Cardiac Outcomes in Isolated Heart and Simultaneous Kidney and Heart Transplants in the United States

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Introduction: Kidney dysfunction is not uncommon in patients with advanced heart failure. Simultaneous kidney and heart transplants (SKHTs) have gained acceptance as a treatment for patients with end-stage heart failure and severe kidney dysfunction. United States saw a rise of 650% in SKHT from 2000 to 2019. Despite increasing number of SKHT, the selection criteria remain poorly defined and vary across transplant centers.

Methods: We evaluated patient and cardiac allograft survival for SKHT and heart transplant alone (HTA) using the United Network for Organ Sharing (UNOS) database. We then performed a subgroup analysis in recipients with post-transplant acute kidney injury requiring renal replacement therapy (RRT) and compared outcomes between SKHT and HTA recipients.

Results: Although patient survival was comparable between SKHT and HTA groups (12.4 vs. 11.3 years), patients dependent on dialysis pretransplant derived greater survival advantage from SKHT as compared with HTA (12.4 vs. 9.9 years). Cardiac graft survival was better in SKHT (12.5 vs. 11.2 years). Among patients who developed acute kidney injury requiring RRT postoperatively, SKHT recipients had a significantly better survival (11.9 vs. 2.7 years).

Conclusion: Our data support consideration of SKHT in dialysis-dependent heart transplant candidates and suggest that patients who are at increased risk of requiring RRT after heart transplant may benefit from SKHT.

T he first combined heart and kidney transplant was performed in 1978.[1] Since then, this combined transplant modality has gained widespread acceptance for patients with end-stage heart failure and concomitant renal disease. Although criteria for isolated organ transplants are well defined, the criteria for combined organ allocation vary based on geographic region and institutional policy. When deciding whether patients should be listed for combined kidney and heart transplant, some authors have recommended an estimated glomerular filtration rate (eGFR) cutoff of <37

ml/min,[2] whereas others have used <40 ml/min.[3] Gill *et al.*[4] suggested using "dialysis dependence" as criteria for combined organ transplantation. Both single-center and previous analyses of the UNOS database have revealed similar patient survival between HTA and SKHT recipients.[2–6] In contrast, simultaneous kidney transplant seems to provide immunoprotection to the cardiac allograft and hence improved cardiac graft outcomes in SKHT recipients when compared with HTA recipients.[2,4,7]

According to the Organ Procurement and Transplantation Network (OPTN)/UNOS data, the number of heart transplants performed every year in the United States increased by 61%, from 2199 in 2000 to 3552 in 2019. Notably, SKHTs increased by 650%, from 29 in 2000 to 219 in 2019.[8] Despite this exponential increase in combined organ transplantation, patient selection criteria remain poorly defined. Therefore, we analyzed the UNOS/OPTN database of heart and combined organ

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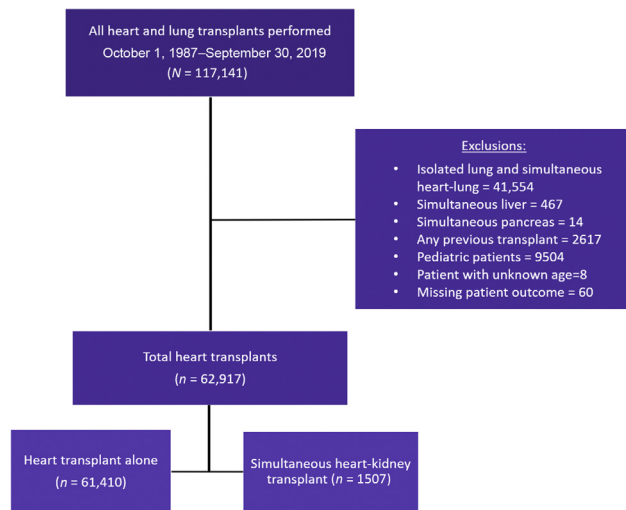
Figure 1. Flowchart revealing inclusion and exclusion criteria.

transplants from 1987 to 2019 to study the outcomes of SKHT versus HTA recipients. We also aimed to identify recipients who would benefit from SKHT as compared with HTA.

METHODS

Study Population and Data Source

The OPTN/UNOS maintains registries for thoracic and abdominal transplants separately, known as the Standard Transplant Analysis and Research files. We used data from the thoracic Standard Transplant Analysis and Research files to identify all adult recipients of first HTA between October 1, 1987, and September 30, 2019. We excluded simultaneous liver ($n = 467$), isolated lung and simultaneous heart-lung ($n = 41,554$), simultaneous pancreas ($n = 14$), any other previous transplant ($n = 2617$), pediatric patients aged <18 years ($n = 9504$), patient with unknown age ($n = 8$), and missing patient status information ($n = 60$). SKHT recipients were confirmed by merging the thoracic data with kidney-pancreas data. A total of 61,410 HTA and 1507 SKHT recipients were included in the final analysis (Figure 1). This study was exempted for full review by the Institutional Review Board at Beth Israel Deaconess Medical Center.

Study Design

This is a retrospective cohort study. We compared the baseline characteristics and outcomes of SKHT and HTA recipients. Outcomes included patient survival, cardiac graft survival, and new post-transplant dialysis requirement. Cox multivariate analysis was performed to compare risk of death and graft loss between SKHT and HTA. For cardiac graft survival, patients were censored for death at the last available follow-up visit. We also stratified patients based on pretransplant

dialysis need and analyzed patient survival between SKHT and HTA. We then performed a logistic regression analysis to identify factors associated with receipt of SKHT as compared with HTA. A separate logistic regression analysis was performed to identify factors associated with new post-transplant dialysis requirement in SKHT and HTA recipients not on pretransplant dialysis.

