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Longitudinal Changes in Kidney Function Following Heart Transplantation: Stanford Experience

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Abstract

Many heart transplant recipients experience declining kidney function following transplantation. We aimed to quantify change in kidney function in heart transplant recipients stratified by pre-transplant kidney function.

230 adult heart transplant recipients between May 1, 2008 and December 31, 2014 were evaluated for up to 5 years post-transplant (median 1 year). Using 19,398 total eGFR assessments, we evaluated trends in estimated glomerular filtration rate (eGFR) in recipients with normal/near normal (eGFR ≥ 45 mL/min/1.73m²) *versus* impaired (eGFR <45 mL/min/1.73m²) kidney function and the likelihood of reaching an eGFR of 20 mL/min/1.73m² after heart transplant.

Baseline characteristics were similar. Immediately following heart transplant, the impaired pre-transplant kidney function group showed a mean eGFR gain of 9.5mL/min/1.73m² (n=193) *versus* a mean decline of 4.9 mL/min/1.73m² (n=37) in the normal/near normal group. Subsequent rates of eGFR decline were 2.2 mL/min/1.73m²/yr *versus* 2.9 mL/min/1.73m²/yr, respectively. The probability of reaching an eGFR of 20 mL/min/1.73m² or less at 1, 5, and 10 years following heart transplant was 1%, 4% and 30% in the impaired group, and $<1\%$, $<1\%$, and 10% in the normal/near normal group.

Estimates of expected recovery in kidney function and its decline over time will help inform decision making about kidney care after heart transplantation.

Keywords

Heart Transplant; Kidney Transplant; Combined/Dual Heart-Kidney Transplant; Kidney/Renal Function

Background:

There are 5 million people in the United States living with heart failure and the prevalence of chronic kidney disease (CKD) is quite high in this group—up to 50%, depending on how

CKD is defined (1). Chronic kidney disease in patients with heart failure is mostly caused by kidney hypoperfusion (from heart failure itself and/or from medications used to treat heart failure including diuretics and renin angiotensin–aldosterone system blockade); recurrent episodes of acute kidney injury; and comorbid conditions including diabetes, hypertension and atherosclerotic disease (2, 3). In a select group of patients with advanced heart failure, heart transplantation is the treatment of choice.

Impaired kidney function before and after heart transplant is associated with a significant increase in the risk of death. Additionally, pre-transplant estimated glomerular filtration rate (eGFR) is independently associated with mortality in both the short and long-term (2–7). An eGFR below 40 mL/min/1.73m² is considered a relative contraindication to heart transplantation unless combined heart-kidney transplant is an option (8). Kidney function in patients awaiting heart transplant is dynamic, particularly in the peri-operative phase, which adds to the uncertainty of dual organ allocation. In patients whose kidney disease is primarily hemodynamically driven, heart-only transplant may result in recovery of kidney function. For patients with moderate to severe CKD from intrinsic kidney disease, combined heart-kidney transplant may be necessary (9). Heart and kidney transplant providers face the challenge of allocating a scarce resource with limited evidence to inform the decision of heart-only versus combined heart-kidney transplantation.

The extent to which impaired kidney function is reversible with improved renal perfusion after successful heart transplantation varies from patient to patient and the degree of reversibility is difficult to assess during the peri-operative period. However, CKD after heart transplantation is common, and many patients may need counselling regarding progression of CKD. We therefore aimed to study longitudinal changes in kidney function among heart transplant recipients with and without impaired pre-transplant kidney function. We hypothesized that heart transplant recipients would experience improvement in kidney function following transplant and sought to quantify the degree of kidney function recovery. We also hypothesized that kidney function following heart transplant would decline steadily over time and sought to measure that rate stratified by pre-transplant kidney function. Understanding the expected changes in kidney function after heart transplantation could help inform decision making regarding kidney care after heart transplantation.

Methods

Study Cohort

We used the Stanford Translational Research Database Environment (STRIDE) to identify a cohort of adults (age ≥ 18) who received heart transplants between May 1, 2008 and December 31, 2014 (10). We obtained demographic variables, information on comorbid conditions, and laboratory data using STRIDE queries. We excluded patients if they received prior or multiple organ transplants, were missing all serum creatinine determinations in the week prior to transplant including the day of transplant, and/or were missing all serum creatinine determinations after transplant. We performed a detailed review of the electronic medical record of each patient to obtain additional transplant characteristics and populate missing laboratory data. We collected and managed study data using REDCap electronic data capture tools hosted at the Stanford Center for Clinical Informatics (11).

