, 95% confidence interval.

TABLE 2. Posttransplant adverse events in propensity score–matched subjects

Adverse events	Age 18-65 (n = 209)	Age > 65 (n = 209)	*P* value
Length of stay, d	19.00 [13.00, 30.00]	21.00 [14.00, 31.00]	.226
Cardiac graft failure	41 (19.6)	41 (20.0)	1.000
Acute heart rejection requiring treatment	11 (5.3)	14 (6.8)	.644
Stroke	8 (3.8)	7 (3.4)	1.000
Dialysis	61 (29.2)	55 (26.8)	.671
Pacemaker	5 (2.4)	3 (1.5)	.747

Values are n (%) or median [interquartile range].

TABLE 3. Multivariable Cox regression analyses of pretransplant characteristics on 7-y posttransplant mortality among entire SHK transplanted cohort

Variable	Hazard ratio (95% CI)	*P* value
Age	1.039 (0.975-1.106)	.2415
Male sex	0.738 (0.532-1.023)	.0681
Functional status		
Total assistance (KPS 10-40)	4.423 (0.090-216.175)	.4537
Some assistance (KPS 50-70)	8.952 (0.157-509.037)	.2877
No assistance (KPS 80-100)	Reference	N/A
Functional status with interaction term for age		
Total assistance (KPS 10-40)	0.976 (0.914-1.041)	.4610
Some assistance (KPS 50-70)	0.965 (0.902-1.033)	.3079
No assistance (KPS 80-100)	Reference	N/A
BMI		
Underweight	0.801 (0.318-2.018)	.6383
Normal	Reference	N/A
Overweight	1.002 (0.724-1.387)	.9905
Obese	1.244 (0.878-1.762)	.2202
Previouscardiac surgery at listing (nontransplant)	1.167 (0.896-1.52)	.2522
History of any non-heart transplant	1.854 (0.883-3.893)	.1030
Any previous malignancy	1.530 (1.024-2.287)	.0379*
Diabetes	1.242 (0.944-1.635)	.1212
Dialysis between listing and transplant	1.177 (0.893-1.553)	.2476
Cigarette use	1.07 (0.823-1.391)	.6132
ECMO at transplant	2.162 (1.077-4.339)	.0302*
After new allocation policy?	1.393 (1.009-1.923)	.0438*
Implantable defibrillator at listing	1.348 (0.964-1.885)	.0807
Infection requiring IV drug therapy at transplant	1.309 (0.918-1.867)	.1373
Transplant center volume	0.994 (0.989-0.999)	.0268*
eGFR at transplant	1.002 (0.996-1.008)	.4519
Ischemic time >4 h	1.190 (0.867-1.634)	.2826
Total days on waitlist	1.000 (0.999-1.000)	.2874
Total bilirubin at transplant	1.025 (1.005-1.044)	.0123*
Donor age	1.012 (1.000-1.024)	.0436*
Donor–recipient sex mismatch	1.024 (0.751-1.395)	.8816

CI, Confidence interval; *KPS*, Karnofsky Performance Score; *N/A*, not available; *BMI*, body mass index; *ECMO*, extracorporeal membrane oxygenation; *IV*, intravenous; *eGFR*, estimated glomerular filtration rate. *Statistically significant value ($P < .05$).

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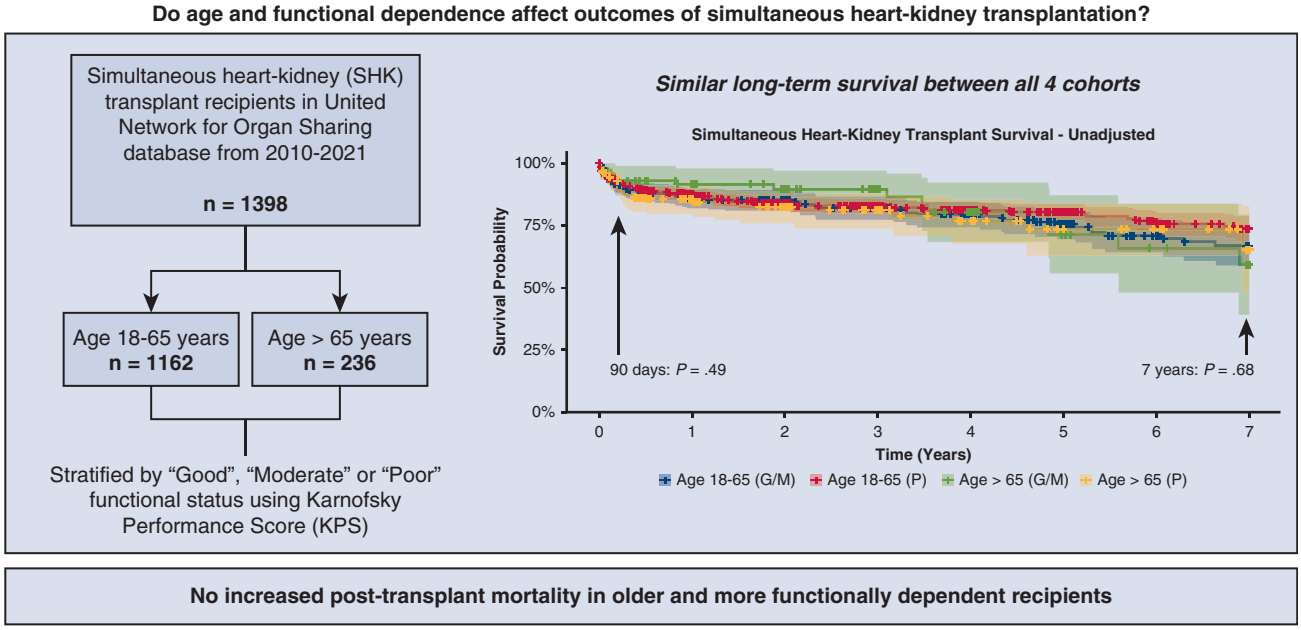

FIGURE 4. Do age and functional dependence affect outcomes of simultaneous heart–kidney (SHK) transplantation? *G/M*, Good/moderate; *P*, poor.

DISCUSSION

This study investigated outcomes after SHK transplant for recipients characterized by both age and functional dependence. The results in this study suggest that similar post-SHK transplant outcomes are achievable in patients aged >65 years relative to patients aged 18 to 65 years (Figure 4), consistent with a previous study that performed a similar analysis of the UNOS dataset with patients from a slightly earlier era.[15] Our study also newly suggests that at least in our cohort, functional dependence does not have a major effect on SHK transplant outcomes. However, it should be noted that long-term survival comparisons involving propensity-matched cohorts showed a numerical difference in survival despite the nonsignificant *P* value, suggesting that these findings may be vulnerable to sample size limitations and should be confirmed with future studies as more older patients receive SHK transplant over time. Although age was found to be significant risk factor for posttransplant mortality in SHK transplants from over a decade ago,[16,17] and functional independence shown to be protective of survival after isolated heart transplant,[4,18] the major differences in baseline characteristics of our unadjusted patient cohorts raise the possibility that our opposing results may be due to more careful selection of older and more functionally dependent SHK recipients in the most recent decade. For example, patients aged >65 years were less likely to be on dialysis before transplant, which was found to be a major risk factor for mortality after SHK transplantation in a previous study and could possibly increase the likelihood of older patients on this life-saving therapy to be "disqualified" from SHK transplantation.[17] However, even with careful selection of patients in determining SHK transplant candidacy, it is known that the average incidence of various events contributing to mortality after cardiac surgery, including stroke, increases with age.[19] Despite our comparison of adverse events immediately after transplant showing no difference between older and younger recipients, as well as our attempt to balance some covariates using propensity matching techniques, there are likely still age-related differences not shown by our analysis.

