Clinical Events and Renal Function in the First Year Predict Long-Term Kidney Transplant Survival

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Key Points

- eGFR at 1 year post transplant is an established predictor of graft failure, but the effects of major intercurrent events are not fully known.
- We assessed the link between 12-month eGFR and long-term graft failure accounting for intercurrent events and competing mortality risks.
- Acute rejection, cardiovascular events, and infectious events were significant risks; 12-month eGFR remained the dominant driver of graft failure.

Abstract

Background Estimated glomerular filtration rate (eGFR) at 1 year post transplantation has been shown to be a strong predictor of long-term graft survival. However, intercurrent events (ICEs) may affect the relationship between eGFR and failure risk.

Methods The OPTN and USRDS databases on single-organ kidney transplant recipients from 2012 to 2016 were linked. Competing risk regressions estimated adjusted subhazard ratios (SHRs) of 12-month eGFR on long-term graft failure, considering all-cause mortality as the competing risk, for deceased donor (DD) and living donor (LD) recipients. Additional predictors included recipient, donor, and transplant characteristics. ICEs examined were acute rejection, cardiovascular events, and infections.

Results Cohorts comprised 25,131 DD recipients and 7471 LD recipients. SHRs for graft failure increased rapidly as 12-month eGFR values decreased from the reference 60 ml/min per 1.73 m². At an eGFR of 20 ml/min per 1.73 m², SHRs were 13–15 for DD recipients and 12–13 for LD recipients; at an eGFR of 30 ml/min per 1.73 m², SHRs were 5.0–5.7 and 5.0–5.5, respectively. Among first-year ICEs, acute rejection was a significant predictor of long-term graft failure in both DD (SHR = 1.63, P < 0.001) and LD (SHR = 1.51, P = 0.006) recipients; cardiovascular events were significant in DD (SHR = 1.24, P < 0.001), whereas non-CMV infections were significant in the LD cohort (SHR = 1.32, P = 0.03). Adjustment for ICEs did not significantly reduce the association of eGFR with graft failure.

Conclusions Twelve-month eGFR is a strong predictor of long-term graft failure after accounting for clinical events occurring from discharge to 1 year. These findings may improve patient management and clinical evaluation of novel interventions.

Introduction

Long-term failure rates of kidney allografts have reduced steadily over the last 15 years. Five-year failure rates for deceased donor (DD) organs fell by nearly half between 1996 and 2012 and now stand at <14%; five-year failure rates for living donor (LD) transplants decreased 46% over the same period and are now <9% (1). Long-term patient survival has also improved, with survival for DD recipients increasing from 8.2 years between 1995 and 1999 to 11.7 years between 2014 and 2017 (2). However, numbers of patients reinitiating dialysis after failed transplants have increased over time—a leading cause of patients receiving dialysis (3,4). Thus, despite recent improvements in immunosuppressant therapy and management of acute rejection (AR) episodes, there remains a need to better understand factors affecting long-term survival.

Kidney function within the first year of transplantation has been consistently identified as a key factor that affects longer-term graft survival (5–16). Indeed, advances in transplant care that reduce graft failure...
risk may work through the mechanism of improving kidney function in the first year after transplant (5). The relationship between kidney function in the year post transplant and long-term allograft survival has been demonstrated in observational studies, with several examining various measures of eGFR and changes in eGFR during the first year (5–8) and others specifically using 12-month eGFR to predict long-term graft failure (9–15). Increases in 12-month eGFR resulting from different interventions have also been shown to improve long-term outcomes in experimental settings, including BENEFIT, ELITE-Symphony, and the FAVORIT trials (17–20).

Several other factors have also been associated with long-term graft survival, including donor type and other donor characteristics, recipient characteristics (e.g., age, sex, comorbidities), and features of the transplant (e.g., HLA mismatch, delayed graft function [DGF], and cold ischemia time) (9–15). In addition, AR events during the first year have been included in some observational studies and have been shown to be associated with long-term graft failure (5,12,14,15,21). However, other intercurrent events (ICEs)—occurring during the first-year post transplant—may also influence long-term graft survival, but these are not fully understood. As one key example, transplant recipients are at high risk for cardiovascular diseases (CVD), which are associated with poor graft function, graft failure, and increased mortality (22–26). More than a third of known causes of death in transplant recipients are due to CVD, with more than two thirds of these due to cerebrovascular accidents, cardiac arrhythmias, or cardiac arrest (1). CVD incidence is largely associated with low eGFR values, with a 15% increase in CVD events for each 5 mL/min per 1.73 m² decrease in eGFR <45 mL/min per 1.73 m². This relationship is notably absent with an eGFR >45 mL/min per 1.73 m² (20). In addition, recipients are at increased risk of viral and bacterial infections due to immunosuppression. Such infections are associated with poor kidney function and poor graft and patient outcomes, including 18% of all known causes of death among transplant recipients (1).

Several studies have demonstrated the association of eGFR at 12 months post transplant with long-term graft failure in addition to identifying additional factors that may also influence graft failure. However, ICEs such as episodes of CVD or serious infections may increase long-term graft failure risk while also adversely impacting kidney function to different extents, thereby potentially changing the relationship between 12-month eGFR and long-term graft failure.

In this study, we aimed to provide a better estimate of the association of 12-month eGFR on long-term graft failure that accounts for ICEs using a competing risk analysis with data from the Organ Procurement and Transplantation Network (OPTN) merged with the administrative claims data from the United States Renal Data System (USRDS) (27).

Materials and Methods
Data Sources
A retrospective cohort of single-organ kidney transplantation recipients in the United States was identified using the OPTN/USRDS database from January 1, 2012, to December 31, 2015. The USRDS database is a joint effort of the National Institute of Diabetes and Digestive and Kidney Disease and the Centers for Medicare and Medicaid Services (CMS) that tracks many descriptive elements for all patients in the United States with ESKD. USRDS registries integrate information from the OPTN, CMS, and Medicare billing claims records (1). These elements are linked with a unique encrypted patient identifier, permitting investigators to combine patient-specific information from multiple tables without revealing patient identity. Therefore, no Institutional Review Board review was required.

Study Population
This study population included adult (i.e., aged ≥18 years) kidney transplant patients with Medicare as their primary payer at time of first transplantation from 2012 to 2015. If patients had multiple kidney transplant procedures in that time period, the first was included. Patients with other organ transplants before the index transplantation were excluded from this study.

Patients who died or experienced graft failure within 12 months post transplantation were excluded from this analysis. Patients without serum creatinine measures before discharge and at 180- and 365-days post transplantation were excluded from this analysis and so were patients without follow-up 1 year post transplantation and those with prior kidney transplants (Figure 1).

