The Survival Benefit of Simultaneous Heart-Kidney Transplantation Extends Beyond Dialysis-Dependent Patients

Arman Kilic, MD, Joshua C. Grimm, MD, Glenn J. R. Whitman, MD, Ashish S. Shah, MD, Kaushik Mandal, MD, John V. Conte, MD, and Christopher M. Sciortino, MD, PhD

Division of Cardiac Surgery, The Johns Hopkins Hospital, Baltimore, Maryland

Background. **This study evaluated the effect of simultaneous heart-kidney transplantation (SHK) on survival stratified by preoperative renal function.**

Methods. **Patients undergoing SHK or heart transplant alone (HTA) between 1992 and 2012 were identified in the United Network for Organ Sharing database. Patients were primarily stratified by the need for dialysis before transplantation. Nondialysis patients were further stratified by preoperative glomerular filtration rate (GFR) and likelihood of postoperative development of renal failure requiring new-onset dialysis (high risk defined as ≥75th percentile according to a previously derived and validated risk score). The primary outcome was 5-year survival, evaluated by Kaplan-Meier and multivariable logistic regression analyses.**

Results. **Included were 665 (2%) SHK and 38,488 (98%) HTA patients. SHK improved 5-year survival in dialysis-dependent patients (69% vs 54%, $p < 0.001$), with no survival difference in patients with a preoperative GFR ≥60 mL/min/1.73 m^2 (84% SHK vs 77% HTA, $p = 0.34$). In patients with a preoperative GFR of less than 60 mL/min/1.73 m^2, being high risk for postoperative new-onset dialysis discriminated those patients who would benefit from SHK (5-year survival low risk: 82% SHK vs 76% HTA, $p = 0.27$; 5-year survival high risk: 86% SHK vs 67% HTA, $p < 0.001$). Risk-adjusted analysis confirmed these findings. SHK comprised only 2.6% of heart transplants in patients with a preoperative GFR of less than 60 mL/min/1.73 m^2 who were at high risk for postoperative renal failure.**

Conclusions. **SHK improves long-term survival not only in dialysis-dependent patients but also in patients with reduced preoperative GFR who are at high risk for postoperative new-onset dialysis. Expansion of SHK into this subset warrants further study, especially considering its low current utilization.**

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Depending on the definition used, acute renal failure can occur in up to 70% of heart transplant patients postoperatively, with chronic renal failure developing in about 10% by 5 years after transplantation [1–4]. Because developing renal failure requiring renal replacement therapy poses a substantial risk of death, reduced quality of life, and increased resource utilization, efforts to reduce its occurrence have been underscored [5–7]. Simultaneous heart-kidney transplantation (SHK) may be one strategy to mitigate this risk. SHK is uncommonly performed in the United States, and patient selection for SHK remains incompletely understood. In this study, we evaluated the effect of SHK on long-term survival compared with heart transplant alone (HTA) after stratifying patients according to preoperative renal function.

Patients and Methods

The Johns Hopkins Hospital Institutional Review Board approved this study.

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Address correspondence to Dr Sciortino, Division of Cardiac Surgery, The Johns Hopkins Hospital, 1800 Orleans St, Sheikh Zayed Tower, Ste 7107, Baltimore, MD 21287; e-mail: csciort2@jhmi.edu.

Data Acquisition

SHK and HTA patients who underwent their transplantation between January 1, 1992, and December 31, 2012, were identified in the United Network for Organ Sharing (UNOS) database. The UNOS registry provides deidentified patient-level data on all solid organ transplants performed in the United States.

Data Analysis

Baseline recipient, donor, and transplant-related characteristics were compared between the SHK and HTA cohorts. Patients were primarily stratified by the need for dialysis before transplantation. Patients who were not receiving dialysis were further stratified according to a preoperative glomerular filtration rate (GFR) of 60 mL/min/1.73 m^2 or more vs less than 60 mL/min/1.73 m^2 and the likelihood of developing postoperative new-onset renal failure requiring dialysis (low vs high risk). Preoperative GFR was calculated using methods previously described [8]. High risk was defined as being in the 75th percentile or greater (score ≥27) of all recipients according to a risk score for postoperative new-onset renal failure requiring dialysis that was previously derived and validated by our group using UNOS data (Table 1) [9].