Definitions

The baseline characteristics included age, gender, race, recipient comorbidities, body mass index, human leukocyte antigen mismatch, pretransplant dialysis, and donor comorbidities. Mechanical cardiac support is a composite of any pretransplant ventricular assist device and/or intra-aortic balloon pump use. For underlying diagnosis, we broadly categorized them into dilated (nonischemic) cardiomyopathy, ischemic cardiomyopathy, restrictive cardiomyopathy, congenital causes, and valvular defects.

Acute cardiac rejection rates were based on determination made in the UNOS data or treatment for rejection within first post-transplant year. New post-transplant dialysis need was identified as reported in the UNOS database.

Statistical Analysis

Baseline characteristics were described using mean ($\pm$SD), median (with interquartile range), or frequencies (percentage) as appropriate. Comparisons between groups were made using the Student t test or Kruskal–Wallis test for continuous variables and χ^2 test for categorical variables. Patient and graft survival were estimated using Kaplan–Meier curves, and the log-rank test was used to compare death-censored graft survival between the 2 groups. Cox regression analysis was used to study the factors associated with cardiac graft failure. All recipient, donor, and transplant factors that were significantly associated with the outcome ($P \leq 0.10$) were included in the multivariate model. Logistic regression analysis was used to study factors associated with receiving SKHT compared with HTA. Missing values were considered as a separate variable in the regression models. All P values were 2-tailed, and values ≤ 0.05 were considered statistically significant. STATA version 15.1, SE (StataCorp LP, College Station, TX) was used for all statistical analyses.

RESULTS

From October 1, 1987, to September 30, 2019, a total of 61,410 adults underwent HTA and 1507 underwent SKHT. Of these, 36,631 HTA and 384 SKHT were performed in the 21 years between 1987 and 2007, whereas 24,779 HTA and 1123 SKHT were performed in the 12
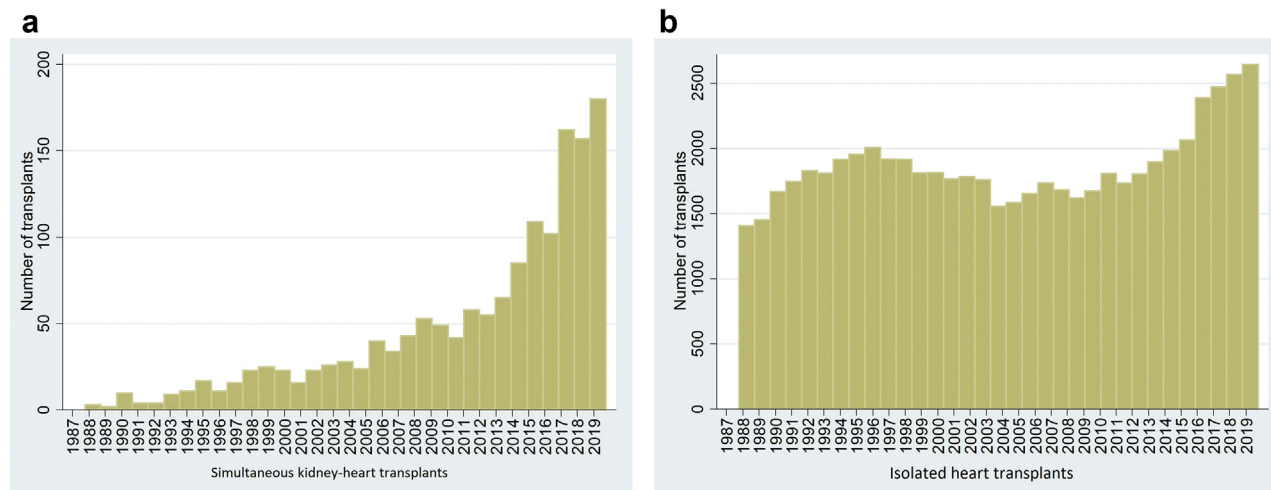
Figure 2. Histograms revealing the trend of number of (a) simultaneous heart and kidney transplants and (b) heart-alone transplants performed annually in the United States from 1987 to 2019.

years between 2008 and September 2019. Although the number of heart transplants performed annually in the United States increased modestly by 61% between 2000 and 2019 (Figure 2b), the number of SKHTs increased by a staggering 650% (Figure 2a).

Baseline Demographics
Baseline Characteristics
Baseline characteristics stratified by HTA versus SKHT are listed in Table 1. There were more males (80.6% vs. 76.3%), African Americans (30% vs. 15.8%), individuals with diabetes (43.8% vs. 18.8%), and patients dependent on dialysis (53.2% vs. 2.8%) in SKHT compared with HTA recipients, whereas HTA recipients were younger (55 vs. 57 years) and had lower body mass index (26 vs. 26.8) as compared with SKHT recipients.

Underlying Diagnoses
The predominant causes of heart failure in both groups were nonischemic dilated cardiomyopathy (45%) and ischemic cardiomyopathy (43%). The only significant difference between the 2 groups was in restrictive cardiomyopathy. Almost 4% of SKHT recipients had restrictive cardiomyopathy as compared with 2% among the HTA recipients.