Patient Baseline Characteristics
The following patient demographics and clinical variables were assessed in this study (Table 1): age at transplantation, sex, race (Black versus non-Black as required and reported by USRDS), body mass index (BMI), history of diabetes, cause of ESKD, calculated panel reactive antibodies (PRA) at time of transplantation, years of dialysis treatment before transplantation, and years of follow-up after 12 months post transplantation. Baseline patient demographics were assessed for the entire sample population and stratified further for patients who experienced graft failure and those who did not over the follow-up period.

In addition to the patient demographics and clinical variables, the following donor variables were also captured: age, sex, race (Black versus non-Black), weight, history of hypertension, history of diabetes, cytomegalovirus (CMV) status, cause of death, and predonation levels of protein in urine and serum creatinine. The following variables during transplantation were considered as potential confounders for this analysis and were therefore captured across the sample population: the year of the transplant procedure, the number of HLA mismatches, cold ischemia time (≤40 or >40 hours), DGF, and receipt of transplant on pump.

ICEs were also considered as potential confounders for the relation between eGFR at 12 months and graft survival (Table 2). These variables included AR events, cardiovascular events, and CMV and other infections within 12 months post transplantation. AR was identified in the OPTN registry data, whereas cardiovascular events and CMV and other infection events were identified by diagnostic codes in the USRDS claims database (Supplemental Table 1). AR is captured by the dichotomous OPTN variable ACUTE_
REJ_EPI, which is reported by transplant centers in follow-up data collection (28,29). Cardiovascular events included were acute myocardial infarction, atrial fibrillation, heart failure, hemorrhagic and ischemic stroke, and unstable angina. CMV infections were identified separately from other serious infections, which captured viral and bacterial infections, including pneumonias. ICD codes do not explicitly account for BK infections, although these are coded as other viral infections in practice and are captured in the codes used.

eGFR Variable Definition
The main predictor variable for this analysis was eGFR at 12 months, whereas 6-month eGFR was used in sensitivity analyses. In this study, eGFR was assessed using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation using serum creatinine (30). In the regression equations, the eGFR variable was constructed as a cubic spline to account for the nonlinear relationship between kidney function and graft failure (15). The eGFR reference value was 60 ml/min per 1.73 m².

Outcome Measures
The primary outcome of interest was graft failure assessed after 12 months post transplant as captured by the OPTN/USRDS database. Model results evaluating 6-month eGFR, including patients and graft surviving to 6 months post transplant and ICEs to 6 months, are included as supplemental analyses.

Statistical Analyses
Descriptive statistics were used to describe the baseline demographic and clinical variables. Continuous variables are described as means and SDs. Categorical variables are described as counts and percentages. Missing continuous variables were imputed using the mean from patients with complete data, and missing categorical variables were included as a separate “unknown” category.

Death was treated as a competing risk when evaluating time to graft failure. Therefore, the subdistribution hazard model, which estimates the effect of covariates on the cumulative incidence function for graft failure alone, was
## Table 1. Baseline recipient, donor and transplant characteristics for deceased donor and living donor cohorts

| Deceased Donor, with Prior Dialysis, with or without Prior Transplant | Living Donor, with or without Prior Dialysis, with or without Prior Transplant |
|---|---|
| **All (N=25,118)** | **Patients with Graft Failure (N=1641)** | **Patients without Graft Failure (N=23,477)** | **All (N=7469)** | **Patients with Graft Failure (N=320)** | **Patients without Graft Failure (N=7149)** |
| **Patients with Graft Failure (N=1641)** | **Patients without Graft Failure (N=23,477)** |
| **All (N=7469)** | **Patients with Graft Failure (N=320)** | **Patients without Graft Failure (N=7149)** |
| **Long-term graft failure rate** | **7%** | **4%** |
| **Recipient characteristics** |  |  |
| eGFR 12 months post transplant (calculated using CKD-EPI formula) |  |  |
| Mean (SD) |  |  |
| With prior dialysis, n (%) |  |  |
| Yes | 25,118 (100) | 1641 (100) | 23,477 (100) | 6202 (83) | 296 (93) | 5906 (83) |
| With prior transplants, n (%) |  |  |
| Yes | 3576 (14) | 270 (17) | 3306 (14) | 830 (11) | 46 (14) | 784 (11) |
| Follow-up time from 1 year post transplantation (years) |  |  |
| Mean (SD) | 2.86 (1.27) | 2.23 (1.27) | 2.90 (1.25) | 2.95 (1.24) | 2.32 (1.20) | 2.98 (1.24) |
| Age group, yr, n (%) |  |  |
| <30 | 1531 (6) | 223 (14) | 1308 (6) | 860 (12) | 92 (29) | 768 (11) |
| 30–45 | 5385 (21) | 433 (26) | 4952 (21) | 1712 (23) | 86 (27) | 1626 (23) |
| 45–59 | 9448 (38) | 572 (35) | 8876 (38) | 2283 (31) | 65 (20) | 2218 (31) |
| 60–74 | 8221 (33) | 382 (23) | 7839 (33) | 2438 (33) | 73 (23) | 2365 (33) |
| ≥75 | 533 (2) | 31 (2) | 502 (2) | 176 (2) | 4 (1) | 172 (2) |
| Sex, n (%) |  |  |
| Men | 15,390 (61) | 1024 (62) | 14,366 (61) | 4662 (62) | 178 (56) | 4484 (63) |
| Race, n (%) |  |  |
| Black | 9157 (37) | 814 (50) | 8343 (36) | 1077 (14) | 71 (22) | 1006 (14) |
| BMI, kg/m² | Mean (SD) | 28.4 (6) | 28.6 (6) | 28.3 (6) | 27.9 (6) | 28.4 (6) | 27.9 (6) |
| Years since dialysis start from transplant (among patients who had prior dialysis) | Mean (SD) | 6.7 (5) | 6.7 (5) | 6.7 (5) | 4.1 (5) | 4.1 (5) | 4.1 (5) |
| Cause of ESKD, n (%) |  |  |
| Polycystic kidney disease | 1663 (7) | 70 (4) | 1593 (7) | 596 (8) | 13 (4) | 583 (8) |
| Diabetes | 6909 (28) | 411 (25) | 6498 (28) | 1841 (25) | 73 (23) | 1768 (25) |
| Glomerulonephritis | 6186 (25) | 469 (29) | 5717 (24) | 2081 (28) | 106 (33) | 1975 (28) |
| Hypertension | 6621 (26) | 447 (27) | 6174 (26) | 1517 (20) | 66 (21) | 1451 (20) |
| Other | 3739 (15) | 244 (15) | 3495 (15) | 1434 (19) | 62 (19) | 1372 (19) |
| History of diabetes, n (%) |  |  |
| Yes | 9064 (36) | 549 (34) | 8515 (36) | 2471 (33) | 96 (30) | 2375 (33) |
| No | 15,977 (64) | 1087 (66) | 14,890 (63) | 4987 (67) | 223 (70) | 4764 (67) |
| Unknown | 77 (0.3) | 5 (0.3) | 72 (0.3) | 11 (0.2) | 1 (0.3) | 10 (0.1) |
| Calculated PRA, n (%) |  |  |
| #80 | 20,499 (82) | 1337 (82) | 19,162 (82) | 6586 (88) | 273 (85) | 6313 (88) |
| ≥80 | 4563 (18) | 303 (19) | 4260 (18) | 428 (6) | 23 (7) | 405 (6) |
| Unknown | 56 (0.2) | 1 (0.1) | 55 (0.2) | 455 (6) | 24 (8) | 431 (6) |
| **Donor characteristics** |  |  |
| Age group, yr, n (%) |  |  |
| ≤10 | 1119 (5) | 60 (4) | 1059 (5) | 0 (0) | 0 (0) | 0 (0) |
| 11–20 | 2226 (9) | 131 (8) | 2095 (9) | 73 (1) | 6 (2) | 67 (1) |
| 21–40 | 9241 (37) | 517 (32) | 8724 (37) | 3025 (41) | 123 (38) | 2902 (41) |
| 41–60 | 10,715 (43) | 772 (47) | 9943 (42) | 3634 (49) | 165 (52) | 3469 (49) |
| >60 | 1817 (7) | 161 (10) | 1656 (7) | 737 (10) | 26 (8) | 711 (10) |
| Sex, n (%) |  |  |
| Men | 15,327 (61) | 957 (58) | 14,370 (61) | 2738 (37) | 120 (38) | 2618 (37) |
| Race, n (%) |  |  |
| Black | 3835 (15) | 340 (21) | 3495 (15) | 882 (12) | 66 (21) | 816 (11) |
| Donor weight, kg | Mean (SD) | 80.6 (25.3) | 81.5 (25.5) | 80.6 (25.3) | 76.8 (15.1) | 77.4 (16.7) | 76.7 (15.1) |
| History of hypertension, n (%) |  |  |
| Yes | 6933 (28) | 588 (36) | 6345 (27) | 269 (4) | 12 (4) | 257 (4) |
| No | 18,053 (72) | 1043 (64) | 17,010 (73) | 7194 (96) | 307 (96) | 6887 (96) |
| Unknown | 132 (0.5) | 10 (0.6) | 122 (0.5) | 6 (0.1) | 1 (0.3) | 5 (0.1) |
used (31). Models including and excluding ICEs were evaluated. Subdistribution hazard ratios (SHRs) and \( P \) values are reported.