As both the number of SHK transplants and fraction of recipients >65 years old have risen over the past 2 decades, the debate about whether SHK transplant is a viable option in older and more functionally dependent recipients will become increasingly relevant in clinical practice. It is especially important to strike a balance between the costs and benefits of medical resource use among these older recipients due to scarcity of organs. Our findings suggest that SHK transplantation may be viewed as a successful therapy for severe kidney disease that is seen more frequently in older patients with heart failure, if these older patients are selected carefully based on comorbidities. Multivariable analysis from this study suggests that patients with history of malignancy, extracorporeal membrane oxygenation, transplant performed at a lower-volume center, greater total

bilirubin, and older donor age should be assessed especially carefully when determining the patient's eligibility for SHK transplantation. Although there are currently no consensus criteria on listing patients for SHK transplantation, our findings align with the 2016 International Society for Heart and Lung Transplantation listing criteria for isolated heart transplantation, which advises that "carefully selected patients >70 years of age may be considered for cardiac transplantation" and "it is reasonable to consider the presence of irreversible renal dysfunction (eGFR <30 mL/min/1.73 m^2) as a relative contraindication for heart transplantation alone."[20]

The high incidence of dialysis immediately after SHK transplantation has mostly been attributed to delayed renal graft function, which commonly is observed after deceased donor kidney transplant.[8,10] Our study did not find differences between the propensity-matched age groups in percentage of recipients requiring dialysis immediately after transplant. However, our unadjusted analyses showed a significantly greater incidence of both acute and long-term dialysis in younger SHK recipients. This may or may not be related to greater rates of pretransplant dialysis among younger recipients in our unadjusted data, or several previous studies showing greater incidence of acute kidney rejection among younger kidney transplant recipients.[21,22] It remains to be investigated whether this possible increased need for both short- and long-term dialysis in younger recipients is associated with adverse outcomes.

This study has several important limitations to highlight. There may be selection bias determining which patients older the age of 65 years undergo SHK transplantation, as older patients with more comorbidities may be excluded from SHK transplant eligibility. This is highlighted by significant differences in pretransplant characteristics seen in the unadjusted cohorts, although we attempted to mitigate these biases through propensity score matching and multivariable Cox analysis in this study. Of note, propensity score matching possibilities were also reduced by the limited number of continuous variables in the UNOS dataset. Moreover, there are inherent limitations to using the UNOS database, as some recipients are lost to follow-up after transplant, not all variables are available for each recipient, and it is impossible to identify recipients who were listed for both organs but became too unstable to receive the second organ after receiving the first one. Finally, there is the unavoidable limitation of much fewer patients older than the age of 65 years having undergone SHK transplantation compared with patients aged 18 to 65 years due to transplant candidate selection practices, with especially low sample size among recipients older than 70 years. Not only did this decrease our statistical power and create difficulty in using propensity-matched cohorts for several analyses, but the inferences and conclusions on post-SHK transplant outcomes among older recipients in this study should therefore only be applied to recipients aged 66 to 69 years at this time, given inability to extrapolate these findings to those aged 70 or older.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://www.aats.org/resources/do-recipient-age-and-functional-dependence-affect-outcomes-of-simultaneous-heart-kidney-transplantation.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: heart transplant, kidney transplant, multiorgan transplant, elderly, frailty

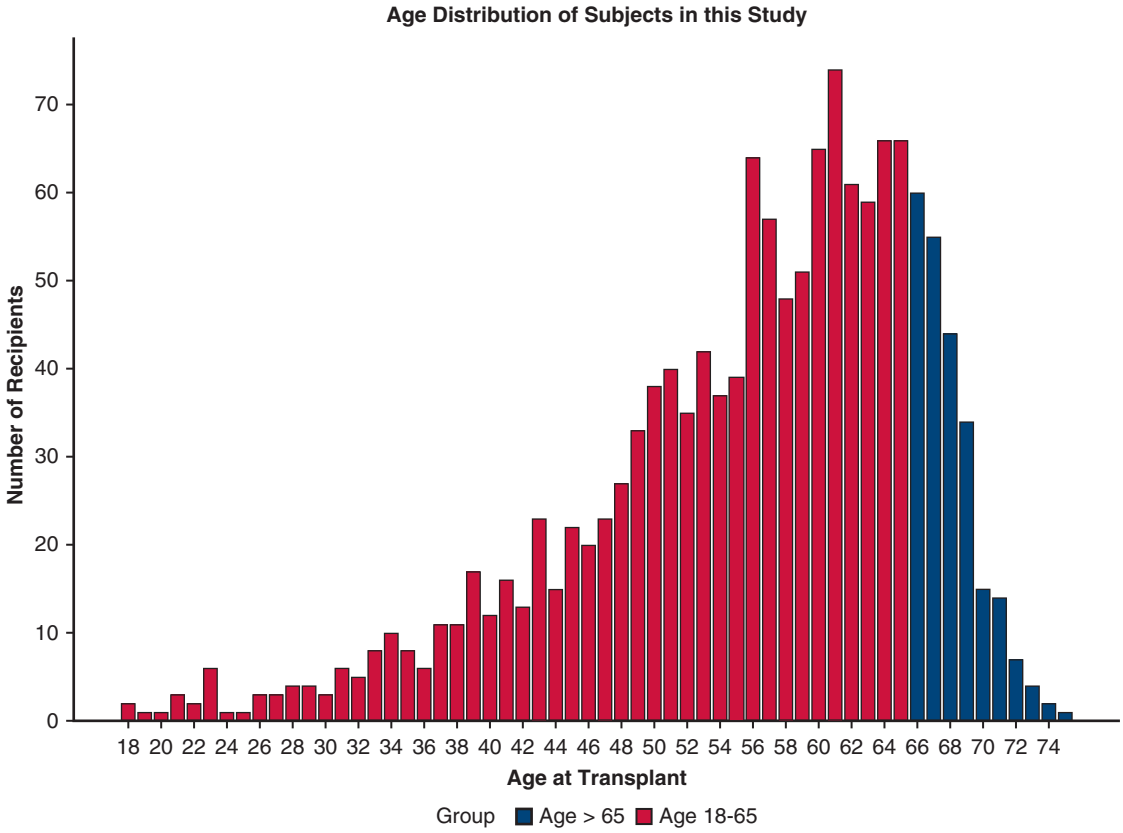


FIGURE E1. Distribution of ages among recipients 18 to 65 years old (*red*) and >65 years old (*blue*) who were included in this study.