Mechanical and Inotropic Support
The use of mechanical cardiac support at the time of transplant was significantly more frequent in the SKHT group (35%) as compared with the HTA group (29%). Left ventricular assist device was the modality of choice with 18.4% SKHT recipients as compared with 14.8% HTA recipients. Intra-aortic balloon pump was used in 11.5% SKHT and 9% HTA recipients ($P =$ 0.001). Similarly, inotropic support was required in a higher number of SKHT recipients (56.4%) as compared with HTA recipients (46.5%) ($P < 0.001$).

Donor Characteristics
The median age of donors in both groups was 29 years, and most were White males. A total of 10% to 12% had hypertension and only 1% to 2% had diabetes. The predominant cause of death was trauma in both groups. Anoxia was more common in donors to the SKHT group (23.7% vs. 15.3%; $P < 0.001$), whereas cerebrovascular disease was more common in donors to the HTA group (23.5% vs. 19.2%; $P < 0.001$) (Table 1). The median left ventricular ejection fraction of donors of both groups was 60%. As expected, most of the transplants were gender matched (75.7% in SKHT vs. 72.5% in HTA; $P = 0.007$) to ensure compatibility between the cardiac graft and recipient thoracic cavity size.

SKHT Versus HTA
Pretransplant dialysis (odds ratio [OR] = 16.1), GFR < 60 ml/min per 1.73 m^2 (OR = 60.6 for GFR < 30, OR = 9.7 for GFR = 30–44, and OR = 2.3 for GFR = 45–59), recipient age > 60 years (OR = 1.4), male gender (OR = 1.8), African American race (OR = 1.7), and recipient diabetes (OR = 2.0) were associated with higher odds of receiving a simultaneous heart-kidney as compared with heart-alone transplant in a multivariate analysis (Table 2).

Post-Transplantation Outcomes
Patient Survival
The overall median patient survival was similar between SKHT (12.4 years) and HTA (11.3 years, $P =$ 0.053) (Figure 3). In patients who were dialysis dependent before transplantation, SKHT recipients had a significantly better median survival compared with HTA recipients (12.4 vs. 9.9 years; $P < 0.01$) (Table 3 and Figure 4). Among the non–dialysis-dependent patients, those with eGFR < 45 had a significantly better

Table 1. Baseline characteristics in patients undergoing simultaneous kidney and heart transplant or heart transplant alone

Total (N = 62,917)	SKHT (n = 1507)	HTA (n = 61,410)	P value
Recipient characteristics			
Age (yr), median (IQR)	57 (49–63)	55 (46–61)	<0.001
Male, %	80.6	76.3	<0.001
African American, %	30	15.8	<0.001
White, %	55.5	74.5	<0.001
BMI, median (IQR)	26.8 (23.4–30.5)	26 (23.1–29.6)	<0.001
Diabetes, % (n)	43.8 (661)	18.8 (11,560)	<0.001
Pretransplant dialysis, %	53.2	2.8	<0.001
GFR (ml/min per 1.73 m², median [IQR]	26.4 [15.3–39.3]	66.1 [50.9–83.6]	0.0001
Median serum creatinine (mg/dl) at transplant [IQR]	2.7 (1.9–4.3)	1.2 (1.0–1.5)	<0.001
HLA mismatch, mean (SD)	4.7 (1.04)	4.6 (1.08)	0.027
Underlying diagnosis			
Congenital, %	25 (1.7)	1458 (2.4)	0.07
Valvular, %	24 (1.6)	1442 (2.4)	0.055
Dilated cardiomyopathy, %	678 (45)	28,031 (45.6)	0.61
Ischemic cardiomyopathy, %	652 (43.3)	26,960 (43.9)	0.62
Restrictive cardiomyopathy, %	60 (4)	1273 (2)	<0.001
Cardiac support			
Mechanical cardiac support, %	35.0	28.9	<0.001
LVAD pretransplant, %	18.4	14.8	<0.001
RVAD pretransplant, %	1.8	1.1	0.009
BiVAD pretransplant, %	1.7	1.0	0.02
VAD, unknown type, pretransplant, %	6.8	6.7	0.89
IABP pretransplant, %	11.5	8.9	0.001
Inotrope use pretransplant, %	56.4	46.5	<0.001
Donor factors			
Age, median (IQR)	29 (22–40)	29 (21–40)	0.054
Male, %	73.7	70.5	0.009
African American, %	13.9	13.2	0.38
White, %	64.0	71.2	<0.001
Hypertension, %	12.5	10.9	0.044
Diabetes mellitus, %	1.7	2.2	0.19
Heart ischemia time, mean (SD), h	3.1 (1.01)	3.0 (1.04)	0.052
Donor cause of death			
Anoxia, % (n)	23.7 (358)	15.3 (9426)	<0.001
Cerebrovascular disease, % (n)	19.2 (289)	23.5 (14,409)	<0.001
Trauma, % (n)	53.9 (813)	52.2 (32,024)	0.19
CNS tumor, % (n)	0.5 (7)	0.7 (437)	0.25
Donor LVEF, %, median (IQR)	60 (55–65)	60 (56–65)	1.00
Donor-recipient gender match, % (n)	75.7 [1140]	72.5 [44,512]	0.007

BiVAD, biventricular assist device; BMI, body mass index; CNS, central nervous system; GFR, glomerular filtration rate; HLA, human leukocyte antigen; HTA, heart transplant alone; IABP, intra-aortic balloon pump; IQR, interquartile range; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; RVAD, right ventricular assist device; SKHT, simultaneous kidney and heart transplant; VAD, ventricular assist device.