Two cohorts were generated for analysis: (1) DD recipients with prior dialysis and with or without prior transplants and (2) LD recipients with or without prior dialysis and with or without prior transplants.

Two regression models were conducted to assess the impact of ICEs on the predictive nature of 12-month eGFR on graft failure. A sensitivity analysis employed 6-month eGFR. This was chosen rather than the change in eGFR from 6 to 12 months due to the degree of collinearity between changes in eGFR and ICEs. The base model included recipient, donor, and transplant covariates. In addition to these variables, the full model included AR events, CVD events, and CMV and other infections. Model fitting was assessed by evaluating Akaike information criterion and the likelihood ratios of the two models. All

### Table 1. (Continued)

| CMV status, n (%) | Deceased Donor, with Prior Dialysis, with or without | Living Donor, with or without | Deceased Donor, with Prior Dialysis, with or without | Living Donor, with or without |
|-------------------|-----------------------------------------------------|--------------------------------|-----------------------------------------------------|--------------------------------|
| Positive          | Patients with Graft Failure (N=1641)                | Patients without Graft Failure (N=23,477) | Patients with Graft Failure (N=320)                | Patients without Graft Failure (N=7149) |
| 15,179 (60)       | 14,152 (60)                                         | 3225 (43)                      | 3102 (43)                                          |
| Negative          | 9843 (39)                                           | 9232 (39)                      | 123 (38)                                           |
| Unknown           | 96 (0.4)                                            | 93 (0.4)                       | 177 (2)                                            |
| Cause of death, n (%) | Patients with Graft Failure (N=1641)                | Patients without Graft Failure (N=23,477) | Patients with Graft Failure (N=320)                | Patients without Graft Failure (N=7149) |
| Anoxia            | 8431 (34)                                           | 7942 (34)                      | 6650 (89)                                          |
| CNS tumor         | 117 (0.5)                                           | 112 (0.5)                      | 50 (7)                                             |
| Cerebrovascular accident | 7352 (29)                                           | 6775 (29)                      | 47 (7)                                             |
| Head trauma       | 8501 (34)                                           | 7984 (34)                      | 307 (4)                                            |
| Other             | 717 (3)                                             | 664 (3)                        | 6363 (89)                                          |
| History of diabetes, n (%) | Patients with Graft Failure (N=1641)                | Patients without Graft Failure (N=23,477) | Patients with Graft Failure (N=320)                | Patients without Graft Failure (N=7149) |
| Yes               | 1879 (8)                                            | 187 (11)                       | 561 (34)                                           |
| No                | 23,110 (92)                                         | 21,670 (92)                    | 260 (4)                                            |
| Unknown           | 129 (0.5)                                           | 115 (0.5)                      | 28 (9)                                             |
| Protein in urine, n (%) | Patients with Graft Failure (N=1641)                | Patients without Graft Failure (N=23,477) | Patients with Graft Failure (N=320)                | Patients without Graft Failure (N=7149) |
| Yes               | 11,436 (46)                                         | 10,682 (46)                    | 1807 (24)                                          |
| No                | 13,508 (54)                                         | 12,629 (54)                    | 76 (24)                                            |
| Unknown           | 174 (0.7)                                           | 166 (0.7)                      | 73 (1)                                             |
| Predonation serum creatinine, mg/dl a | Mean (SD) 1.16 (0.98) | 1.16 (0.99) | 0.82 (0.25) | 0.82 (0.25) |