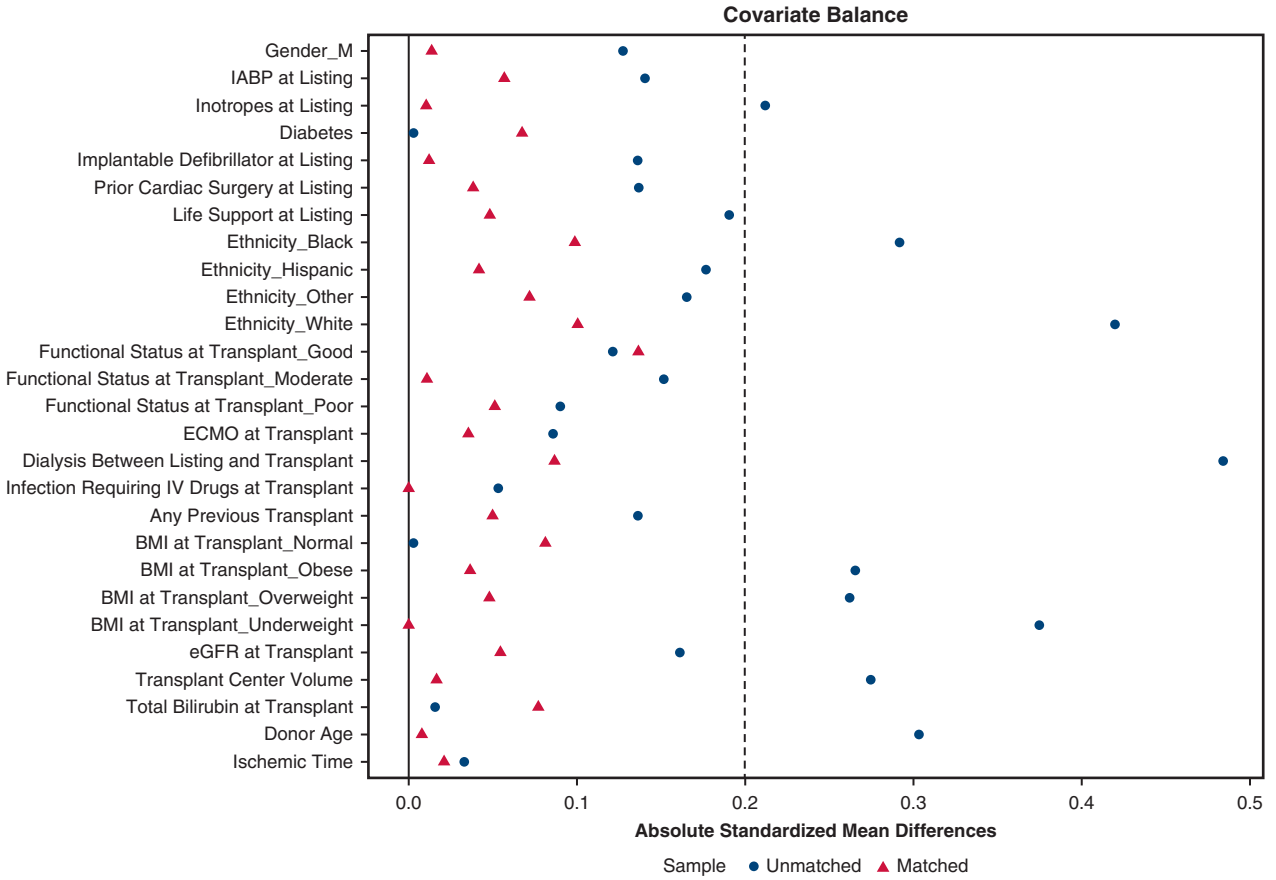
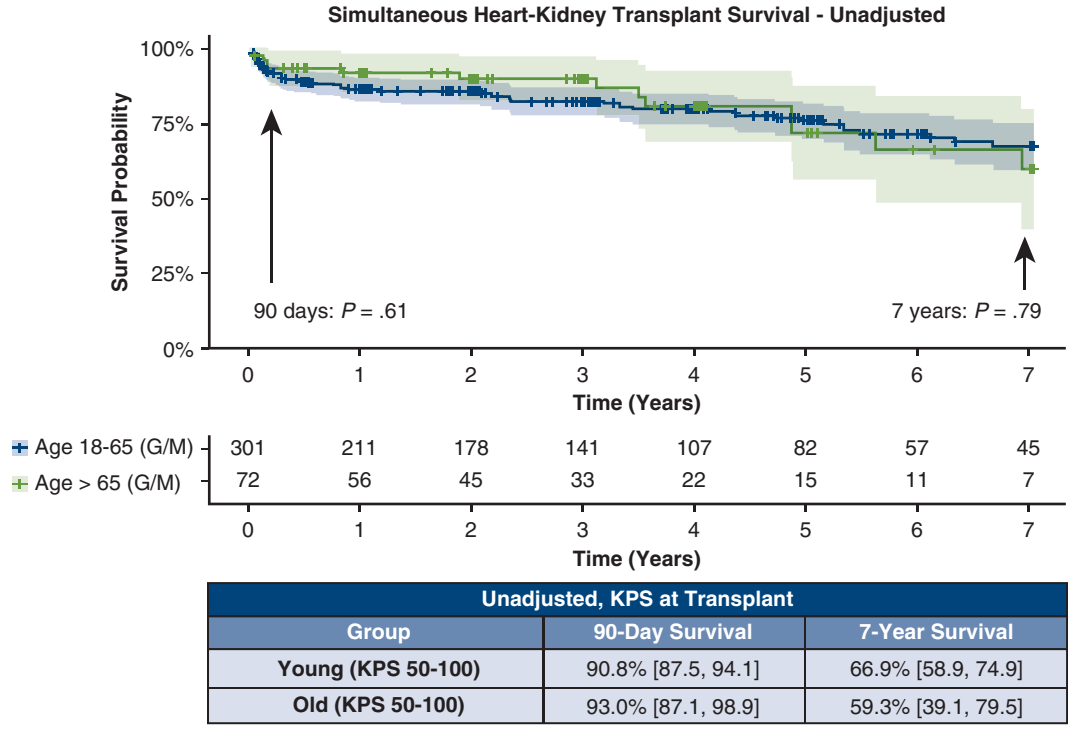
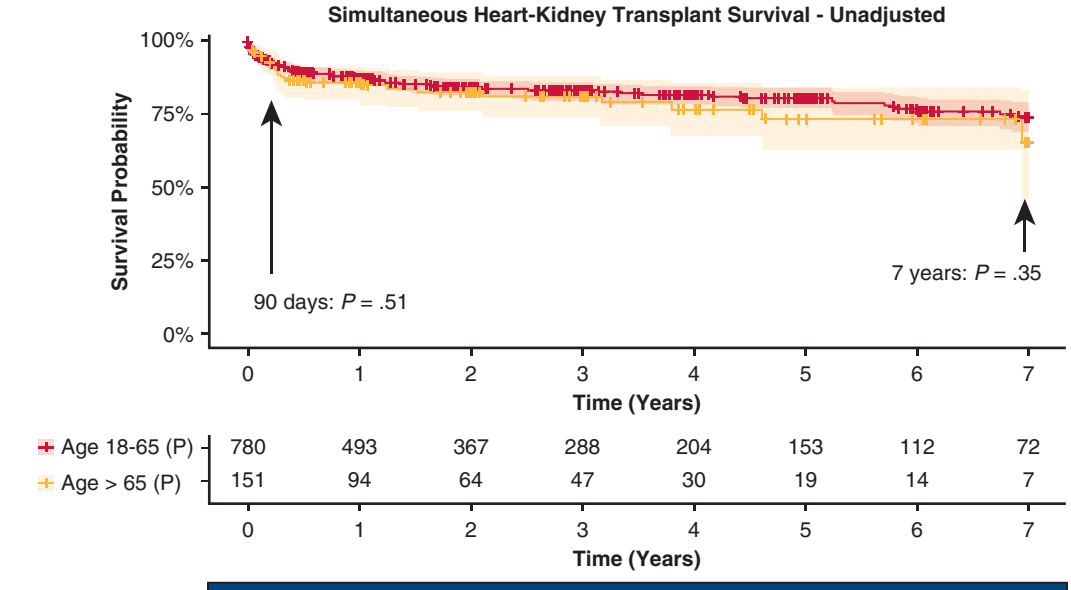


FIGURE E2. Covariate balance of propensity matching model used in this study evaluated by absolute value of standard mean difference. *IABP*, Intra-aortic balloon pump; *ECMO*, extracorporeal membrane oxygenation; *BMI*, body mass index; *eGFR*, estimated glomerular filtration rate.



Unadjusted, KPS at Transplant		
Group	90-Day Survival	7-Year Survival
Young (KPS 50-100)	90.8% [87.5, 94.1]	66.9% [58.9, 74.9]
Old (KPS 50-100)	93.0% [87.1, 98.9]	59.3% [39.1, 79.5]

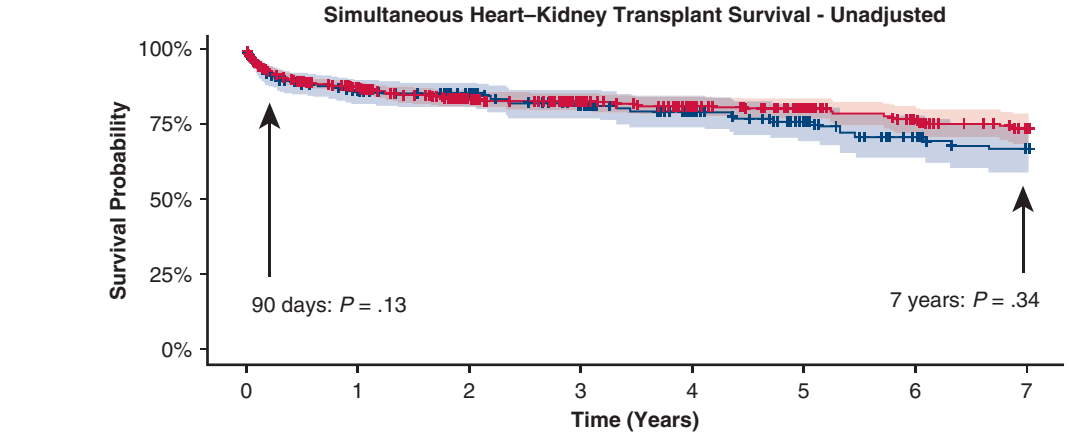
A

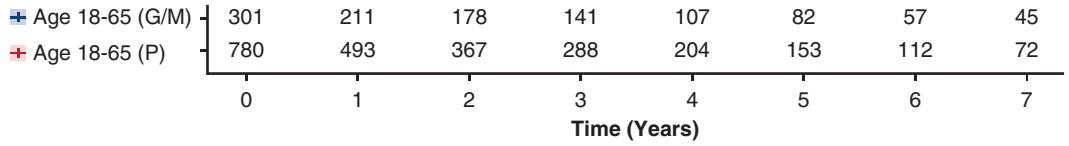


Unadjusted, KPS at Transplant		
Group	90-Day Survival	7-Year Survival
Young (KPS 10-40)	91.8% [89.8, 93.8]	73.8% [68.6, 78.9]
Old (KPS 10-40)	86.9% [81.4, 92.4]	65.2% [47.5, 82.9]