Table 2. Factors associated with receiving SKHT as compared with HTA

Factors	Univariate OR [95% CI]	P value	Multivariate OR [95% CI]	P value
Pretransplant dialysis	39.6 [35.4–44.3]	<0.001	16.1 [13.9–18.6]	<0.001
GFR (ml/min per 1.73 m²)				
<30	114.2 [84.7–153.8]	<0.001	60.6 [44.2–83.1]	<0.001
30–44	10.9 [8.0–14.8]	<0.001	9.7 [7.1–13.4]	<0.001
45–59	2.38 [1.70–3.32]	<0.001	2.3 [1.6–3.2]	<0.001
60–89	1.10 [0.78–1.56]	0.57	1.12 [0.79–1.59]	0.53
≥90	1.0		1.0	
Missing GFR	0.24 [0.13–0.45]	<0.001	0.30 [0.16–0.55]	<0.001
Age (yr)				
18–29	0.62 [0.47–0.82]	0.001	1.04 [0.72–1.50]	0.85
30–59	1.0		1.0	
>60	1.47 [1.32–1.63]	<0.001	1.38 [1.21–1.59]	<0.001
Male gender	1.29 [1.13–1.46]	<0.001	1.81 [1.54–2.14]	<0.001
African American race	2.27 [2.03–2.55]	<0.001	1.73 [1.38–2.16]	<0.001
White race	0.43 [0.38–0.47]	<0.001	0.60 [0.49–0.73]	<0.001
Diabetes mellitus	3.37 [3.03–3.73]	<0.001	2.00 [1.74–2.29]	<0.001
Mechanical cardiac support	1.32 [1.19–1.47]	<0.001	0.95 [0.83–1.10]	0.49
Inotrope use	1.48 [1.34–1.65]	<0.001	0.97 [0.85–1.11]	0.70

GFR, glomerular filtration rate; HTA, heart transplant alone; OR, odds ratio; SKHT, simultaneous kidney and heart transplant.
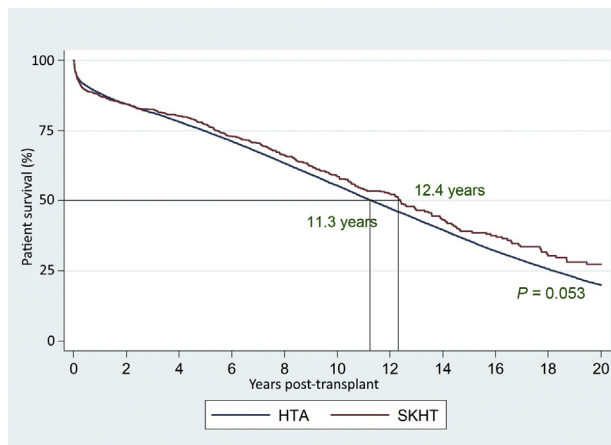
compared with 1987 to 2007 whereas it did not change for SKHT recipients (see Supplementary Figure S1).

As compared with HTA, the following factors were associated with improved patient survival in SKHT recipients (Table 4): pretransplant dialysis (hazard ratio [HR] = 1.52 [1.40–1.65]); eGFR < 30 (HR 1.74 [1.60–1.88]) or eGFR 30–44 (HR 1.37 [1.30–1.45]) or eGFR 45–59 (HR = 1.20 [1.14–1.26]); age 18–29 years (HR = 1.29 [1.21–1.37]) or age > 60 years (HR = 1.22 [1.18–1.26]); African American race (HR = 1.38 [1.29–1.46]); diabetes mellitus (HR = 1.26 [1.22–1.30]); and mechanical cardiac support (HR = 1.08 [1.04–1.12]). Transplant procedure performed between 2008 and 2019 was associated with decreased survival for SKHT recipients as compared with HTA recipients (HR = 0.72 [0.69–0.74]).

Cardiac Graft Survival

The median cardiac graft survival in SKHT recipients was 12.5 years, significantly better than the 11.2 years in HTA recipients (P = 0.008) (Figure 6). Among the non–dialysis-dependent patients, those with eGFR < 45 had a significantly better cardiac graft survival with SKHT as compared with HTA (13 vs. 10.2 years; P < 0.0001) (Figure 7).

In a 5-year follow-up, 18.6% cardiac grafts failed in the SKHT recipients as compared with 24% in the HTA recipients. As compared with functioning cardiac grafts in the HTA group, new post-transplant dialysis

patient survival with SKHT as compared with HTA (12.4 vs. 10 years; P < 0.0001). Patients with eGFR ≥ 45 did not derive any survival advantage from SKHT as compared with HTA (Figure 5). Similarly, use of mechanical cardiac support at the time of transplant did not affect patient survival.

When stratified for eras, survival of HTA recipients improved significantly between 2008 and 2019 as

Figure 3. Kaplan–Meier curve of overall patient survival in SKHT and HTA recipients. HTA, heart transplant alone; SKHT, simultaneous kidney and heart transplant.
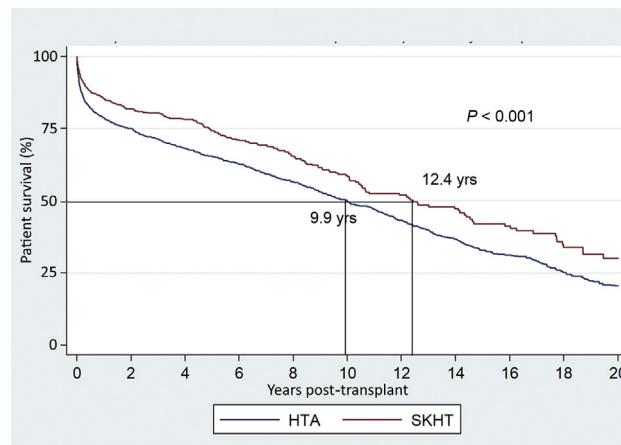
need (HR = 3.37 [3.20–3.54]), pretransplant dialysis (HR = 1.45 [1.33–1.57]), mechanical cardiac support (HR = 1.51 [1.45–1.57]), age < 30 years (HR = 1.30 [1.21–1.38]) or >60 years (HR = 1.09 [1.05–1.13]), and GFR < 30 ml/min (HR = 1.28 [1.17–1.40]) or GFR 30–59