**Transplant characteristics**

| Year of transplant, n (%) | Deceased Donor, with Prior Dialysis, with or without | Living Donor, with or without |
|---------------------------|-----------------------------------------------------|--------------------------------|
| 2012                      | Patients with Graft Failure (N=1641)                | Patients without Graft Failure (N=23,477) |
| 6022 (24)                 | 5439 (23)                                           | 1834 (25)                      |
| 2013                      | 6041 (24)                                           | 1907 (26)                      |
| 2014                      | 6211 (25)                                           | 2876 (39)                      |
| 2015                      | 6844 (27)                                           | 1807 (24)                      |
| Number of HLA mismatches, n (%) | Patients with Graft Failure (N=1641)                | Patients without Graft Failure (N=23,477) |
| 5801 (231)                | 5456 (23)                                           | 76 (24)                        |
| 9281 (37)                 | 8705 (37)                                           | 1731 (24)                      |
| 6                         | 7945 (39)                                           | 9038 (39)                      |
| Unknown                   | 791 (1)                                             | 278 (1)                        |
| CIT, hr, n (%) | Deceased Donor, with Prior Dialysis, with or without | Living Donor, with or without |
| 16,802 (67)               | Patients with Graft Failure (N=1641)                | Patients without Graft Failure (N=23,477) |
| 7722 (31)                 | 7229 (31)                                           | 2736 (38)                      |
| 454 (2)                   | 417 (2)                                             | 140 (44)                       |
| Unknown                   | 140 (0.6)                                           | 125 (0.5)                      |
| DGF status, n (%) | Deceased Donor, with Prior Dialysis, with or without | Living Donor, with or without |
| 7084 (28)                 | Patients with Graft Failure (N=1641)                | Patients without Graft Failure (N=23,477) |
| 561 (34)                  | 6523 (28)                                           | 232 (3)                        |
| Received on pump, n (%)  | Deceased Donor, with Prior Dialysis, with or without | Living Donor, with or without |
| 7876 (31)                 | Patients with Graft Failure (N=1641)                | Patients without Graft Failure (N=23,477) |

BMI, body mass index; CIT, cold ischemia time; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CMV, cytomegalovirus; CNS, central nervous system; DGF, delayed graft function; PRA, panel reactive antibodies.

| Continuous variables with missing values were imputed using the mean from patients with complete data. The proportions of patients with missing values on these measures were <1% with exception of calculated PRA in the living donor cohort (6%). |
analyses were performed using SAS v9.4 (SAS Institute, Cary, NC). Note that the terms “predict” and “predictor” are used in the conventional sense of explaining an observed trend in an outcome by a correlation with other parameters not as a part of a prediction score to estimate risk for individual patients.

**Results**

**Study Population**

Initially, 67,648 patients who underwent kidney transplantation from 2012 to 2015 were identified in the linked OPTN/USRDS database. Following the attrition inclusion and exclusion criteria, a total of 33,549 patients were identified for this study (Figure 1). In creating the two cohorts described above, 25,118 patients met the criteria for DD, and 7469 patients met the criteria for LD in the 12-month analyses.

**Patient Characteristics**

**DD Cohort**

A total of 25,118 patients were captured in DD cohort with a prior history of dialysis, with or without prior transplants. The comprehensive characteristics of the DD cohort are shown in Table 1. The percentages of patients who received a kidney transplant are distributed evenly across study years (2012–2015). Approximately one third of patients developed DGF, and one third of patients received their kidney on pulsatile perfusion.

Most of these patients received kidneys from men (61%), non-Black donors (85%), aged between 21 and 60 (80%). Overall, 28% of the donor population had hypertension, 8% had diabetes, and 60% had positive CMV infections. Head trauma, cerebral anoxia, and cerebrovascular accidents were the three leading causes of death for these donors.

DD recipients had 6.7 years of history of prior dialysis on average, and 3576 (14%) of those patients had at least one prior transplantation. Most DD recipients were ≥45 years old (73%), men (61%), and non-Black (64%) and had no history of diabetes (64%). Overall, DD recipients had a mean follow-up time of 2.9 years (SD=1.3 years) after 1 year post transplantation and a mean BMI of 28.4 kg/m² (SD=5.5 kg/m²), and 82% of DD recipients had a calculated PRA of <80. Diabetes, glomerulonephritis, and hypertension were the three leading causes of ESKD in DD recipients. Of these patients, 1641 (7%) experienced graft failure over the follow-up period, with higher failure rates among those with low 12-month eGFR levels. Mean eGFR at 12 months post transplantation for the overall cohort was 61.6 ml/min per 1.73 m² (SD=25.3 ml/min per 1.73 m²), with a substantially lower mean eGFR in patients with graft failure compared with those without (46.6 versus 62.7; SD=25.3 versus 21.5).

Overall, from discharge to 12 months post transplantation, 9% of DD cohort patients experienced AR, 22% of them had CVD, 13% had CMV infections, and 33% had other infections. All of the ICEs occurred in a higher frequency in patients with graft failure than in those without (Table 2).

**LD Cohort**

A total of 7469 of the patients identified in this analysis met the criteria for the LD cohort: patients who received an LD kidney, with or without prior history of dialysis, and with or without prior transplants. The comprehensive characteristics of the LD cohort are presented in Table 1. Most received kidneys from women (63%), non-Black donors (88%), aged between 21 and 60 (89%). The percentages of patients who received a transplant are distributed evenly across study years (2012–2015). Approximately 4% of LD recipients developed DGF.

In general, 83% (n=6202) of LD recipients had a history of prior dialysis (mean=4.1 years; SD=5.3 years), and 11%
of those patients had at least one prior transplantation. Most LD recipients were ≥45 years old (66%), men (62%), and non-Black (86%) and had no history of diabetes (67%). Overall, LD recipients had a mean follow-up time of 3 years (SD = 1.2 years) after 1 year post transplantation, and a mean BMI of 28 kg/m² (SD = 5.6 kg/m²). Diabetes, glomerulonephritis, and hypertension were the three leading causes of ESKD in LD recipients. Of these patients, 320 (4%) experienced graft failure over the follow-up period. Mean eGFR at 12 months post transplantation for the overall cohort was 62.8 ml/min per 1.73 m² (SD = 19.6 ml/min per 1.73 m²), with a substantially lower mean eGFR in patients with graft failure compared with those without (52.5 versus 63.3; SD = 24.2 versus 19.3).

Overall, from discharge to 12 months post transplantation, 8% of LD recipients experienced AR, 16% had a CVE, 9% had CMV infections, and 26% had other infections. AR and other infection events occurred in a higher frequency in patients with graft failure than in those without, whereas CVD and CMV infections had a similar rate of occurrence between the two groups (Table 2).

