Combined heart-kidney transplant improves post-transplant survival compared with isolated heart transplant in recipients with reduced glomerular filtration rate: Analysis of 593 combined heart-kidney transplants from the United Network Organ Sharing Database

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Objective: Criteria for simultaneous heart-kidney transplant (HKTx) recipients are unclear. We characterized the evolution of combined HKTx in the United States over time compared with isolated heart transplantation (HTx) and determined factors maximizing post-transplant survival. We focused on whether a threshold estimated glomerular filtration rate (eGFR) could be identified that justified combined transplantation.

Methods: A supplemented United Network Organ Sharing Dataset identified HTx and HKTx recipients from 2000 to 2010. eGFR was calculated for HTx and recipients were grouped into eGFR quintiles. Time-related mortality was compared among recipients, with multivariable factors sought using Cox proportional hazard regression models.

Results: We identified 26,183 HTx recipients, of whom 593 were HKTx recipients. HTx increased modestly over time (3.6%), whereas prevalence of HKTx increased dramatically (147%). Risk-unadjusted survival was similar among HTx recipients (8.4 $\pm$ 0.04 years) and HKTx recipients (7.7 $\pm$ 0.2 years) ($P = .76$). Isolated HTx recipients in the lowest eGFR quintile had decreased survival ($P < .001$), but those in the third eGFR quintile had superior survival, suggesting a benefit in this subgroup. HTx recipients in the lowest eGFR quintile (eGFR less than mean 37 mL/minute) had worse survival than combined HKTx recipients (7.1 ± 0.07 vs 7.7 ± 0.2; $P < .001$). Multivariable factors for increased mortality among HTx recipients included lower eGFR, higher recent panel reactive antibody score, older age, African American race, diabetes, longer ischemic time, and certain diagnoses.

Conclusions: Performance of combined HKTx is increasing out of proportion to isolated HTx. eGFR is an important determinant of improved HTx survival. Combined HKTx recovers post-transplant survival in patients with eGFR <37 mL/minute and can be recommended in this subgroup. (J Thorac Cardiovasc Surg 2014;147:456-61)

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The first report of simultaneous combined heart and kidney transplantation (HKTx) using the same donor was by Norman and colleagues in 1978.[1] Combined organ transplantation has since become an accepted therapy for combined kidney and cardiac failure, which frequently exist together. Although several single-institution studies have been published,[2-4] contemporary national outcomes for HKTx recipients are not known. Additionally, there are no uniformly agreed upon criteria for selecting a combined organ transplant strategy over sequential or isolated organ transplant. We sought to characterize the evolution of HKTx relative to isolated heart transplantation (HTx) in the United States and determine those factors that maximize post-transplant survival. We were particularly interested in whether a threshold estimated glomerular filtration rate (eGFR) could be identified that justified combined transplantation.

METHODS

All HTx and HKTx recipients from 2000 to 2010 were identified using a supplemented United Network for Organ Sharing (UNOS) dataset, termed

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Abbreviations and Acronyms
eGFR = estimated glomerular filtration rate
HKTx = combined heart-kidney transplant
HTx = heart transplant
LVAD = left ventricular assist device
UNOS = United Network for Organ Sharing

UNOS–Standard Transplant Analysis and Research. All HKTx procedures were performed either as simultaneous procedures, or performed sequentially within 24 hours of 1 another. The eGFR among HTx recipients was estimated using the widely accepted 4-variable Modification of Diet in Renal Disease formula for adults[5-7] and the Schwartz formula for recipients younger than age 13 years.[8,9] The 4-Modification of Diet in Renal Disease formula incorporates serum creatinine, age, race, and sex, and has been validated for patients with chronic renal disease. The Schwartz formula (eGFR = [k · height/serum creatinine]), includes a constant, k, that varies with age to account for variable muscle mass. The serum creatinine used in all calculations was obtained at the most proximate measurement before transplantation. The eGFR was then log-transformed and recipients were grouped into eGFR quintiles. Continuous variables are reported as mean ± standard deviation, or as medians with range, and are compared across groups using the Student t test (for normal distribution) or the Wilcoxon rank sum test (for non-normal distribution). Comparisons among categorical variables are presented as percentages and frequencies and were compared across groups using the χ^2 test or Fisher exact test as appropriate. The prevalence of HKTx compared with isolated HTx over time was calculated for each year of the study period. Time-related survival from HTx or HKTx were described using the Kaplan-Meier method, and risk-unadjusted differences among groups were determined using the log-rank test. Particular attention was directed at investigating an eGFR threshold at which combined HKTx survival provided a benefit over isolated HTx. Multivariable factors for time-related death were sought using Cox proportional hazard regression models. Variables considered in multivariable models are reported in Table E1. In all cases, variable transformations were explored and optimized to provide optimum calibration, and year was included in all models to account for a possible era effect. SAS software, version 9.2 (SAS Institute Inc, Cary, NC) was used for all analyses. Institutional review board approval was obtained under an expedited review for de-identified existing data.