Table 3. Patient and cardiac graft survival outcomes

Outcomes	SKHT	HTA	P value
Median cardiac graft survival in yr [IQR]	12.51 [5.4–….]	11.2 [4.7–18.5]	0.008
Median overall patient survival in yr [IQR]	12.4 [5.4–…]	11.3 [4.9–18.2]	0.053
Median cardiac graft survival in non–dialysis-dependent recipients with eGFR < 45 ml/min per 1.73 m² [IQR]	13 [6.4–…]	10.2 [3.5–…]	<0.0001
Median cardiac graft survival in non–dialysis-dependent recipients with eGFR ≥ 45 ml/min per 1.73 m² [IQR]	12.2 [5.3–…]	11.5 [5.0–…]	0.95
Median patient survival in pretransplant dialysis-dependent recipients [IQR]	12.4 [4.9–…]	9.9 [1.9–18.1]	<0.001
Median patient survival in non–dialysis-dependent recipients with eGFR < 45 ml/min per 1.73 m² [IQR]	12.4 [6.4–…]	10.0 [3.6–…]	<0.0001
Median patient survival in non–dialysis-dependent recipients with eGFR ≥ 45 ml/min per 1.73 m² [IQR]	12.2 [5.3–…]	11.6 [5.2–…]	0.69
Median patient survival in recipients requiring mechanical cardiac support [IQR]	13	12.04	0.35
New post-transplant dialysis			
Non–dialysis-dependent recipients requiring post-transplant dialysis; % (n)	46.4 (700)	6.6 (4097)	<0.001
Median patient survival in recipients with new post-transplant dialysis; yr [IQR]	11.9 [4.3– ….]	2.7 [0.11–12.8]	<0.001

Note. The "…" reflects that the third quartile extends beyond the period of observation and therefore could not be calculated.
eGFR, estimated glomerular filtration rate; HTA, heart transplant alone; IQR, interquartile-quartile range; SKHT, simultaneous kidney and heart transplant.

Figure 4. Kaplan–Meier curve of patient survival in SKHT and HTA recipients on dialysis before transplantation. HTA, heart transplant alone; SKHT, simultaneous kidney and heart transplant; yrs, years.

ml/min (HR = 1.06 [1.01–1.13]) were significantly associated with cardiac graft loss at 5 years.

Among the HTA recipients, 17.2% received treatment for acute rejection episode in the first post-transplant year as compared with 7.2% in SKHT recipients (*P* < 0.001).

When stratified for eras, cardiac graft survival of HTA recipients improved significantly between 2008 and 2019 as compared with 1987 to 2007 whereas it did not change for SKHT recipients (see Supplementary Figure S2).
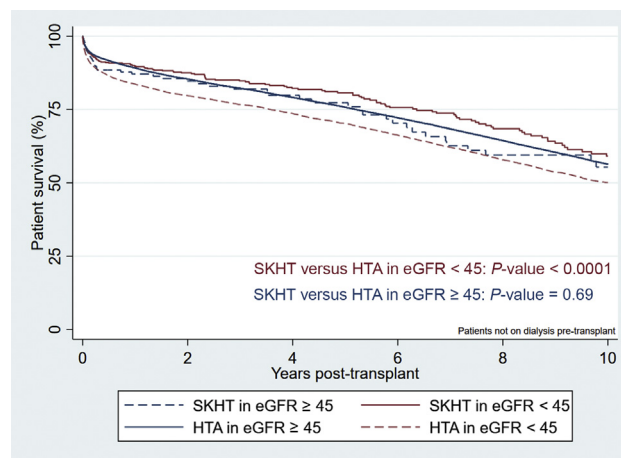
Subgroup Analysis
Post-Transplant Dialysis

Patients who were not on dialysis before transplant but newly required dialysis post-transplant were analyzed separately. A significantly higher number of SKHT recipients (46.4%) not on dialysis pretransplant ended