Subdistribution Hazard Models for Prediction of Graft Failure

eGFR at 12 months post transplantation was a strong and statistically significant predictor of graft failure in all three subdistribution hazard models for both DD and LD cohorts. The full model with ICEs was a statistically significantly better fit of the data compared with the model with only recipient, donor, and transplant covariates (Supplemental Table 2). Detailed SHR estimates for all of the covariates are presented in Table 3 (DD) and Table 4 (LD). The effects of nonlinear transformation (cubic spline) terms of eGFR are shown in Figure 2 (DD) and Figure 3 (LD), which represent the estimated SHRs of graft failure at different values of 12-month eGFR, with a reference of 60 ml/min per 1.73 m². Adjusted SHRs are substantially higher for low 12-month eGFR levels (indicating higher failure risk). There are some differences in overall eGFR failure results in the base model versus the full model, with ICEs in Figures 2 and 3. Comparing Figure 2, A and B for the DD cohort, for example, at an eGFR of 30 ml/min per 1.73 m², the SHR is 5.7, whereas for the full model, the SHR drops to 5. Given the nonlinear relationship between eGFR and survival, the differences at an eGFR of 45 ml/min per 1.73 m² reduce to 1.6 versus 1.5. For the LD cohort (Figure 3, A and B), the differences in adjusted hazard are 5.5 and 5 at 30 ml/min per 1.73 m² and reduce to 1.6 and 1.5 at 45 ml/min per 1.73 m².

In the full model for DD recipients, the relative hazard of graft failure increased 7% with an eGFR of 55 ml/min per 1.73 m² (SHR = 1.07; 95% CI, 1.02 to 1.12) and 20% with an eGFR of 50 ml/min per 1.73 m² (SHR = 1.20; 95% CI, 1.07 to 1.33). The relative hazard of graft failure doubled when eGFR at 12-month post transplantation was <40 ml/min per 1.73 m². In contrast, recipients with an eGFR of 75 ml/min per 1.73 m² at 12 months post transplantation experienced a 21% reduced hazard of graft failure (SHR = 0.79; 95% CI, 0.67 to 0.93). Similarly, in LD recipients, the relative hazard of graft failure increased 6% with an eGFR of 55 ml/min per 1.73 m² (SHR = 1.06; 95% CI, 0.93 to 1.21) and 19% with an eGFR of 50 ml/min per 1.73 m² (SHR = 1.19; 95% CI, 0.90 to 1.55). The relative hazard of graft failure doubled when eGFR at 12 months post transplantation was <41 ml/min per 1.73 m². Recipients with an eGFR of 75 ml/min per 1.73 m² at 12 months post transplantation experienced a 33% reduced hazard of graft failure (SHR = 0.67; 95% CI, 0.48 to 0.94).

To aid interpretation of the adjusted relationship between 12-month eGFR and long-term graft failure (Figures 2 and 3), complete listings of the SHRs for unit eGFR levels from 15 to 75 ml/min per 1.73 m² are provided (Supplemental Table 3). These results show that for patients with 12-month eGFRs of 40 ml/min per 1.73 m², a mean increase of 1.5 ml/min per 1.73 m² was associated with at least a 20% reduction in graft failure risk for either DD or LD recipients (Supplemental Figure 1).

We conducted sensitivity analyses to evaluate the relationship between eGFR and graft failure under differing model assumptions. Models predicting graft failure using eGFR levels at 6 months post transplant and ICEs from discharge to 6 months were run for both cohorts (Supplemental Tables 4 and 5 and Supplemental Figures 2 and 3). Adjusted SHRs on 6-month eGFR were lower than those for 12-month eGFR at lower eGFR levels (e.g., at 30 ml/min per 1.73 m², SHR = 5 at 12 months versus 3.6 at 6 months). Adjusted SHRs on all other predictors were very similar between 6- and 12-month models, except for CMV and other infection events, which were statistically significant (P = 0.0459 and P = 0.003, respectively) in the 6-month but not the 12-month model. Differences between the base and full model results at lower eGFR levels (Supplemental Figures 2, A and B, and 3, A and B) were similar to those in the 12-month analyses. Separate prediction models using 12-month eGFR were run for DD recipients identified as of Black race and those who identified as non-Black (Supplemental Table 6 and Supplemental Figure 4), which showed that mean SHRs on 12-month eGFR were nominally lower for Black versus non-Black recipients (e.g., at 30 ml/min per 1.73 m², SHR = 4.6 for Black recipients versus 5.6 for non-Black recipients) with overlapping 95% confidence intervals over the range of eGFRs evaluated.

Discussion

Traditional analyses of allograft outcome are often limited to clinical characteristics available either before or at the time of transplantation. Although these factors are clearly important and relevant to clinical decision making and long-term allograft function, the contribution of subsequent clinical events are often not incorporated in studies evaluating long-term graft survival. Whereas previous analyses have attempted to understand the implications of AR episodes on long-term allograft survival, our current analysis also incorporates the effect of additional common early complications such as infections and cardiovascular events and impaired kidney function in the first year to evaluate the cumulative risks at the end of the first year on longer-term outcomes. The primary findings quantify the applicable risks associated with ICEs and kidney function conditional on one-year graft survival among kidney transplant recipients. These findings provide evaluation of
### Table 3. Regression results: adjusted SHRs for the prediction of graft failure using 12-month eGFR in the DD cohort (N=25,118)