Comparison Groups

We defined impaired kidney function as having a baseline eGFR under 45 mL/min/1.73m² in the week prior to heart transplant. We chose a cut-off point of eGFR < 45 (stage 3b CKD or higher) as indicating impaired kidney function based on the low likelihood of misclassification at this level (relative to <60 mL/min/1.73m²) and because this population is considered to require more frequent monitoring by clinical practice guidelines, owing in part to higher rates of progression to advanced or end-stage kidney disease (12–15).

Outcomes

The primary outcome was eGFR trend over time in patients with normal or near normal pre-transplant kidney function compared to those with impaired kidney function. As a secondary outcome we examined the cumulative incidence of CKD by stage at 6 and 12 months. We defined CKD stage according to KDIGO (stage 3a is an eGFR of 45–59; stage 3b, eGFR 30–44, stage 4, eGFR 15–29, and stage 5, eGFR < 15 mL/minute/1.73m²) (14). Estimated glomerular filtration rate was calculated according to the 4-variable Modification of Diet and Renal Disease Study (MDRD-4) formula [eGFR = 186 x Serum Creatinine^{-1.154} x Age^{-0.203} x 1.210 (Black) x 0.742 (Female)] (16). Lastly, we compared mortality rates in the two comparison groups.

Immunosuppression

Patients received induction therapy with 500 mg of intravenous methylprednisolone when coming off bypass and 1 mg/kg (maximum dose: 125 mg) of rabbit antithymocyte globulin therapy, on post-operative days 1, 2, and 3. The daily maintenance immunosuppressive regimen included tacrolimus (initiated at 0.5 mg twice daily) and mycophenolate mofetil (initiated at 1,000 mg twice daily). We target a tacrolimus trough of 10–15 ng/ml in the first 6 months. Prednisone was initiated at 1 mg/kg/day and tapered to 0.5 mg/kg/day by month 6 and to 0.1 mg/kg/day by month 12. Dose adjustments were made as indicated by adverse effects and/or acute rejection (17).

Statistical Analysis—We analyzed our data using SAS statistical software, version 9.4. Continuous variables are presented as means with 95 percent confidence intervals or median with 25th, 75th percentile range. We compared group characteristics using the two-sample (Student's) t-test for normally distributed variables and the Wilcoxon rank-sum test for variables that were not normally distributed. Categorical variables are presented as frequencies and percentages and compared by the chi-square test or Fisher Exact test as applicable. P-values less than or equal to 0.05 were considered statistically significant.

We performed a longitudinal analysis of eGFR from 3 years prior to transplant to 5 years post-transplant excluding the month immediately post-transplant given day-to-day fluctuations in serum creatinine concentrations. We applied a log transformation to eGFR to normalize the distribution of the data. We assumed a linear mixed model with a multivariate normal distribution for log eGFR with an auto regressive correlation structure for the variance. This approach accounted for the within-subject correlation between measurements. The model included an indicator for transplant status (pre-versus post-transplant), time from transplant (treated as a continuous variable in days), and group (normal/near normal versus

impaired kidney function). We included a 3-way interaction between time, transplant status, and group and all nested 2-way interactions in the model. Predicted means and associated 95% confidence intervals of eGFR were plotted by group and days post transplant. Predicted values of eGFR were also tabulated for specific baseline values at 1 month, 1 year, 5 years and 10 years post transplant. We estimated the probability of having an eGFR below 10 and 20 mL/min/1.73m² using model parameter estimates. Distribution of log eGFR and residuals from the model were examined for normality. Log eGFR was assumed to have a linear trend over time, however we also examined nonlinear specifications for time. We found the results to be robust to the assumptions of the model. To explore the possible role of regression to the mean in our model, we applied the approach of Barnett et al (18).

In separate models we estimated the cumulative incidence of CKD stage (1–2, 3a, 3b, 4, 5) at 6 and 12 months post transplant adjusting for the competing risk of death. The cumulative incidence functions were estimated by nonparametric methods. We tested for differences between groups using Gray's test of homogeneity. We created figures of the cumulative incidence of ESRD and death stratified by treatment group over the full 5 years of follow-up post transplant.