Figure 5. Kaplan–Meier curve of patient survival in non–dialysis-dependent SKHT and HTA recipients, stratified on eGFR. HTA, heart transplant alone; eGFR, estimated glomerular filtration rate; SKHT, simultaneous kidney and heart transplant.
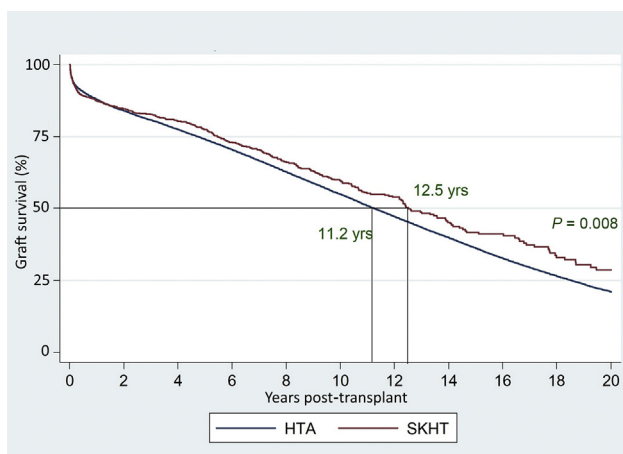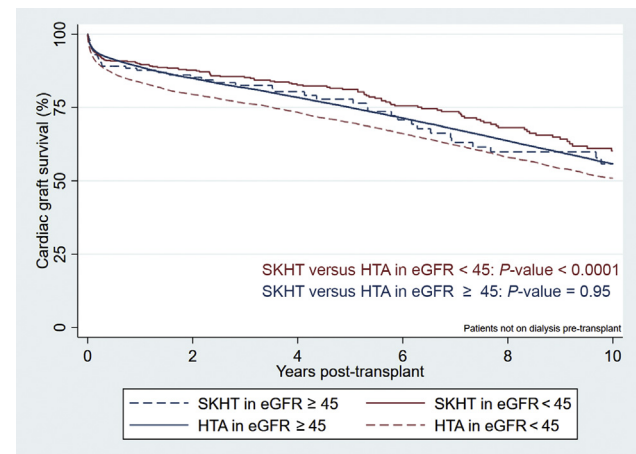
Table 4. Cox regression for patient survival in SKHT as compared with HTA recipients at 10-year follow up

Factors	Hazard ratio [95% CI]	P value
Pretransplant dialysis	1.52 [1.40–1.65]	<0.001
eGFR at transplant (ml/min per 1.73 m^2)		
<30	1.74 [1.60–1.88]	<0.001
30–44	1.37 [1.30–1.45]	<0.001
45–59	1.20 [1.14–1.26]	<0.001
60–89	1.05 [1.00–1.10]	0.054
≥90	1.0	
Missing GFR	1.36 [1.26–1.46]	<0.001
Age in yr		
18–29	1.29 [1.21–1.37]	0.001
30–59	1.0	
>60	1.22 [1.18–1.26]	<0.001
Male gender	1.01 [0.97–1.05]	0.55
African American race	1.38 [1.29–1.46]	<0.001
White race	1.03 [0.98–1.10]	0.164
Diabetes mellitus	1.26 [1.22–1.30]	<0.001
Mechanical cardiac support	1.08 [1.04–1.12]	<0.001
Transplant between 2008 and 2019	0.72 [0.69–0.74]	<.001

eGFR, estimated glomerular filtration rate; GFR, glomerular filtration rate; HTA, heart transplant alone; SKHT, simultaneous kidney and heart transplant.

up requiring post-transplant dialysis as compared with HTA recipients (6.6%; $P < 0.001$). The median survival time of this subgroup of SKHT recipients was significantly longer at 11.9 years when compared with 2.7 years in the similar subgroup of HTA recipients ($P < 0.001$) (Table 3 and Figure 8).
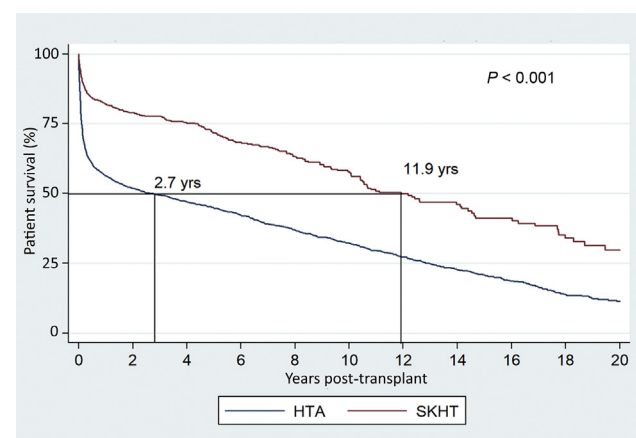
Age < 30 years (OR = 1.27 [1.10–1.47]), higher body mass index (OR = 1.02 [1.01–1.02]), reduced GFR (OR = 9.46 [8.34–10.7] for GFR < 30, OR = 2.68 [2.38–3.02] for 30–44, OR = 1.99 [1.78–2.22] for GFR = 45–59, and OR = 1.3 [1.17–1.44] for 60–89), mechanical cardiac support (OR = 1.58 [1.51–1.73]), recipient diabetes (OR = 1.15 [1.07–1.24]), inotropic support (OR = 1.11 [1.04–1.18]), previous sternotomy (OR = 1.61 [1.51–1.73]), African American donor (OR = 1.1 [1.0–

Figure 7. Kaplan–Meier curve of cardiac graft survival in non–dialysis-dependent SKHT and HTA recipients, stratified on eGFR. HTA, heart transplant alone; eGFR, estimated glomerular filtration rate; SKHT, simultaneous kidney and heart transplant.

1.2]), and donor history of hypertension (OR = 1.4 [1.3–1.5]) were significant risk factors for requiring dialysis post-transplant in multivariate analysis (Table 5). Donor male gender seemed to be associated with reduced risk of requiring post-transplant dialysis (OR = 0.83 [0.77–0.89]).

DISCUSSION

In this study, we evaluated post-transplant outcomes of patients who received SKHT and HTA. Furthermore, we analyzed the same outcomes in a subgroup of patients who required RRT after transplantation. We found similar patient survival between SKHT and HTA but improved cardiac graft survival in SKHT as compared with HTA recipients. The survival in patients requiring RRT post-transplant was significantly

Figure 6. Kaplan–Meier curve of cardiac graft survival in SKHT and HTA recipients. HTA, heart transplant alone; SKHT, simultaneous kidney and heart transplant; yrs, years.