| Category                                      | Base: Recipient, Donor and Transplant Variables | Full: Base+ICEs |
|-----------------------------------------------|-------------------------------------------------|----------------|
| **eGFR (see Figure 2)**                      |                                                 |                |
| **Recipient variables**                       |                                                 |                |
| With prior transplants (reference: no)       |                                                 |                |
| Yes                                           | 1.095                                           | 1.104          |
| Age (yr; reference: <30)                     |                                                 |                |
| 30–44                                         | 0.405                                           | 0.416          |
| 45–59                                         | 0.260                                           | 0.266          |
| 60–74                                         | 0.169                                           | 0.174          |
| 75+                                           | 0.197                                           | 0.199          |
| Sex (reference: women)                       |                                                 |                |
| Men                                           | 1.116                                           | 1.108          |
| Race (reference: non-Black)                  |                                                 |                |
| Black                                         | 1.557                                           | 1.561          |
| BMI (kg/m²; polynomial)                      |                                                 |                |
| BMI (1)                                       | 0.799                                           | 0.799          |
| BMI (2)                                       | 1.007                                           | 1.007          |
| BMI (3)                                       | 1.000                                           | 1.000          |
| LN (years since dialysis up to transplant; continuous) | 1.008                                           | 0.850          |
| Cause of ESKD (reference: other)             |                                                 |                |
| Polycystic kidney disease                    | 0.858                                           | 0.860          |
| Diabetes                                      | 1.215                                           | 1.189          |
| Glomerulonephritis                            | 1.067                                           | 1.064          |
| Hypertension                                  | 1.075                                           | 1.076          |
| Calculated PRA (reference: ≥80)              |                                                 |                |
| <80                                           | 1.059                                           | 1.100          |
| **Donor variables**                           |                                                 |                |
| Age (yr; reference: >60)                     |                                                 |                |
| ≤10                                           | 1.229                                           | 1.189          |
| 11–20                                         | 1.237                                           | 1.203          |
| 21–40                                         | 1.019                                           | 0.992          |
| 41–60                                         | 0.893                                           | 0.886          |
| Sex (reference: women)                       |                                                 |                |
| Men                                           | 0.976                                           | 0.978          |
| Race (reference: non-Black)                  |                                                 |                |
| Black                                         | 1.245                                           | 1.235          |
| LN (donor weight; continuous)                |                                                 |                |
| History of hypertension (reference: no)      |                                                 |                |
| Yes                                           | 1.169                                           | 1.178          |
| Unknown                                       | 0.887                                           | 0.785          |
| CMV status (reference: negative)             |                                                 |                |
| Positive                                      | 0.997                                           | 1.000          |
| Unknown                                       | 0.575                                           | 0.556          |
| Cause of death (reference: other)            |                                                 |                |
| Anoxia                                        | 0.885                                           | 0.899          |
| CNS tumor                                     | 0.723                                           | 0.708          |
| Cerebrovascular accident                      | 0.889                                           | 0.903          |
| Head trauma                                   | 0.939                                           | 0.956          |
| History of diabetes (reference: no)          |                                                 |                |
| Yes                                           | 1.329                                           | 1.345          |
| Unknown                                       | 1.728                                           | 1.958          |
| Protein in urine (reference: no)             |                                                 |                |
| Yes                                           | 1.060                                           | 1.059          |
| Unknown                                       | 0.617                                           | 0.647          |
| Predonation serum creatinine (mg/dl; continuous) | 0.983                                           | 0.980          |
important factors associated with subsequent graft losses among recipients in a contemporary cohort. Results also confirm that kidney function at 1 year remains prominently associated with other early 1-year post transplant complications and other baseline donor, recipient, and transplant characteristics.

Notably, both cardiovascular events and infections are much more common in the first year than ARs (as the basis of definitions in these data). Both ARs and cardiovascular events remained significantly associated with an increased risk of graft failure among DD recipients after adjusting for the 12-month eGFR, suggesting that these events may have long-term adverse implications independent of the effects on kidney function. In addition, the association of graft failure in DD recipients with 12-month eGFR persisted even after the inclusion of these ICEs, underscoring the clinical significance of the patients’ eGFR at the 12-month post transplantation mark (Table 3 and Figure 2). Infections were not associated with increased risk of long-term graft failure, perhaps in part because infections are often minor short-term events, but when they are more severe or prolonged, they tend to result in reductions in immunosuppression, which may in turn alter the risk of an AR.

Although early ARs and CMV and other infections in the first year were associated with inferior outcomes among LD recipients, cardiovascular events were not. The effect of ICEs was stronger in the 6-month models (Supplemental Table 4) for the DD cohort, with all ICEs significantly associated with increased failure risk, whereas in the LD cohort, ICE results were similar to the 12-month models. The attenuated effect of ICEs in DD recipients over time may be due to ICEs primarily contributing to early graft failure in this cohort. The source of differential associations of acute infections and cardiovascular events between recipients of LD and DD kidneys is unclear and may be important for prospective research. Relatedly, the lack of an independent effect of DGF is notable, given the strong univariate relationship between DGF and failure. This likely is due to the relationship between DGF and both AR and eGFR at 12 months; accounting for these factors substantially attenuates the independent effect of DGF.

Not surprisingly, lower eGFR at 12 months, particularly eGFR consistent with CKD stages 3b, 4, and 5, is associated with a higher incidence of early graft failure (Figures 2 and 3). The risk of allograft failure increased in both LD and DD recipients at lower eGFRs. Although this relationship was slightly attenuated when considering ICEs, the association persisted in both LD and DD cohorts, suggesting the value of 12-month estimates of eGFR as an independent predictor of long-term allograft function. It is also noteworthy that the association of 12-month eGFR extended to

Table 3. (Continued)

| Category | Base: Recipient, Donor and Transplant Variables | Full: Base+ICEs |
|----------|-----------------------------------------------|----------------|
| Transplant variables | SHR | P Value | SHR | P Value |
| Year of transplant (reference: 2012) | | | | |
| 2013 | 1.008 | 0.91 | 0.999 | 0.99 |
| 2014 | 1.017 | 0.83 | 1.018 | 0.81 |
| 2015 | 1.002 | 0.99 | 0.981 | 0.82 |
| Number of HLA mismatches (reference: 6) | | | | |
| <5 | 0.870 | 0.05 | 0.894 | 0.12 |
| 5 | 0.854 | 0.008 | 0.871 | 0.02 |
| Unknown | 0.922 | 0.77 | 0.964 | 0.89 |
| CIT (reference: >40) | | | | |
| ≤20 | 0.975 | 0.88 | 0.948 | 0.76 |
| 20–40 | 0.888 | 0.49 | 0.868 | 0.41 |
| Unknown | 1.035 | 0.93 | 1.013 | 0.97 |
| DGF status (reference: no) | | | | |
| Yes | 1.024 | 0.68 | 1.036 | 0.54 |
| Received on pump (reference: no) | | | | |
| Yes | 0.923 | 0.16 | 0.922 | 0.15 |
| ICEs—discharge to 12 mo | | | | |
| AR events (reference: no) | | | | |
| Yes | — | — | 1.629 | <0.0001 |
| Unknown | — | — | 0.878 | 0.63 |
| CVD events (reference: no) | | | | |
| Yes | — | — | 1.238 | 0.0006 |
| CMV infections (reference: no) | | | | |
| Yes | — | — | 1.037 | 0.63 |
| Other infections (reference: no) | | | | |
| Yes | — | — | 1.068 | 0.23 |