B

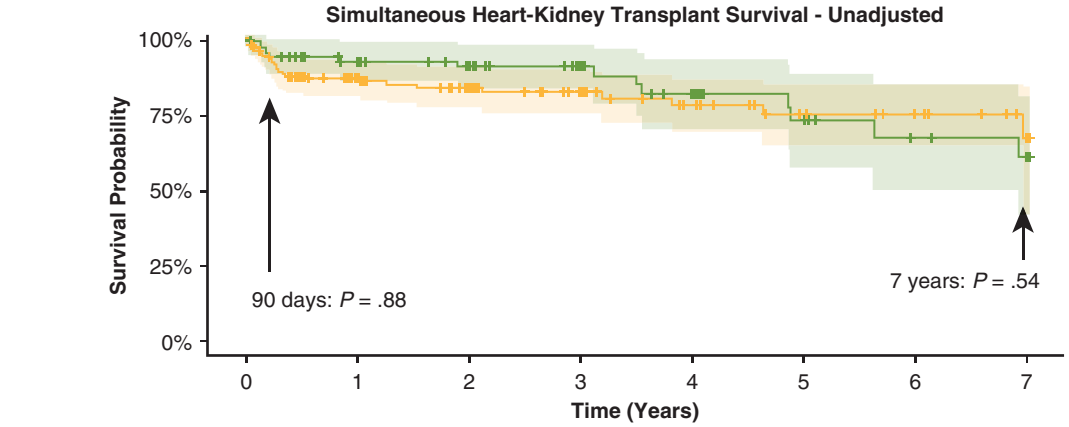
FIGURE E3. Pairwise comparisons of Kaplan-Meier curves from Figure 3 showing post-SHK transplant survival with 95% confidence interval and *P* values among unadjusted cohorts stratified by KPS at time of transplant. Recipients age >65 years with KPS 50 to 100 (*green*), age >65 years with KPS 10 to 40 (*yellow*), age 18 to 65 years with KPS 50 to 100 (*blue*), and age 18 to 65 years with KPS 10 to 40 (*red*) at 90 days and 7 years' posttransplant. *G/M*, Good/moderate; *KPS*, Karnofsky Performance Score.

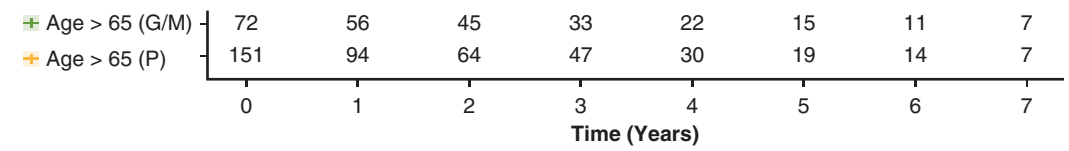




Unadjusted, KPS at Transplant		
Group	**90-Day Survival**	**7-Year Survival**
Young (KPS 50-100)	90.8% [87.5, 94.1]	66.9% [58.9, 74.9]
Young (KPS 10-40)	91.8% [89.8, 93.8]	73.8% [68.6, 78.9]

C

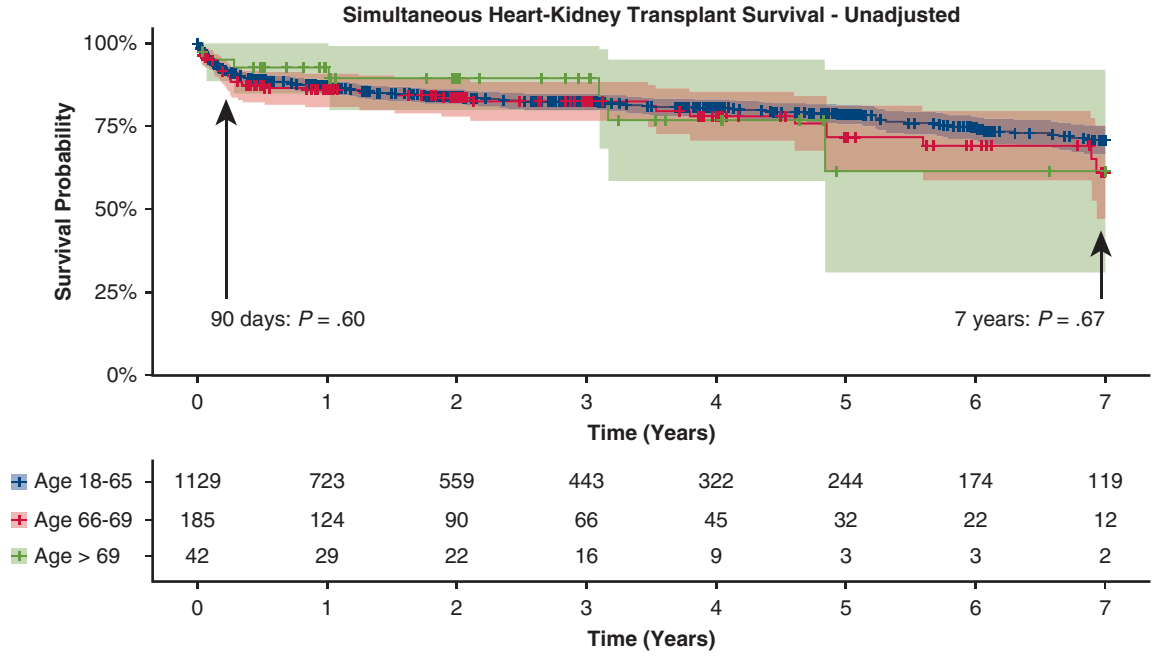




Unadjusted, KPS at Transplant		
Group	**90-Day Survival**	**7-Year Survival**
Old (KPS 50-100)	93.0% [87.1, 98.9]	59.3% [39.1, 79.5]
Old (KPS 10-40)	86.9% [81.4, 92.4]	65.2% [47.5, 82.9]

D

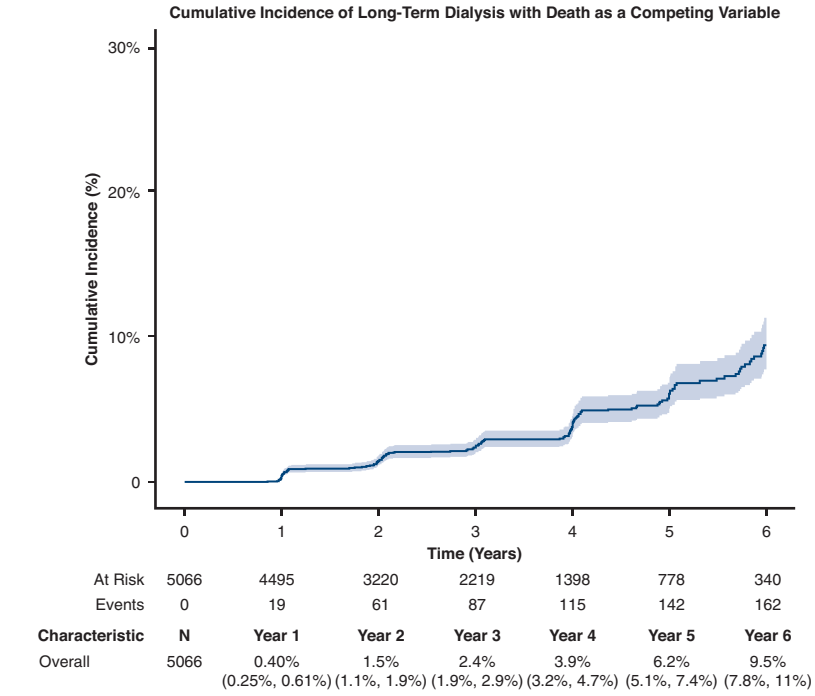
FIGURE E3. Continued.