Results:

Of the 251 records identified on STRIDE, 230 were included in the analysis. We excluded three previous transplant recipients, 16 with missing baseline creatinine, and two for inconsistent waitlist information. One-hundred and ninety-three (84%) heart transplant recipients had normal or near normal pre-transplant kidney function and 37 (16%) had impaired pre-transplant kidney function. The groups were reasonably well balanced with respect to baseline characteristics (Table 1). The mean age was 51.4 and 58.9 in the normal/near-normal and impaired kidney function groups, respectively. There were no statistically significant differences in race, marital status, smoking status, baseline comorbidities, total ischemic time, waitlist days and calculated panel reactive antibodies. The most common etiology of heart failure was idiopathic dilated cardiomyopathy with 32.6% in the normal kidney function group and 35.1% in the impaired kidney function group. Ischemic cardiomyopathy was the second most common cause of heart failure in both groups. Ventricular assist devices were present in 22.8% versus 10.8% of the normal/near-normal and impaired groups. Of note, there was no significant difference in baseline characteristics of the 21 excluded patients compared to the 230 patients included in the study.

We examined the cumulative incidence of CKD by stage at 6 month and 1 year stratified by pre-transplant kidney function (Tables 3). At 6 months, 26% in the normal/near-normal kidney function group had CKD stage 3b or higher (including deaths) *versus* 57% in the impaired kidney function group. At 12 months, cumulative incidence of CKD stage 3b or higher remained relatively stable at 28% in the normal/near-normal kidney function group and 59% in the abnormal kidney function group. At 1 year post transplant there were no patients living with end-stage renal disease (ESRD); however, 11% of patients in the impaired group and 6% in the normal group had died.

Discussion:

Understanding longitudinal changes in kidney function following heart transplantation is important in optimizing kidney care after heart transplantation, timely referral for kidney transplantation and preparation for dialysis. Several studies have identified characteristics such as older age, female sex, hypertension, diabetes, pre-and early post-transplant kidney dysfunction as determinants of CKD following heart transplant (2, 3, 19–21). Following transplantation, calcineurin inhibitor use has been associated with progressive decline in kidney function (2, 3, 20, 22–25). Although it is well known that kidney function declines following heart transplant, our study is the first to model the trajectory of kidney function using a longitudinal analysis with granular laboratory data available in the electronic medical record.

We demonstrate that heart-only transplant can initially result in improved kidney function in recipients with impaired pre-transplant kidney function, with an eGFR gain of 9.5 mL/min/1.73m² in the first month. In contrast, rather than an improvement, a decline in eGFR of 4.9 mL/min/1.73m² was seen in the group with normal/near normal kidney function. A possible explanation is that the hemodynamic improvement from a heart transplant exceeds the negative hemodynamic effects of calcineurin inhibitors in the kidney impaired group, while the reverse may hold in the normal/near normal group.

We also quantified the rate of kidney function decline following heart transplant. For our cohort, this was 2.9 mL/min/1.73m²/year in the normal/near-normal group and 2.2 mL/min/1.73m²/year in the impaired group. Table 2 shows representative cases of kidney function change over time, starting with the pre-transplant baseline eGFR. A patient with a pre-transplant eGFR of 22 mL/min/1.73m² would be expected to have an eGFR of 28 mL/min/1.73m² after heart-only transplant and reach an eGFR of 21 mL/min/1.73m² in 5 years. Patients with CKD can be listed for kidney transplant once they have a sustained eGFR of 20 mL/min/1.73m² or less. This information, taken in context with waitlist times in the transplant region as well as estimated post-transplant survival may aid in early referral to nephrologists for CKD care, referral for kidney transplantation, and counseling regarding kidney transplant candidacy.

In line with other studies, we demonstrate a high incidence of CKD stage 3b and higher following heart transplant, which reached more than half of patients at 12 months who were transplanted with impaired kidney function (6, 19). Patients with more advanced CKD (i.e. stage 3b and higher) have higher rates of morbidity and mortality in the years following transplantation (3). Our study shows that 4% of the patients with impaired kidney function prior to heart transplantation had advanced CKD that would qualify them for kidney transplant listing five years after transplantation. In contrast, fewer than 1% of patients with normal/near normal had CKD advanced enough for kidney transplant listing. Patients with impaired renal function prior to transplantation appear to reach advanced stages of CKD (3b or higher) around 1–3 years post-transplant. This represents a critical time where heart transplant providers can refer patients to nephrology for co-management, aiming to slow down progression to ESRD and early/pre-emptive listing for kidney transplant when applicable.

Patients with intrinsic kidney disease from diabetes, hypertension and atherosclerotic vascular disease have an irreversible component to their kidney disease that will not be recovered by restoring hemodynamic function with heart transplantation. We found a similar prevalence of these risk factors in both groups, but our sample size was too small to permit a sub-analysis. We also evaluated the effect of VAD support in our preliminary analysis, however, our sample size precluded meaningful analysis (n=4 for abnormal eGFR, n=44 for normal eGFR).