AR, acute rejection; BMI, body mass index; CI, confidence interval; CIT, cold ischemia time; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CMV, cytomegalovirus; CNS, central nervous system; CVD, cardiovascular disease; DD, deceased donor; DGF, delayed graft function; ICEs, intercurrent events; PRA, panel reactive antibodies; SHR, subdistribution hazard ratio.
Table 4. Regression results: adjusted SHRs for the prediction of graft failure using 12-month eGFR in the LD cohort (N=7469)

| Category                  | Base: Recipient, Donor, and Transplant Variables | Full: Base+ICEs |
|---------------------------|-------------------------------------------------|-----------------|
|                           | SHR | P Value | SHR | P Value |
| **eGFR (see Figure 3)**   |     |         |     |         |
| **Recipient variables**   |     |         |     |         |
| With prior transplants (reference: no) |     |         |     |         |
| Yes                       | 1.178 | 0.38 | 1.200 | 0.3293 |
| Age (yr; reference: <30) |     |         |     |         |
| 30–44                     | 0.370 | <0.001 | 0.367 | <0.001 |
| 45–59                     | 0.191 | <0.001 | 0.191 | <0.001 |
| 60–74                     | 0.211 | <0.001 | 0.215 | <0.001 |
| 75+                       | 0.175 | 0.001 | 0.164 | 0.001 |
| Sex (reference: women)    |     |         |     |         |
| Men                       | 0.864 | 0.22 | 0.879 | 0.29 |
| Race (reference: non-Black) |     |         |     |         |
| Black                     | 1.184 | 0.43 | 1.132 | 0.56 |
| BMI (kg/m²; polynomial)   |     |         |     |         |
| BMI (1)                   | 0.744 | 0.29 | 0.752 | 0.3 |
| BMI (2)                   | 1.010 | 0.27 | 1.010 | 0.28 |
| BMI (3)                   | 1.000 | 0.29 | 1.000 | 0.3 |
| With prior dialysis (reference: no) |     |         |     |         |
| Yes                       | 1.788 | 0.008 | 1.732 | 0.01 |
| Cause of ESKD (reference: other) |     |         |     |         |
| Polycystic kidney disease | 0.690 | 0.24 | 0.695 | 0.25 |
| Diabetes                  | 1.186 | 0.39 | 1.192 | 0.38 |
| Glomerulonephritis        | 1.004 | 0.98 | 1.029 | 0.86 |
| Hypertension              | 1.022 | 0.91 | 1.085 | 0.67 |
| Calculated PRA (reference: ≥80) |     |         |     |         |
| <80                       | 1.086 | 0.75 | 1.112 | 0.68 |
| Unknown                   | 1.174 | 0.62 | 1.177 | 0.61 |
| **Donor variables**       |     |         |     |         |
| Age (yr; reference: >60)  |     |         |     |         |
| 11–20                     | 2.051 | 0.09 | 1.926 | 0.11 |
| 21–40                     | 1.240 | 0.39 | 1.234 | 0.4 |
| 41–60                     | 1.310 | 0.24 | 1.311 | 0.23 |
| Sex (reference: women)    |     |         |     |         |
| Men                       | 1.295 | 0.1 | 1.26 | 0.13 |
| Race (reference: non-Black) |     |         |     |         |
| Black                     | 1.538 | 0.05 | 1.575 | 0.04 |
| LN (donor weight; continuous) | 0.881 | 0.73 | 0.884 | 0.73 |
| History of hypertension (reference: no/unknown) |     |         |     |         |
| Yes                       | 0.971 | 0.93 | 0.949 | 0.86 |
| CMV status (reference: negative) |     |         |     |         |
| Positive                  | 1.135 | 0.29 | 1.143 | 0.27 |
| Unknown                   | 1.535 | 0.21 | 1.557 | 0.2 |
| Protein in urine (reference: no) |     |         |     |         |
| Yes                       | 0.871 | 0.63 | 0.860 | 0.61 |
| Unknown                   | 0.883 | 0.59 | 0.897 | 0.63 |
| Predonation serum creatinine (mg/dl; continuous) | 0.885 | 0.69 | 0.863 | 0.7 |
| **Transplant variables**  |     |         |     |         |
| Year of transplant (reference: 2012) |     |         |     |         |
| 2013                      | 0.727 | 0.03 | 0.731 | 0.03 |
| 2014                      | 0.679 | 0.02 | 0.691 | 0.03 |
| 2015                      | 0.792 | 0.26 | 0.824 | 0.35 |
| Number of HLA mismatches (reference: 6) |     |         |     |         |
| <5                        | 0.817 | 0.2 | 0.841 | 0.27 |
| 5                         | 1.088 | 0.56 | 1.111 | 0.47 |
| Unknown                   | 1.219 | 0.74 | 1.225 | 0.73 |
| DGF status (reference: no) |     |         |     |         |
| Yes                       | 1.498 | 0.08 | 1.489 | 0.08 |
higher ranges of function such that it is not solely an indicator of rapid decline to graft failure but prognostic for long-term decline and progression to ESKD. Thus, interventions to maintain function or attenuate rates of decline remain critically important, even among patients who are not acutely at risk of kidney failure. The benefits of improved eGFR do diminish substantially at 45 ml/min per 1.73 m², but there continues to be a slight although

Table 4. (Continued)

| Category                  | Base: Recipient, Donor, and Transplant Variables | Full: Base+ICEs |
|---------------------------|--------------------------------------------------|-----------------|
| ICEs—discharge to 12 mo  | SHRs                                             | P Value         |
| AR events (reference: no)| -                                                | -               |
| Yes                       | -                                                | 1.508 0.01      |
| Unknown                   | -                                                | 0.488 0.32      |
| CVD events (reference: no)| -                                                | 1.136 0.43      |
| Yes                       | -                                                | 0.674 0.07      |
| CMV infections (reference: no)| -                                             | 1.317 0.03      |
| Yes                       | -                                                |                |
| Other infections (reference: no)| -                                 |                |

AR, acute rejection; BMI, body mass index; CI, confidence interval; CIT, cold ischemia time; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CMV, cytomegalovirus; CNS, central nervous system; CVD, cardiovascular disease; DGF, delayed graft function; ICEs, intercurrent events; LD, living donor; PRA, panel reactive antibodies; SHR, subdistribution hazard ratio.

Figure 2. Regression results: relative subdistribution hazard ratio (SHR) for eGFR values by 12-month eGFR post transplantation, deceased donor cohort (N=25,118).

Figure 3. Regression results: relative SHR for eGFR values by 12-month eGFR post transplantation, living donor cohort (N=7469).
This analysis also builds upon the evidence supporting the utility of 12-month eGFR as a surrogate end point for graft failure in kidney transplant clinical trials. Consistent with prior literature, graft failure rates are strongly associated with a patient’s 12-month eGFR level (5,10–12,14,15,17–20). However, in addition, the association of level of eGFR also varies in a nonlinear manner, which may be an important consideration for use as an end point and projected risk of subsequent graft failure. How this nonlinearity is accounted for and interpreted in the comparison of mean values across treatment arms in a clinical trial will likely be dependent on specifics of clinical trial design. For example, our analysis (Supplemental Table 3 and Supplemental Figure 1) indicates that for a cohort of patients with a mean 12-month eGFR of ≤45 ml/min per 1.73 m², an increase in eGFR of 5 ml/min per 1.73 m² would be associated with at least a 20% reduction in long-term graft failure relative risk for either DD or LD recipients. Achieving a similar relative risk reduction for recipients at 60 ml/min per 1.73 m² would, on average, require increases in eGFR level of up to 15 ml/min per 1.73 m². These will be important considerations for trial design, given the need for the use of surrogate end points to evaluate novel interventions.