Group	90-Day Survival	7-Year Survival
Age 18-65	91.4% [89.7, 93.0]	70.9% [66.5, 75.2]
Age 66-69	89.4% [84.9, 93.9]	61.0% [46.8, 75.1]
Age > 69	92.7% [84.8, 100.0]	61.4% [30.7, 92.1]

Values are probability [95% CI]

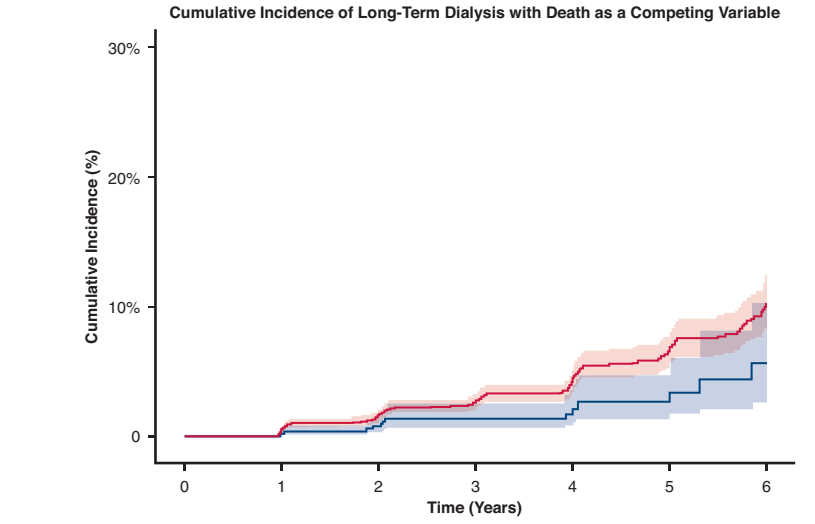
FIGURE E4. Kaplan-Meier survival analysis with 95% confidence interval and *P* values of patients aged 18 to 65 years (*blue*) versus 66 to 69 years (*red*) versus ≥70 years (*green*) at 90 days and 7 years' post-SHK transplant. 95% *CI*, 95% Confidence interval.



At Risk	5066	4495	3220	2219	1398	778	340
Events	0	19	61	87	115	142	162

Characteristic	N	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Overall	5066	0.40% (0.25%, 0.61%)	1.5% (1.1%, 1.9%)	2.4% (1.9%, 2.9%)	3.9% (3.2%, 4.7%)	6.2% (5.1%, 7.4%)	9.5% (7.8%, 11%)

A



Age > 65							
At Risk	846	755	535	364	225	121	54
Events	0	1	5	8	10	12	14
Age 18-65							
At Risk	4220	3740	2685	1855	1173	657	286
Events	0	18	56	79	105	130	148

Characteristic	N	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	*P*-value
group_age	5066							.020
Age > 65		0.13% (0.01%, 0.71%)	0.73% (0.28%, 1.6%)	1.3% (0.62%, 2.5%)	2.1% (1.0%, 3.9%)	3.3% (1.6%, 6.0%)	5.6% (2.6%, 10%)	
Age 18-65		0.45% (0.28%, 0.71%)	1.6% (1.2%, 2.1%)	2.6% (2.1%, 3.2%)	4.3% (3.5%, 5.2%)	6.7% (5.5%, 8.1%)	10% (8.3%, 12%)	
Gray's Test								

B

FIGURE E5. Cumulative 6-year incidence of long-term dialysis with death as a competing risk with 95% confidence interval among (A) entire unadjusted cohort and (B) unadjusted cohort stratified by age group 18 to 65 years versus >65 years. *P*-value computed by the *Fine-Gray* test.

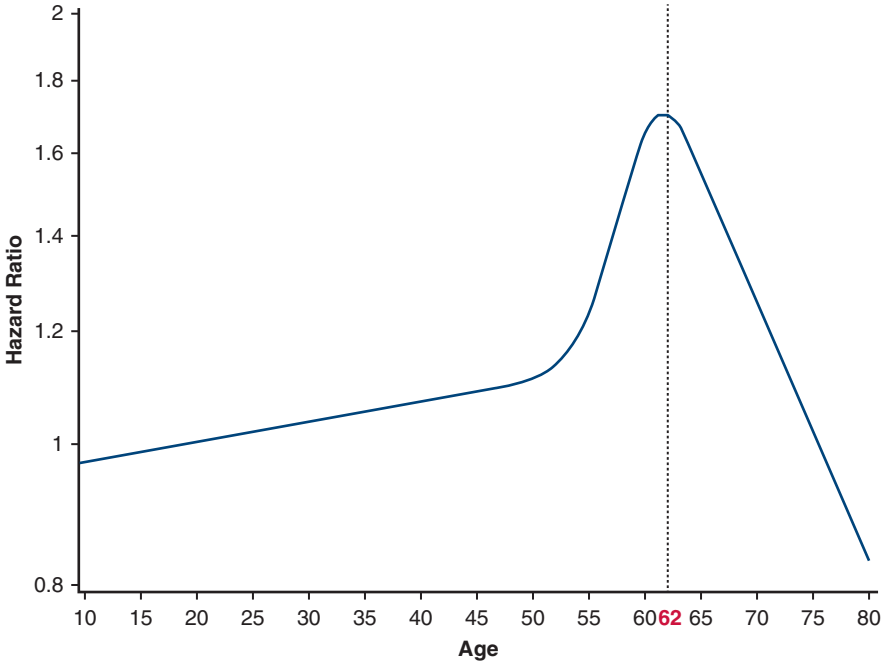


FIGURE E6. Restricted cubic spline regression model of recipient age versus HR of post-SHK transplant long-term mortality.

TABLE E1. Follow-up information within each age group

	Age 18-65 y (n = 1162)	Age >65 y (n = 236)
Median [interquartile range] follow-up time, d	730.0 [182.0, 1693.0]	729.0 [225.5, 1425.8]
Number (%) of recipients without follow-up	33 (2.8%)	9 (3.8%)

TABLE E2. Missing values for each variable used in propensity score matching and/or multivariable analyses

Variable	n (%)	Operation
After new allocation policy?	0 (0%)	N/A
Age	0 (0%)	N/A
Any previous malignancy	5 (0.4%)	Excluded from analysis
Blood type	4 (0.3%)	Excluded from analysis
BMI	0 (0%)	N/A
Cardiac output at transplant	146 (10.4%)	Excluded from analysis
Cardiac surgery between listing and transplant	32 (2.3%)	Excluded from analysis
Cigarette use	4 (0.3%)	Excluded from analysis
Creatinine at transplant	30 (2.1%)	Excluded from analysis
Diabetes at listing	6 (0.4%)	Excluded from analysis
Dialysis between listing and transplant	35 (2.5%)	Excluded from analysis
Donor age	0 (0%)	N/A
Donor hematocrit	14 (1.0%)	Excluded from analysis
Donor history of cigarette use	24 (1.7%)	Excluded from analysis
Donor history of diabetes	8 (0.6%)	Excluded from analysis
Donor history of heavy alcohol use	35 (2.5%)	Excluded from analysis
Donor history of hypertension	9 (0.6%)	Excluded from analysis
Donor protein in urine	22 (1.6%)	Excluded from analysis
Donor–recipient sex mismatch	0 (0%)	N/A
ECMO at transplant	30 (2.1%)	Excluded from analysis
eGFR at transplant	30 (2.1%)	Excluded from analysis
Ethnicity	0 (0%)	N/A
Functional status at transplant	81 (5.8%)	Excluded from analysis
Gender	0 (0%)	N/A
History of any non-heart transplant	0 (0%)	N/A
IABP at listing	0 (0%)	N/A
Implantable defibrillator at listing	18 (1.3%)	Excluded from analysis
Infection requiring IV drug therapy	41 (2.9%)	Excluded from analysis
Inotropes at listing	0 (0%)	N/A
Ischemic time	57 (4.1%)	Excluded from analysis
Life support at listing	3 (0.2%)	Excluded from analysis
Most recent creatinine at listing	7 (0.5%)	Excluded from analysis
Prior cardiac surgery at listing (non-transplant)	22 (1.6%)	Excluded from analysis
Total bilirubin	35 (2.5%)	Excluded from analysis
Total days on waitlist	0 (0%)	N/A
Transplant center identifier	0 (0%)	N/A
Ventilator between listing and transplant	49 (3.5%)	Excluded from analysis

N/A, Not available; *BMI*, body mass index; *ECMO*, extracorporeal membrane oxygenation; *eGFR*, estimated glomerular filtration rate; *IABP*, intra-aortic balloon pump.