Figure 8. Kaplan–Meier curve of patient survival in SKHT and HTA recipients not on pretransplant dialysis but newly requiring dialysis after transplantation. HTA, heart transplant alone; SKHT, simultaneous kidney and heart transplant; yrs, years.

Table 5. Univariate and multivariate logistic regression for risk of new post-transplant dialysis requirement among SKHT and HTA recipients not on dialysis pretransplant

Factors	Univariate		Multivariate	
	OR [95% CI]	*P* value	OR [95% CI]	*P* value
Recipient factors				
Age				
18–29	0. 88 [0.77–1.01]	0.07	1.27 [1.10–1.47]	0.001
30–59	1.0		1.0	
≥60	1.37 [1.29–1.46]	<0.001	1.004 [0.94–1.07]	0.885
Male gender	1.07 [0.98–1.14]	0.05	1.22 [1.13–1.32]	<0.001
White race	0.74 [0.70–0.80]	<0.001	0.84 [0.76–0.93]	0.001
African American race	1.31 [1.22–1.42]	<0.001	1.05 [0.94–1.18]	0.35
BMI	1.05 [1.042–1.054]	<0.001	1.02 [1.01–1.02]	<0.001
GFR (ml/min per 1.73 m^2)				
<30	8.71 [7.72–9.82]	<0.001	9.46 [8.34–10.7]	<0.001
30–44	2.52 [2.25–2.82]	<0.001	2.68 [2.38–3.02]	<0.001
45–59	1.89 [1.70–2.10]	<0.001	1.99 [1.78–2.22]	<0.001
60–89	1.24 [1.12–1.38]	<0.001	1.30 [1.17–1.44]	<0.001
≥90	1.0		1.0	
Missing	0.12 [0.094–0.15]	<0.001	0.24 [0.19–0.32]	<0.001
Diabetes mellitus	1.89 [1.77–2.02]	<0.001	1.15 [1.07–1.24]	<0.001
Previous sternotomy	2.30 [2.17–2.44]	<0.001	1.61 [1.51–1.73]	<0.001
Transplant factors				
HLA mismatch	1.02 [0.99–1.05]	0.19		
Mechanical cardiac support	1.77 [1.67–1.89]	<0.001	1.58 [1.51–1.73]	<0.001
Inotropic support	1.33 [1.25–1.41]	<0.001	1.11 [1.04–1.18]	0.001
Donor factors				
Age	1.02 [1.015–1.020]	<0.001	1.01 [1.005–1.01]	<0.001
African American race	1.17 [1.08–1.27]	<0.001	1.10 [1.006–1.20]	0.035
Male gender	0.88 [0.82–0.94]	<0.001	0.83 [0.77–0.89]	<0.001
Hypertension	2.39 [2.26–2.52]	<0.001	1.40 [1.30–1.51]	<0.001

BMI, body mass index; GFR, glomerular filtration rate; HLA, human leukocyte antigen; HTA, heart transplant alone; OR, odds ratio; SKHT, simultaneous kidney and heart transplant.

better in those who received SKHT as compared with HTA.

Heart and kidneys are physiologically interdependent organs, and hence, failure of either could affect the other, referred to as the cardiorenal syndromes.[9] Systemic diseases such as diabetes mellitus, hypertension, and amyloidosis can also affect both these organs by common pathophysiologic mechanisms. SKHT accounted for 6% of all heart transplants in 2019, as compared with only 1.3% in 2000.[8]

In our analysis of 1507 SKHT from the UNOS/OPTN database, we found excellent overall patient and graft survival. The median survival of 12.4 years in SKHT recipients and 11.3 years in HTA recipients is consistent with those of previous single-center[6,10,11] and large database studies.[2–4]

Improved Patient Survival With SKHT

Our data analysis reveals that as compared with HTA, patients who received SKHT were more likely to be dialysis dependent pretransplant or had reduced renal function. They were also more likely to be African Americans, 60 years old or older, and have diabetes mellitus (Table 2).

Although patient survival was not significantly different between SKHT and HTA recipients, there was a trend toward improved survival with SKHT ($P = 0.053$). This finding is in line with that of previous analysis of the UNOS database by Gill et al.[4] and Chou et al.[7] The lower incidence of acute cardiac rejection in SKHT recipients (7.2%) as compared with HTA recipients (17.2%) may in part be responsible for this survival advantage. Hence, SHKT may be a superior option as compared with HTA in heart transplant candidates with severe renal dysfunction, especially patients with eGFR < 45 ml/min per 1.73 m^2.

Notably, our analysis revealed a significant survival advantage with SKHT compared with HTA among the subgroup of recipients who were on dialysis before transplantation (median = 12.4 years compared with 9.9 years). This may be reflective of poor hemodynamics owing to intradialytic hypotension,[12] interdialytic fluid gain,[13] and increased systemic inflammation associated with dialysis.[14,15] Another possible explanation is reduced left ventricular hypertrophy and ischemia in transplanted patients as compared with patients on dialysis.[16] There was no

significant survival difference in recipients with eGFR $\geq$ 45 ml/min per 1.73 m^2 (12.2 vs. 11.6 years).