Studies show that mortality is much higher in heart-only transplant recipients who become dialysis dependent compared to a matched group of patients who are not on dialysis. In addition, heart-only transplant recipients on dialysis have significantly lower survival than a matched group of patients with end-stage-renal disease on dialysis (2–4, 26). These data suggest that expedited kidney transplant or combined heart-kidney transplant might be preferred in candidates with advanced CKD. In our study, mortality was 6% for near normal and 11% in the impaired patients in the first year ($p<.05$), but over the course of 5 years mortality reached 20% and was not significantly different between the normal/near-normal and impaired kidney function groups.

Hong and colleagues recently published their findings from a cohort of 17,459 heart transplant recipients, showing that an $\text{eGFR} < 34 \text{ mL/min/1.73m}^2$ was associated with worse post-transplant survival (27). This is in line with the revised heart transplant listing criteria from the 2016 International Society for Heart and Lung Transplantation, stating that an eGFR under $40 \text{ mL/min/1.73m}^2$ is a relative contraindication to listing for heart-only transplant. Karamalou and colleagues identified an eGFR threshold of $< 37 \text{ mL/min/1.73m}^2$ as deriving the greatest benefit from combined heart-kidney transplants (28). While we did not aim to determine an exact eGFR threshold that derives benefit from combined heart-kidney transplant, we demonstrate that, despite the initial gain in kidney function seen in heart transplant recipients with impaired kidney function, there is still significant decline in kidney function over time that should prompt careful consideration of dual-organ candidacy before proceeding with heart-only transplant.

Decisions regarding kidney allocation depend on the health providers' ability to predict recovery of kidney function following heart transplant as well as long-term kidney function trajectory. A recent publication by Goupil and colleagues highlights the difficulty in selecting patients for combined heart-kidney transplants (29). With studies showing good outcomes for heart-kidney transplants (30–34), with the decreased rates of organ rejection in multi-organ transplant recipients (thought to be related to induction of partial immune tolerance, although the mechanisms are not completely understood), it is foreseeable that demand for kidneys in heart transplant candidates with impaired kidney function will continue to rise. In the over three decades since the first combined heart-kidney transplant (35), there are no consensus guidelines to help cardiologists, cardiothoracic surgeons, or nephrologists select patients most likely to benefit from combined organ transplantation. Based on data from the Organ Procurement and Transplantation Network as of December 31, 2016, combined heart-kidney transplants represent less than 1% of heart transplants per year. However, the rates of heart-kidney transplants have increased by 400% in the past 15 years, while heart-only transplants have increased by 25% in the same time. We need more

studies to quantify the change in kidney function with heart transplant alone to develop evidence-based guidelines.

Limitations

Limitations of this study include a relatively small sample size, which precluded assessment of predictors of kidney function recovery in multivariate analyses. While Stanford is one of the largest heart transplant centers in the country, results may not be generalizable to the broader heart transplant population. As with all observational data, results may be influenced by variables we did not measure. For example, proteinuria, kidney size and kidney biopsy data were not routinely assessed prior to transplantation and therefore were not available for analysis. There are also limitations in using creatinine-based equations such as the MDRD-4 to calculate eGFR, our main measure of kidney function in this study. Of concern is the overestimation of kidney function in the heart transplant population who often have reduced muscle mass and creatinine generation. In addition, heart transplant candidates experience wide fluctuations in serum creatinine during episodes of heart failure exacerbations, prompted in part by diuresis and inotrope use, rendering creatinine-based equations less reliable in measuring kidney function during and soon after exacerbations. It is possible that differential use of calcineurin inhibitors for immunosuppression in patients with impaired versus normal/near normal kidney function could have influenced results. We generally target a serum trough tacrolimus concentration of 10–15 ng/ml during the first 6 months post-heart transplant. For patients with acute kidney injury, we target levels at the lower end of that range hoping to facilitate recovery of kidney function. This differential may create a selection bias, however, in the long term, both groups are treated similarly and we believe that any effect of early differences in calcineurin inhibitor dosing would be minimal in the context of our overall findings. It is possible that there is some bias in the estimates due to regression to the mean, a common statistical problem among models with repeated observations. We estimated the bias due to RTM (18) to be approximately 1.07 units of eGFR, which would slightly attenuate the estimates of immediate gain/loss in eGFR post transplant, however this does not fully explain our results.