TABLE E3. Comparison of baseline characteristics among propensity score–matched versus –unmatched SHK transplant recipients aged 18 to 65 years

Characteristics	Matched (n = 209)	Unmatched (n = 953)	*P* value
Recipient			
Male sex, n (%)	179 (85.6)	757 (79.4)	.050
BMI at transplant, n (%)			<.001*
Underweight	1 (0.5)	33 (3.5)	
Normal	62 (29.7)	330 (34.6)	
Overweight	102 (48.8)	297 (31.2)	
Obese	44 (21.1)	293 (30.7)	
Diabetes, n (%)	103 (49.3)	431 (45.5)	.355
Cigarette use, n (%)	87 (41.6)	349 (36.7)	.210
Cerebrovascular disease, n (%)	18 (8.7)	59 (6.2)	.266
Any history of malignancy, n (%)	18 (8.6)	79 (8.3)	1.000
Any previous non-heart transplant, n (%)	3 (1.4)	25 (2.6)	.444
Previous cardiac surgery at listing, n (%)	98 (46.9)	351 (37.5)	.014*
Ethnicity, n (%)			<.001*
Black	45 (21.5)	393 (41.2)	
Hispanic	14 (6.7)	94 (9.9)	
White	144 (68.9)	390 (40.9)	
Other	6 (2.9)	76 (8.0)	
Functional status at listing, n (%)			.226
Good	18 (8.6)	75 (7.9)	
Moderate	66 (31.6)	290 (30.4)	
Poor	121 (57.9)	538 (56.5)	
Functional status at transplant, n (%)			<.001*
Good	16 (7.7)	61 (6.4)	
Moderate	54 (25.8)	170 (17.8)	
Poor	139 (66.5)	650 (68.2)	
Medical condition (%)			.036*
Hospitalized (not in ICU)	39 (18.7)	179 (18.8)	
In ICU	91 (43.5)	456 (47.8)	
Not hospitalized	79 (37.8)	294 (30.8)	
Dialysis between listing and transplant, n (%)	65 (31.1)	472 (51.1)	<.001*
Any history of dialysis, n (%)	80 (38.3)	526 (56.6)	<.001*
Implantable defibrillator at listing, n (%)	169 (80.9)	683 (72.8)	.020*
Infection requiring IV drug therapy at transplant, n (%)	27 (12.9)	135 (14.7)	.575
ECMO at transplant, n (%)	3 (1.4)	33 (3.5)	.190
IABP at listing, n (%)	24 (11.5)	68 (7.1)	.049*
IABP at transplant, n (%)	28 (13.4)	142 (14.9)	.654
Inotropes at listing, n (%)	61 (29.2)	382 (40.1)	.004*
Inotropes at transplant, n (%)	93 (44.5)	423 (44.4)	1.000
Ventricular assist device at transplant, n (%)	66 (31.6)	351 (37.8)	.109
Life support at listing, n (%)	114 (54.5)	638 (67.1)	.001*
Life support at transplant, n (%)	168 (80.4)	775 (83.4)	.341
Transplant center volume	30.00 [17.00, 48.00]	20.00 [13.00, 37.00]	<.001*
Ischemic time	3.20 [2.50, 3.70]	3.20 [2.50, 3.80]	.672
Days on waitlist	74.00 [25.00, 248.00]	72.00 [19.00, 270.00]	.703
eGFR at transplant	26.99 [16.57, 40.74]	25.98 [15.02, 40.14]	.344
Creatinine at transplant	2.60 [1.82, 3.90]	2.68 [1.90, 4.20]	.333
Total bilirubin at transplant	0.70 [0.50, 1.10]	0.70 [0.50, 1.10]	.902
Cardiac output at transplant	4.60 [3.80, 5.92]	4.70 [3.70, 5.77]	.734
Donor			
Donor–recipient sex mismatch (%)	56 (26.8)	217 (22.8)	.249
Donor diabetes, n (%)	7 (3.4)	18 (1.9)	.287
Donor history of heavy alcohol use, n (%)	48 (23.4)	144 (15.5)	.009*

(Continued)

TABLE E3. Continued

Characteristics	Matched (n = 209)	Unmatched (n = 953)	*P* value
Donor history of cigarette use, n (%)	36 (17.5)	91 (9.7)	.002*
Donor history of hypertension, n (%)	32 (15.5)	109 (11.5)	.146
Donor clinical infection, n (%)	166 (79.4)	739 (78.6)	.869
Donor age	35.00 [26.00, 44.00]	29.00 [22.00, 38.00]	<.001*
Donor BMI	27.18 [23.71, 30.99]	26.65 [23.32, 30.35]	.151
Donor creatinine	0.90 [0.70, 1.20]	0.90 [0.70, 1.20]	.900
Donor LV ejection fraction	60.00 [58.00, 65.00]	60.00 [56.00, 65.00]	.197

Values are n (%) or median [interquartile range]. *BMI*, Body mass index; *ICU*, intensive care unit; *IV*, intravenous; *ECMO*, extracorporeal membrane oxygenation; *IABP*, intra-aortic balloon pump; *eGFR*, estimated glomerular filtration rate; *LV*, left ventricular. *Statistically significant value ($P < .05$).

TABLE E4. Comparison of baseline characteristics among propensity score–matched versus –unmatched SHK transplant recipients aged >65 years

Characteristics	Matched (n = 209)	Unmatched (n = 27)	*P* value
Recipient			
Male sex, n (%)	178 (85.2)	26 (96.3)	.197
BMI at transplant, n (%)			.505
Underweight	1 (0.5)	0 (0.0)	
Normal	70 (33.5)	13 (48.1)	
Overweight	97 (46.4)	10 (37.0)	
Obese	41 (19.6)	4 (14.8)	
Diabetes, n (%)	96 (45.9)	10 (38.5)	.608
Cigarette use, n (%)	93 (44.5)	12 (48.0)	.904
Cerebrovascular disease, n (%)	20 (9.6)	1 (3.8)	.544
Any history of malignancy, n (%)	29 (13.9)	2 (7.7)	.568
Any previous non-heart transplant, n (%)	2 (1.0)	1 (3.7)	.775
Previous cardiac surgery at listing, n (%)	94 (45.0)	15 (71.4)	.037*
Ethnicity, n (%)			.407
Black	54 (25.8)	5 (18.5)	
Hispanic	12 (5.7)	3 (11.1)	
White	134 (64.1)	19 (70.4)	
Other	9 (4.3)	0 (0.0)	
Functional status at listing, n (%)			.285
Good	20 (9.6)	1 (3.7)	
Moderate	65 (31.1)	8 (29.6)	
Poor	120 (57.4)	16 (59.3)	
Functional status at transplant, n (%)			<.001*
Good	10 (4.8)	2 (7.4)	
Moderate	55 (26.3)	5 (18.5)	
Poor	144 (68.9)	11 (40.7)	
Medical condition (%)			<.001*
Hospitalized (not in ICU)	41 (19.6)	8 (29.6)	
In ICU	97 (46.4)	7 (25.9)	
Not hospitalized	71 (34.0)	7 (25.9)	
Dialysis between listing and transplant, n (%)	57 (27.3)	3 (13.6)	.258
Any history of dialysis, n (%)	63 (30.1)	6 (25.0)	.774
Implantable defibrillator at listing, n (%)	168 (80.4)	20 (83.3)	.941
Infection requiring IV drug therapy at transplant, n (%)	27 (12.9)	1 (4.5)	.423
ECMO at transplant, n (%)	4 (1.9)	0 (0.0)	1.000
IABP at listing, n (%)	28 (13.4)	1 (3.7)	.257
IABP at transplant, n (%)	40 (19.1)	1 (3.7)	.085
Inotropes at listing, n (%)	62 (29.7)	6 (22.2)	.563
Inotropes at transplant, n (%)	95 (45.5)	7 (25.9)	.085
Ventricular assist device at transplant, n (%)	62 (29.7)	9 (40.9)	.398
Life support at listing, n (%)	119 (56.9)	14 (53.8)	.928
Life support at transplant, n (%)	162 (77.5)	18 (81.8)	.847
Transplant center volume	25.00 [17.00, 48.00]	40.00 [13.00, 86.00]	.208
Ischemic time	3.10 [2.40, 3.60]	4.00 [2.90, 4.30]	.009*
Days on waitlist	55.00 [16.00, 181.00]	45.00 [19.50, 180.50]	.920
eGFR at transplant	30.84 [21.35, 40.75]	33.96 [21.78, 56.65]	.191
Creatinine at transplant	2.20 [1.70, 2.98]	2.09 [1.35, 3.03]	.311
Total bilirubin at transplant	0.80 [0.50, 1.20]	0.60 [0.50, 1.00]	.534
Cardiac output at transplant	4.66 [3.84, 5.90]	4.86 [3.90, 5.61]	.954
Donor			
Donor–recipient sex mismatch (%)	49 (23.4)	8 (29.6)	.640
Donor diabetes, n (%)	5 (2.4)	2 (7.4)	.402
Donor history of heavy alcohol use, n (%)	58 (28.4)	5 (18.5)	.391