RESULTS

Patient Characteristics

We identified 26,183 HTx recipients, of whom 593 were HKTx recipients. Although the frequency of isolated HTx increased modestly over time (3.6%), the prevalence of HKTx increased dramatically (147%) over time (Figure 1, *A* and *B*). Demographics and clinical characteristics of the study patients segregated by recipient type are shown in Table 1. The median patient age was 52 years (range 0-77 years). HKTx recipients had higher serum creatinine at the time of transplant (3.4 ± 2.8 mg/dL vs 1.2 ± 0.7 mg/dL), were older (51 ± 13 years vs 45 ± 20 years), and had a higher prevalence of diabetes (40% vs 36%), compared with HTx recipients ($P < .001$ for all). A lower proportion of HKTx recipients were on left ventricular assist device (LVAD) support compared with HTx recipients (15.2% vs 20.4%; $P = .003$), although other types of inotropic or mechanical circulatory support were similar among both groups. Wait-list times were not significantly different among recipient groups (HTx: 193 ± 351 days vs HKTx: 212 ± 322 days; $P = .14$).

Among isolated HTx recipients, the mean eGFR for grouped quintiles in ascending order was: 36.6 ± 8.9 mL/minute, 54.8 ± 4.1 mL/minute, 68.9 ± 4.2 mL/minute, 87.1 ± 6.6 mL/minute, and 140.3 ± 56.4 mL/minute, respectively. eGFR was negatively correlated with diabetes, white ethnicity, being a man, and age. The most prevalent diagnoses overall included dilated cardiomyopathy (72%), ischemic cardiomyopathy (5%), and congenital heart disease (7%). The majority of patients were white (70%) and men (73%).

Renal Failure Requiring Dialysis Among Recipients

Following transplant, 155 (26%) of the combined HKTx recipients required dialysis within 30 days, compared with 2181 (9%) of the isolated HTx recipients. Among isolated HTx recipients, 609 (22%) of 2758 patients in the lowest GFR quintile required early dialysis, compared with 16% (1115 out of 6962) and 11% (1836 out of 15781) of patients in the next 2 quintiles. Logistic regression analysis of patients receiving isolated heart transplant, including renal function indices (c statistic, 0.67) revealed that a higher eGFR reduced the risk of post-transplant early dialysis (odds ratio, 0.647; 95% confidence interval, 0.574-0.72; $P < .001$) Patients in the lowest eGFR quintile had a significantly increased risk of needing dialysis (odds ratio, 2.093; 95% confidence interval, 1.835-2.386; $P < .001$).

Influence of eGFR on Post-Transplant Survival

Overall survival at 1 and 5 years for the entire cohort was 88% and 73%, respectively. Risk-unadjusted survival was similar among HTx (8.4 ± 0.04 years) and HKTx recipients (7.7 ± 0.2 years; $P = .76$) (Figure 2). Isolated HTx recipients in the lowest eGFR quintile had significantly decreased survival compared with the other HTx groups ($P < .001$), whereas those in the third eGFR quintile had superior survival, suggesting a benefit in this subgroup (Figure 3).

Compared with patients receiving combined HKTx, isolated HTx recipients in the lowest eGFR quintile (mean eGFR <37 mL/minute) had significantly worse median survival (7.1 ± 0.07 years vs 7.7 ± 0.2 years; $P < .001$) (Figure 4). Multivariable analysis demonstrated that lower eGFR (log-transformed; hazard ratio, 0.83; $P < .001$), higher recent panel reactive antibody (hazard ratio, 1.001; $P < .001$), older age (hazard ratio, 1.002; $P = .03$), African American race (hazard ratio, 1.55; $P < .001$), diabetes (hazard ratio, 1.17; $P < .001$), longer ischemic time (hazard ratio, 1.08; $P < .001$), and certain diagnoses were risk factors for increased mortality among HTx recipients (Table E2).