Improved Cardiac Graft Survival in SKHT Recipients

One-year cardiac graft survival was similar between HTA and SKHT recipients. The rate of acute cardiac graft rejection in SKHT recipients was lower at 7.2% as compared with 17.2% in HTA recipients. This is consistent with previous reports suggesting cardiac immunoprotection accorded by the simultaneously transplanted kidney.[4,7] Of note, Chou et al.[7] revealed similar immunoprotection accorded by a simultaneously transplanted liver.[7] The long-term cardiac graft survival was significantly better in the SKHT group at 5- and 10-years post-transplant as compared with HTA recipients. This improved cardiac graft survival may in turn improve overall patient survival among the combined organ transplant recipients. A definitive mechanism for this partial immunologic tolerance is not known.

Post-Transplant Dialysis

Patients not on pretransplant dialysis but newly requiring dialysis post-transplant had a significantly greater survival in the SKHT group (11.9 years compared with 2.7 years in HTA). When compared with recipients not requiring dialysis, those who required dialysis post-transplant were more likely younger than 30 years, had preexisting renal dysfunction, had previous sternotomy, and required either ventricular assist device and/or intra-aortic balloon pump support.

Reoperative sternotomy is associated with increased transplant surgery time owing to previous adhesions and hence elevates risk of intraoperative renal ischemia.[17] Similarly, requiring mechanical cardiac support with ventricular assist devices or intra-aortic balloon pump predisposes to renal ischemia and increases the risk of renal failure requiring dialysis post-transplant.[18]

Notably, HTA recipients with a GFR < 30 ml/min and between 30 and 44 ml/min were 9.5 times and 2.7 times more likely to require dialysis post-transplant, respectively. These data suggest considering patients with severe preexisting renal dysfunction for a simultaneous kidney transplant. The improved survival translates into increased utility of these organs in an era wherein the demand for organs far exceeds the supply. Along similar lines, Russo et al.[19] recommended a GFR cutoff < 33 ml/min, Karamlou et al.[2] <37 ml/min, Raichlin et al.[3] <40 ml/min, and Kilic et al.[20] <60 ml/min. In addition to these conflicting recommendations, the potential of renal recovery after cardiac

transplantation makes it difficult to derive a standardized GFR cutoff that would justify SKHT as compared with HTA.[21] Therefore, some authors have promulgated a staged approach of kidney transplant in HTA recipients who have persistent kidney dysfunction.[22] Our data suggest that non–dialysis-dependent patients with eGFR $\geq$ 45 may be good candidates for a staged approach if they continue to have persistent RRT requirement post-HTA.

Although only 6.6% of non–dialysis-dependent HTA recipients newly required dialysis post-transplant as compared with 46.4% of SKHT recipients, we contend that most of the latter group had delayed graft function and hence required dialysis only temporarily. This explains the significantly better patient survival in this group of SKHT recipients. We are limited to speculation because of the lack of more specific data in the UNOS/OPTN heart transplant database.

This study will help providers identify heart transplant recipients at risk of post-transplant renal failure requiring dialysis and hence prioritize them for combined organ transplantation. In addition, these data hint at patients who are not at high risk of renal failure after HTA and can be monitored postoperatively for a staged kidney transplant if at all required.

Limitations

In any retrospective analysis, there are certain limitations that should be considered while interpreting results. We used 2 different data files of the UNOS/OPTN database, the thoracic and kidney transplant files. There were discrepancies in the reporting of some variables between these 2 data files. We attempted to minimize the impact of such discrepancies by merging the 2 data sets and limiting our multivariate analysis to the thoracic data set. Despite our best efforts, there may be residual selection bias in the retrospective analysis.

Second, diagnoses of various comorbidities and outcomes such as cardiac rejection are reported by individual transplant centers based on their criteria.

Finally, new post-transplant dialysis includes all recipients who required any form of dialysis after cardiac transplantation. There is no distinction, in the database, between short-term dialysis versus long-term dialysis dependence. Ideally, we would have excluded patient who required only short-term dialysis for acute kidney injury after HTA/SKHT and delayed graft function after SKHT.

CONCLUSION

In summary, we found that recipients of both SKHT and HTA have comparable patient survival with trend toward better survival with SKHT. Among patients who were on pretransplant dialysis or had an eGFR < 45 ml/

min per 1.73 m^2, SKHT offered a significant survival advantage as compared with HTA. This was not found in recipients with eGFR $\geq$ 45 ml/min per 1.73 m^2. We also found that 6.6% of non–dialysis-dependent HTA recipients newly required dialysis after HTA, and this cohort had a significantly worse survival when compared with a similar cohort of SKHT recipients. Risk factors associated with new post-transplant dialysis requirement were preexisting renal dysfunction, previous sternotomy, age $<$ 30 years, and mechanical cardiac support. Furthermore, we reveal that a simultaneously transplanted kidney reduces acute rejection of the cardiac allograft.

We believe that our results will enable better selection of candidates for simultaneous kidney and heart transplantation and guide universal policy for such combined organ transplantation. Further research is needed to prospectively identify candidates at higher risk of renal failure and/or poor renal recovery after isolated heart transplant. These patients may benefit from sequential kidney transplant after heart transplantation.

DISCLOSURE

ACKNOWLEDGMENTS

DATA AVAILABILITY

The data that support the findings of this study are openly available in the UNOS/OPTN database at https://optn.transplant.hrsa.gov/data/.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1. Kaplan–Meier curve of patient survival in SKHT and HTA performed between 1987 and 2007 versus between 2008 and 2019.

Figure S2. Kaplan–Meier curve of cardiac graft survival in SKHT and HTA performed between 1987 and 2007 versus between 2008 and 2019.

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