(Continued)

TABLE E4. Continued

Characteristics	Matched (n = 209)	Unmatched (n = 27)	*P* value
Donor history of cigarette use, n (%)	25 (12.3)	2 (7.4)	.676
Donor history of hypertension, n (%)	36 (17.3)	1 (3.7)	.122
Donor clinical infection, n (%)	158 (77.1)	19 (76.0)	1.000
Donor age	33.00 [25.00, 44.00]	28.00 [21.00, 38.00]	.104
Donor BMI	26.51 [23.50, 30.24]	26.45 [23.88, 31.00]	.634
Donor creatinine	0.90 [0.71, 1.16]	1.00 [0.80, 1.30]	.101
Donor LV ejection fraction	60.00 [60.00, 65.00]	60.00 [59.00, 65.00]	.900

Values are n (%) or median [interquartile range]. *BMI*, Body mass index; *ICU*, intensive care unit; *IV*, intravenous; *ECMO*, extracorporeal membrane oxygenation; *IABP*, intra-aortic balloon pump; *eGFR*, estimated glomerular filtration rate; *LV*, left ventricular. *Statistically significant value ($P < .05$).

TABLE E5. Univariable Cox analysis of pretransplant characteristics on 7-year posttransplant mortality among entire SHK transplanted cohort

Variable	Hazard ratio (95% CI)	*P* value
Age	1.013 (0.999-1.026)	.0614
Female sex	1.412 (1.042-1.913)	.0258*
Ethnicity		
White	Reference	N/A
Black	0.855 (0.643-1.138)	.2822
Other	0.941 (0.650-1.362)	.7459
Functional status		
Total assistance (KPS 10-40)	1.123 (0.671-1.881)	.6585
Some assistance (KPS 50-70)	1.282 (0.737-2.230)	.3799
No assistance (KPS 80-100)	Reference	N/A
Previouscardiac surgery at listing (non-transplant)	1.114 (0.862-1.441)	.4087
History of any non-heart transplant	1.984 (1.053-3.737)	.0340*
Cardiac surgery between listing and transplant	0.856 (0.623-1.175)	.3351
Any previous malignancy	1.534 (1.040-2.264)	.0309*
Diabetes at listing	1.284 (0.995-1.655)	.0543
Cerebrovascular disease	1.070 (0.653-1.753)	.7878
Dialysis between listing and transplant	1.102 (0.854-1.423)	.4551
Cigarette use	1.066 (0.823-1.381)	.6266
After new allocation policy	1.595 (1.177-2.161)	.0026*
Implantable defibrillator at listing	1.399 (1.011-1.936)	.0428*
Infection requiring IV drug therapy at transplant	1.330 (0.953-1.856)	.0937
ECMO at listing	0.572 (0.142-2.305)	.4325
ECMO at transplant	2.510 (1.366-4.612)	.0030*
IABP at listing	0.832 (0.484-1.429)	.5045
IABP at transplant	1.217 (0.844-1.753)	.2927
Inotropes at listing	0.836 (0.638-1.096)	.1945
Inotropes at transplant	0.849 (0.657-1.099)	.2140
Life support at listing	0.827 (0.639-1.072)	.1508
Life support at transplant	0.906 (0.655-1.253)	.5510
VAD at listing	1.017 (0.758-1.365)	.9087
VAD at transplant	0.943 (0.723-1.230)	.6634
Transplant center volume	0.995 (0.990-0.999)	.0258*
BMI	1.036 (1.010-1.063)	.0069*
Cardiac output at transplant	1.022 (0.945-1.104)	.5913
Creatinine at transplant	1.019 (0.970-1.070)	.4551
eGFR at transplant	1.003 (0.998-1.009)	.2258
Ischemic time >4 h	1.289 (0.945-1.757)	.1085
Total days on waitlist	1.000 (0.999-1.000)	.3002
Total bilirubin at transplant	1.028 (1.010-1.046)	.0021*
Donor age	1.010 (0.999-1.022)	.0789
Donor–recipient sex mismatch	1.073 (0.800-1.440)	.6375
Donor history of heavy alcohol use	0.972 (0.693-1.362)	.8678
Donor BMI	0.991 (0.969-1.014)	.4492

(Continued)

TABLE E5. Continued

Variable	Hazard ratio (95% CI)	*P* value
Donor BUN	0.997 (0.988-1.007)	.5593
Donor clinical infection	1.070 (0.785-1.458)	.6704
Donor creatinine	0.913 (0.735-1.134)	.4114
Donor diabetes	0.813 (0.303-2.185)	.6822
Donor cigarette use	1.080 (0.723-1.612)	.7084
Donor cocaine use	0.761 (0.538-1.078)	.1243
Donor hypertension	1.246 (0.870-1.785)	.2293
Donor LV ejection fraction	1.001 (0.982-1.021)	.9232

Variables with $P < .10$ in this table, as well as other variables that were highly clinically relevant, were selected for multivariable analysis. *CI*, Confidence interval; *N/A*, not available; *KPS*, Karnofsky Performance Score; *IV*, intravenous; *ECMO*, extracorporeal membrane oxygenation; *IABP*, intra-aortic balloon pump; *VAD*, ventricular assist device; *BMI*, body mass index; *eGFR*, estimated glomerular filtration rate; *BUN*, blood urea nitrogen; *LV*, left ventricular. *Statistically significant value ($P < .05$).

TABLE E6. Comparison of baseline characteristics among unmatched SHK transplant recipients aged 18 to 65 y (n = 1162) and aged >65 y (n = 236)