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Table 1. Risk Score for Postoperative New-Onset Renal Failure Requiring Dialysis After Heart Transplantation

Component	Points Assigned
Age ≥60 years	5
Heart failure etiology	
Dilated cardiomyopathy	0
Ischemic heart disease	0
Congenital heart disease	16
Other	6
Creatinine clearance, mL/L/min	
≥60	0
30–59	8
<30	15
Serum bilirubin, mg/dL	
<1	0
1–1.9	5
2–2.9	6
≥3	7
Body mass index, kg/m^2	
<18.5	0
18.5–24.9	0
25–29.9	0
30–34.9	5
≥35	6
Diabetes mellitus	5
Mechanical ventilation	9
Intensive care unit	5
Recent infection	6
Blood transfusion on waiting list	6
Donor age, y	
<30	0
30–49	5
≥50	7
Biatrial anastomosis	5
Ischemic time, h	
<4	0
4–5.9	6
≥6	8
Total points possible	100

A trend analysis was performed. In this analysis, the proportions of heart transplant recipients undergoing SHK vs HTA for each of the stratified cohorts was compared between an early (transplant between 1992 and 2002) and late era (transplant between 2003 and 2012). Changes in the proportion of SHK performed between the early and late era were reported as a factor of the baseline proportion in the early era.

The primary outcome was 5-year survival. Survival was modeled using the Kaplan-Meier method. Survival curves were compared between those undergoing SHK vs HTA within each stratified cohort using the log-rank test. Multivariable logistic regression analysis that risk-adjusted for other recipient, donor, and transplant-related variables that were associated with 5-year mortality in univariate logistic regression (exploratory $p < 0.20$) and had less than 20% missing data was performed to evaluate the independent effect of SHK on survival.

Continuous variables were compared using the unpaired Student t test. Categoric variables were compared using the χ^2 test. A two-tailed p value of less than 0.05 was considered statistically significant. All data and statistical analyses were performed with Stata 11 software (StataCorp LP, College Station, TX).

Results

Baseline Characteristics

A total of 39,153 heart transplants were identified during the study period, including 665 SHKs (2%) and 38,488 HTAs (98%). Demographic data were similar between the SHK and HTA cohorts, with the exception of race, with a higher proportion of SHK patients being African American (Table 2). Recipient factors related to preoperative renal disease were also different, as expected. The average serum creatinine was more than double, and the mean GFR was approximately half in the SHK vs HTA cohort. A higher percentage of SHK patients were also diabetic. The overall renal failure risk score was significantly higher in patients undergoing SHK. A comparison of distributions according to preoperative renal function showed a significantly lower percentage of SHK patients had a GFR of 60 mL/min/1.73 m^2 or greater (6% vs 64%) and a higher percentage were receiving dialysis before transplantation (56% vs 2%) compared with HTA patients ($p < 0.001$).

The donor variables for the SHK and HTA groups were relatively well matched (Table 2). Terminal creatinine was significantly lower in patients undergoing SHK. Donor cigarette use was also less frequent in the SHK cohort. There were several differences in transplant-related variables. Moreover, patients undergoing SHK were more frequently matched for sex and cytomegalovirus status with their donor but were matched for race less frequently. The biatrial technique was used less frequently in SHK recipients. Mean ischemic times were comparable.

The renal failure risk score was predictive of postoperative renal failure requiring dialysis for the overall study population (odds ratio [OR], 1.07; $p < 0.001$), with patients having a score of greater than 20 being at threefold increased risk compared with those with a score of 20 or less (OR, 3.01; $p < 0.001$). A subanalysis of patients completely external to the original UNOS derivation cohort (external cohort who received a transplant between 1992 and 1999 or between 2011 and 2012, original cohort who received a transplant between 2000 and 2010) found that the renal failure risk score had similar predictive capability (OR, 1.07, $p < 0.001$). Patients with a score of greater than 20 were again found to be at nearly threefold increased risk of postoperative renal failure in this external subset (OR, 2.83; $p < 0.001$).

Trend Analysis

The overall use of SHK more than doubled between the early and late era (1.0% to 2.5%; $p < 0.001$). The significant increase in the use of SHK was observed in each of the