Determining true baseline kidney function is challenging given fluctuations in serum creatinine as mentioned; we used the lowest serum creatinine value in the week prior to transplant to calculate baseline eGFR. Our study could have been strengthened by assessing cardiac outcomes such as rejection, ejection fraction and allograft vasculopathy; however, these data were not readily available. We had data on all-cause but not cause-specific mortality; thus, we are unable to comment on death from cardiac causes.

Conclusions:

In this cohort, we determined that heart transplant recipients with impaired pre-transplant kidney function transiently gain 9.5 ml/min/1.73m² of eGFR with heart-only transplant. Heart transplant recipients with normal/near-normal pre-transplant kidney function experience a decline in kidney function of 4.9 ml/min/1.73m² during this same period. Kidney function then declines steadily over time in both groups, albeit at a slightly faster rate in those with normal/near-normal pre-transplant kidney function. This information helps

inform decision making for kidney care after heart transplantation. More studies in larger heart transplant populations are needed to refine these estimates.

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4. Financial disclosures: None
5. STRIDE “*STRIDE (Stanford Translational Research Integrated Database Environment) is a research and development project at Stanford University to create a standards-based informatics platform supporting clinical and translational research*”.
6. REDCap. “*REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources*”.

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Figure 1.

depicts the longitudinal changes of eGFR and serum creatinine over time stratified by baseline kidney function. Kidney function declined in both groups over time, but the group with impaired pre-transplant kidney function demonstrated improvement in kidney function in the first month following transplant with an average eGFR gain of 9.5 (95% CI: 6.6, 12.6) mL/min/1.73m² compared with a decline of 4.9 (95% CI: 3.2, 6.6) mL/min/1.73m² in the normal/near-normal kidney function group ($p < .001$). Estimated glomerular filtration rate subsequently declined at a rate of 2.9 (95% CI: 2.8, 3.0) mL/min/1.73m²/year in the normal/near-normal group and 2.2 (95% CI: 1.8, 2.6) mL/min/1.73m²/year in the impaired group. The probability of reaching an eGFR of 20 mL/min/1.73m² or below (a point at which patients are eligible for kidney transplant listing) at 1, 5, and 10 years after heart transplant was <1%, 4%, and 30% in the impaired group and <1%, <1% and 10% in the normal/near normal group. In Table 2 we present some hypothetical cases with baseline eGFR's of 22, 33, 44, and 66. The patients with baseline values between 22 and 44 show an immediate increase in eGFR 1 month post transplant but a more rapid decline out to 10 years post transplant compared to the patient with a baseline eGFR of 66. To quantify the regression to the mean effect, we measured the overall mean (3.996) standard deviation (.437), and correlation (0.18) among log eGFR measurements in our cohort. This gave a regression to the mean effect on the log eGFR of only 0.07 (this translates to a difference in eGFR of 1.07 units).

Figure 2. shows the cumulative incidence of CKD stage 5, ESRD (top) and death (bottom) for abnormal and normal kidney function at baseline over the 5 years of follow-up. The figures are adjusted for competing risk of death and CKD and show the p-value for the Grays test of homogeneity. Patients with an abnormal baseline eGFR have a higher incidence of CKD ($p=0.01$) and a similar incidence of death ($p=0.9$) when compared to patients with normal or near normal kidney function at baseline.

Table 1 –
Baseline Characteristics stratified by pre-transplant kidney function.