Recipient characteristics	Age 18-65 y (n = 1162)	Age >65 y (n = 236)	*P* value
Recipient			
Male sex, n (%)	936 (80.6)	204 (86.4)	.042*
Diabetes, n (%)	534 (46.2)	106 (45.1)	.824
Cigarette use, n (%)	436 (37.6)	105 (44.9)	.044*
Cerebrovascular disease, n (%)	77 (6.7)	21 (9.0)	.266
Any history of malignancy, n (%)	97 (8.4)	31 (13.2)	.027*
Any previous non-heart transplant, n (%)	28 (2.4)	3 (1.3)	.401
Previous cardiac surgery at listing, n (%)	449 (39.2)	109 (47.4)	.025*
Ethnicity, n (%)			<.001*
Black	438 (37.7)	59 (25.0)	
Hispanic	108 (9.3)	15 (6.4)	
White	534 (46.0)	153 (64.8)	
Other	82 (7.1)	9 (3.8)	
Functional status at listing, n (%)			.522
Good	93 (8.0)	21 (8.9)	
Moderate	356 (30.6)	73 (30.9)	
Poor	659 (56.7)	136 (57.6)	
Functional status at transplant, n (%)			.092
Good	77 (6.6)	12 (5.1)	
Moderate	224 (19.3)	60 (25.4)	
Poor	789 (67.9)	155 (65.7)	
Medical condition, n (%)			.837
Hospitalized (not in ICU)	218 (18.8)	49 (20.8)	
In ICU	547 (47.1)	104 (44.1)	
Not hospitalized	373 (32.1)	78 (33.1)	
Dialysis between listing and transplant, n (%)	537 (47.4)	60 (26.0)	<.001*
Any history of dialysis, n (%)	606 (53.3)	69 (29.6)	<.001*
Implantable defibrillator at listing, n (%)	852 (74.3)	188 (80.7)	.047*
Infection requiring IV drug therapy at transplant, n (%)	162 (14.4)	28 (12.1)	.424
ECMO at transplant, n (%)	36 (3.1)	4 (1.7)	.335
IABP at listing, n (%)	92 (7.9)	29 (12.3)	.040*
IABP at transplant, n (%)	170 (14.6)	41 (17.4)	.330
Inotropes at listing, n (%)	443 (38.1)	68 (28.8)	.008*
Inotropes at transplant, n (%)	516 (44.4)	102 (43.2)	.793
Ventricular assist device at transplant, n (%)	417 (36.6)	71 (30.7)	.102
Life support at listing, n (%)	752 (64.8)	133 (56.6)	.021*
Life support at transplant, n (%)	943 (82.9)	180 (77.9)	.091
BMI	26.90 [23.40, 30.70]	26.15 [23.90, 28.90]	.213
Transplant center volume	22.00 [13.00, 38.00]	25.00 [14.75, 48.00]	<.001*
Ischemic time	3.20 [2.50, 3.80]	3.20 [2.40, 3.80]	.791
Days on waitlist	72.00 [20.00, 266.00]	52.00 [16.75, 181.75]	.035*
eGFR at transplant	26.20 [15.30, 40.16]	31.43 [21.35, 41.99]	<.001*
Creatinine at transplant	2.67 [1.90, 4.08]	2.20 [1.70, 2.99]	<.001*
Total bilirubin at transplant	0.70 [0.50, 1.10]	0.80 [0.50, 1.20]	.121
Cardiac output at transplant	4.70 [3.70, 5.80]	4.70 [3.85, 5.84]	.944
Donor			
Donor–recipient sex mismatch, n (%)	273 (23.5)	57 (24.2)	.894
Donor diabetes, n (%)	25 (2.2)	7 (3.0)	.603
Donor history of heavy alcohol use, n (%)	192 (17.0)	63 (27.3)	<.001*
Donor history of cigarette use, n (%)	127 (11.1)	27 (11.7)	.889
Donor history of hypertension, n (%)	141 (12.2)	37 (15.7)	.172
Donor clinical infection, n (%)	905 (78.8)	177 (77.0)	.602
Donor age	30.00 [22.00, 39.00]	32.00 [25.00, 44.00]	.001*

(Continued)

TABLE E6. Continued

Recipient characteristics	Age 18-65 y (n = 1162)	Age >65 y (n = 236)	*P* value
Donor BMI	26.70 [23.39, 30.51]	26.50 [23.60, 30.29]	.922
Donor creatinine	0.90 [0.70, 1.20]	0.90 [0.75, 1.17]	.703
Donor LV ejection fraction	60.00 [57.00, 65.00]	60.00 [60.00, 65.00]	.327

Values are n (%) or median [interquartile range]. *ICU*, Intensive care unit; *IV*, intravenous; *ECMO*, extracorporeal membrane oxygenation; *IABP*, intra-aortic balloon pump; *BMI*, body mass index; *eGFR*, estimated glomerular filtration rate; *LV*, left ventricular. *Statistically significant value ($P < .05$).

TABLE E7. Posttransplant adverse events in unadjusted cohorts

Adverse events	Age 18-65 y (n = 1162)	Age >65 y (n = 236)	*P* value
Length of stay, d	20.00 [14.00, 32.00]	21.00 [14.00, 31.00]	.714
Cardiac graft failure	215 (19.0%)	47 (20.7%)	.627
Acute heart rejection requiring treatment	49 (4.3%)	14 (6.2%)	.309
Stroke	36 (3.2%)	7 (3.1%)	1.000
Dialysis	375 (33.3%)	59 (26.0%)	.038*
Pacemaker	22 (2.0%)	3 (1.3%)	.712

Values are n (%) or median [interquartile range]. *Statistically significant value ($P < .05$).

TABLE E8. Comparison of frequency of dialysis between listing and transplant versus dialysis immediately posttransplant in recipients 18 to 65 years old and >65 years old

	Unadjusted		Propensity score-matched	
Dialysis	Age 18-65 y (n = 1162)	Age >65 y (n = 236)	Age 18-65 y (n = 209)	Age >65 y (n = 209)
Pretransplant	47.4%	26.0%	31.1%	27.3%
Posttransplant	33.3%	26.0%	29.2%	26.8%
Difference (post–pre)	−14.1%	0.0%	−1.9%	−0.5%

Values are % of patients with data available for the variable.

TABLE E9. Multivariable logistic regression of pretransplant characteristics on need for dialysis immediately after transplant among entire SHK transplanted cohort

Variable	Odds ratio (95% CI)	*P* value
Age	0.997 (0.983-1.012)	.7060
Female sex	1.087 (0.756-1.562)	.6522
Blood type		
A	Reference	N/A
B	1.029 (0.681-1.556)	.6337
AB	1.083 (0.569-2.061)	.9203
O	1.356 (0.985-1.866)	.1055
Ethnicity		
White	Reference	N/A
Black	0.976 (0.713-1.337)	.1040
Hispanic	0.673 (0.391-1.158)	.4649
Other	0.573 (0.305-1.076)	.1870
Functional status at transplant		
Total assistance (KPS 10-40)	1.275 (0.721-2.254)	.0990
Some assistance (KPS 50-70)	0.881 (0.473-1.642)	.2511
No assistance (KPS 80-100)	Reference	N/A
Transplant center volume		
High	0.807 (0.537-1.213)	.0728
Medium	1.114 (0.709-1.750)	.2127
Low	Reference	N/A
BMI		
Underweight	0.662 (0.225-1.952)	.2401
Normal	Reference	N/A
Overweight	1.215 (0.862-1.711)	.4424
Obese	1.620 (1.108-2.370)	.0185*
Cardiac surgery between listing and transplant	1.120 (0.780-1.608)	.5397
Cardiac output at transplant	0.994 (0.914-1.081)	.8949
Dialysis between listing and transplant	2.887 (2.091-3.985)	<.0001*
Diabetes at listing	1.142 (0.850-1.534)	.3771
ECMO at transplant	1.693 (0.675-4.242)	.2615
Inotropes at listing	0.913 (0.677-1.230)	.5494
Ventilator between listing and transplant	1.495 (1.026-2.179)	.0365*
After new allocation policy?	1.542 (1.148-2.070)	.0040*
Infection requiring IV drug therapy at transplant	1.128 (0.752-1.692)	.5605
Most recent creatinine at listing	1.042 (0.968-1.122)	.2753
Creatinine at transplant	1.094 (0.992-1.205)	.0710
eGFR at transplant	1.005 (0.996-1.013)	.3076
Ischemic time >4 h	1.454 (1.031-2.051)	.0331*
Donor age	1.025 (1.010-1.040)	.0007*
Donor hematocrit	0.973 (0.947-1.001)	.0564
Donor history of cigarette use	1.182 (0.752-1.857)	.4683
Donor history of hypertension	1.220 (0.805-1.850)	.3480
Donor history of diabetes	0.506 (0.186-1.377)	.1822
Donor protein in urine	0.926 (0.702-1.222)	.5874

CI, Confidence interval; *N/A*, not available; *KPS*, Karnofsky Performance Score; *BMI*, body mass index; *ECMO*, extracorporeal membrane oxygenation; *IV*, intravenous; *eGFR*, estimated glomerular filtration rate. *Statistically significant value ($P < .05$).

TABLE E10. Posttransplant cause of death at 90 days and at most recent follow-up

	90 days			Most recent follow-up		
Cause of death	**Age 18-65 y (n = 90)**	**Age >65 y (n = 18)**	***P* value**	**Age 18-65 y (n = 190)**	**Age >65 y (n = 41)**	***P* value**
Cardiovascular	9 (10.0%)	1 (5.6%)	.882	20 (10.5%)	4 (9.8%)	1.000
Cerebrovascular	10 (11.0%)	1 (5.6%)	.776	15 (7.9%)	2 (4.9%)	.733
Pulmonary	5 (5.6%)	2 (11.1%)	.727	20 (10.5%)	4 (9.8%)	1.000
Graft failure	6 (6.7%)	2 (11.1%)	.869	9 (4.7%)	2 (4.9%)	1.000
Infection	28 (31.1%)	9 (50.0%)	.204	46 (24.2%)	14 (34.1%)	.263
Other	32 (35.6%)	3 (16.7%)	.198	80 (42.1%)	15 (36.6%)	.634

Values are n (%).