Baseline Characteristics	eGFR 45 mL/min/1.73m ² (N = 193)	eGFR < 45 mL/min/1.73m ² (N = 37)	P-value
Age	51.4 (13.6)	58.9 (9.3)	0.0001
Women	57 (29.5%)	13 (35.1%)	0.50
Hispanic/Latino	20 (10.4%)	3 (8.1%)	1.00
Primary Race			0.94
White	107 (55.4%)	22 (59.5%)	
Black	21 (10.9%)	4 (10.8%)	
Asian	22 (11.4%)	3 (8.1%)	
Unknown/Other	43 (22.3%)	8 (21.6%)	
Marital Status			0.11
Single	47 (24.4%)	5 (13.5%)	
Married	129 (66.8%)	26 (70.3%)	
Divorced	10 (5.2%)	2 (5.4%)	
Other	7 (3.6%)	4 (10.8%)	
Never Smoker	109 (56.5%)	17 (45.9%)	0.23
Comorbidities			
Diabetes	111 (57.5%)	17 (45.9%)	0.19
Stroke	31 (16.1%)	5 (13.5%)	0.70
Hypertension	153 (79.3%)	25 (67.6%)	0.12
Atherosclerosis	42 (21.8%)	11 (29.7%)	0.29
Primary Heart Failure (HF) Etiology			0.99
Dilated cardiomyopathy	63 (32.6%)	13 (35.1%)	
Ischemic cardiomyopathy	39 (20.2%)	9 (24.3%)	
Familial Cardiomyopathy	12 (6.2%)	1 (2.7%)	
Hypertrophic	13 (6.7%)	2 (5.4%)	
Amyloid	15 (7.8%)	3 (8.1%)	
Restrictive	14 (7.3%)	3 (8.1%)	
Other	37 (19.2%)	6 (16.3%)	
Ventricular Assist Device (VAD)	44 (22.8%)	225 (195–272.5) [‡]	0.12
Total Ischemic Time	236 (211–275) [‡]	1.8 (1.6–2.0) [*]	0.36
Baseline serum creatinine (mg/dL)	1.1 (1.0–1.4)	37.6 (32–40.7) [*]	<.0001
Baseline eGFR (mL/min/1.73m ²)	62.9 (51.8–77.1)	134 (130–139)	<.0001
Baseline Sodium (mmol/L)	135 (133–138)	3.6 (3.4–3.9)	0.50
Baseline Albumin (mg/dL)	3.6 (3.2–3.9)	46 (18–110)	0.18
Waitlist Days	53 (15–132)	4 (0–66) ^{##}	0.46
cPRA (%) [#]	22 (2–59) ^{##}		0.63

Continuous variables presented as mean (standard deviation) or median (25th, 75th quartile) as appropriate. Categorical variables presented as percent.

* P-value < 0.05.

[‡] Missing Data = 1–10%

^{##} Missing data: >20%.

[#] Calculated Panel Reactive Antibody

Table 2

Predicted eGFR* and 95% confidence interval post-transplant based on longitudinal model

Baseline	1 month post	1 year post	5 years post	10 years post
22	27.8 (26.0, 29.7)	26.4 (24.4, 28.6)	21.2 (15.9, 28.4)	16.2 (8.97, 29.1)
33	41.6 (39.0, 44.5)	39.6 (36.6, 42.9)	31.8 (23.8, 42.7)	24.2 (13.5, 43.7)
44	55.5 (51.9, 59.3)	52.8 (48.8, 57.2)	42.5 (31.7, 56.9)	32.3 (17.9, 58.3)
66	61.1 (59.5, 62.9)	58.3 (56.5, 60.1)	47.2 (42.7, 52.2)	36.3 (29.7, 44.4)

* eGFR is in ml/minute/1.73m²

Calculate predicted eGFR for 30 days post transplant (eGFR₃₀) from baseline eGFR (eGFR₀) as follows:

Near Normal eGFR₃₀ = $\exp(\ln(\text{eGFR}_0) - 0.72 - .051 * \text{years})$

Impaired eGFR₃₀ = $\exp(\ln(\text{eGFR}_0) + 0.24 - .054 * \text{years})$

Table 3 –

Cumulative incidence* (%) of CKD stage (and 95% confidence interval) *** at 6 months and 1 year post transplant.

(A) 6 months post transplant		
CKD Stage	Normal/near normal kidney function	Impaired kidney function
1–2	49.7 (42.6, 56.5)	18.9 (8.0, 33.4) **
3a	23.8 (18.1, 30.0)	24.3 (11.8, 39.3)
3b	15.0 (10.4, 20.4)	32.4 (17.7, 48.0) **
4	6.7(3.8, 10.9)	16.2 (6.3, 30.1)
5	0.5 (0.04, 2.9)	0
Died	4.2 (1.9, 7.7)	8.1 (2.0, 19.9)
(B) 1 year post transplant		
CKD Stage	Normal/near normal kidney function	Impaired kidney function
1–2	43.0 (36.0, 49.9)	10.8 (3.3, 23.4) **
3a	29.5 (23.3, 36.1)	29.7 (15.4, 45.5)
3b	17.1 (12.1, 22.8)	35.1 (19.6, 51.1) **
4	4.2 (1.9, 7.7)	13.5 (4.8, 26.8) **
5	0	0
Died	6.2(3.4, 10.2)	10.8(3.3, 23.4) **

* estimated by nonparametric methods adjusting for the competing risk of death.

** Gray test of homogeneity for cumulative incidence functions p-value<.05

*** pointwise confidence intervals at 6 months and 1 year post transplant