Given the strong association of eGFR with long-term end points and the consideration of kidney function in clinical decision making and clinical trials, the role of a patient’s race in eGFR estimation is a critical concern. At the time of this study, an NKF/ASN initiative was initiated with the aim, in part, to reassess inclusion of race in eGFR equations and its implications for diagnosis and care of kidney disease and to provide tools for all stakeholders to ensure health care equity (32). There is some evidence that genetic heritage may play a role in serum creatinine levels. However, subjective labels of race used in eGFR equations is an inappropriate proxy measure fraught with potential for suboptimal patient care. The race-pooled models accounting for race assignment (Table 3) indicate that Black DD recipients do have higher graft failure risk after multivariate adjustment, which may reflect the contribution of the multiplier in the CKD-EPI equation for Black race or factors related to access to appropriate care unobserved in the OPTN/USRDS dataset. Black recipients of LD kidneys did not have higher adjusted failure rates (Table 4). Race-stratified models for DD recipients (Supplemental Table 6) showed all predictors of graft failure were similar between Black and non-Black recipients with the exception of donor history of hypertension and diabetes. The adjusted predictive value of 12-month eGFR was not statistically different between Black and non-Black recipients (Supplemental Figure 4). The associations included in the current results should be consistent by specific GFR equations, including the newly revised CKD-EPI (33,34). However, further research and policy considerations for measuring and integrating kidney function measures into care for transplant recipients that are equitable and clinically appropriate will continue to be critically important.

Our analysis also employs advancements over prior observational studies, which have largely used proportional hazards regression in graft failure predictions. Because patient death with a functioning graft is a competing risk to graft failure, the standard proportional hazards approach may lead to biased results by assuming that each covariate affects graft failure and death in the same way. Thus, one of the unique features of our analysis is the use of a competing risks analytic framework (31). This approach can yield unique findings relative to use of censored models or composite end points with Cox regression in predicting long-term graft failure by accounting for cases in which a recipient dies with a functioning graft. Not accounting for this competing risk may result in biased estimates of the relationship between eGFR and long-term graft failure.

Important limitations of these findings include the potential for residual confounding associated with factors not available in the study databases. In addition, given the study inclusion criteria, risks may not be generalizable to all intended populations. For example, the study excluded patients with graft failure in the first-year post transplantation, and our results will not apply to such patients. More generally, this study was not designed to answer questions about management of individual patients because the relationships demonstrated in this large-cohort analysis may differ among patients in clinical practice. Both OPTN and USRDS claims data lack granularity regarding certain data elements, and this lack of specificity may be important for prospective study. For example, ARs were considered a single end point for the purpose of this study but clearly have a wide spectrum of etiology and clinical consequences. An exploration of how our findings might vary by type of AR event would be valuable; however, the availability and completeness of OPTN data on types of AR events are very limited. Further, these analyses are limited by the immunologic and histologic data available in OPTN, although we were able to control for calculated PRA, HLA mismatches, donor proteinuria, and terminal serum creatinine, which had limited explanatory power. Additionally, the mean follow-up period in our analysis is shorter than the typical graft survival period. However, a key challenge in this area is that there is a continued upward trend in patient and graft survival and a downward trend in measures of donor and recipient risk factors, which is explained by substantial and ongoing improvements in the transplant process and management of transplant recipients (33,35).

Thus, it is likely that the relationship between renal function and long-term graft survival is too changing over relatively short periods of time, and we sought to conduct our analysis for transplant recipients receiving contemporary standard of care. Finally, our aim was to test the relationship between eGFR and graft failure in the context of ICEs occurring in the post transplant period. This clearly differs from efforts to create novel prediction tools for everyday clinical practice at the time of organ allocation and transplantation (12). Thus, validation of the predictive power of the models in other populations will be important to complement the current findings.

Cumulatively, these analyses indicate that kidney function at 1 year post transplant is a strong predictor of long-term graft survival, independent of recipient, donor, and transplant characteristics and the effect of ICEs. ICEs also have a sustainable risk for graft failure among patients
with 1-year survival independent of kidney function level. In addition, results were generally consistent by donor type and recipient race. These findings may inform the design of clinical trials and should be tested in prospective settings.

Disclosures

F. Corvino reports being an employee of Genesis Research and having ownership interest in Genesis Research. S. Mohan reports consultancy for Angion Biomedica; research funding from Angion Biomedica and the NIH (NIDDK, NIHMD, and NIBIB); being deputy editor of Kidney International Reports (ISN); being vice chair of UNOS; and being a member of the SRTR Visiting Committee and the Angion Pharma scientific advisory board. B. Nordyke reports being an employee of Angion Biomedica at the time of writing. J. Schold reports consultancy agreements with Guidry and East, Novartis, Sanofi, and the Transplant Management Group; honoraria from Novartis and Sanofi; being a Data Safety Monitoring Board Member—Bristol Myers Squibb and Nephrosant; and participating in a speaker’s bureau for Sanofi. W. Wang reports being an employee of Genesis Research; consultancy for Genesis Research; and ownership interest in Apple, BMS, and Snapchait. Z. Wu reports being an employee of Genesis Research.

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Author Contributions

F. Corvino was responsible for the formal analysis; F. Corvino, S. Mohan, J. Schold, W. Wang, and Z. Wu were responsible for validation; F. Corvino and Z. Wu curated the data and were responsible for the software and visualization; S. Mohan, R. Nordyke, and J. Schold were responsible for conceptualization and investigation, and wrote the original draft of the manuscript; S. Mohan, R. Nordyke, and W. Wang were responsible for resources; S. Mohan and J. Schold were responsible for the methodology; R. Nordyke was responsible for project administration and supervision; and all authors reviewed and edited the manuscript.

Supplemental Material

This article contains supplemental material online at http://kidney360.asnjournals.org/lookup/suppl doi:10.34067/KID.0007342021/-/DCSupplemental.

Supplemental Table 1. Codes for intercurrent events.

Supplemental Table 2. Model fit statistics.

Supplemental Table 3. Listing of adjusted eGFR subdistribution hazard ratios by eGFR level. Models with base and intercurrent event variables.

Supplemental Table 4. Regression results: adjusted subdistribution hazard ratios for the prediction of graft failure using 6-month eGFR in the deceased donor cohort (N=25,950).

Supplemental Table 5. Regression results: adjusted subdistribution hazard ratios for the prediction of graft failure using 6-month eGFR in the living donor cohort (N=7645).

Supplemental Table 6. Regression results: adjusted subdistribution hazard ratios for the prediction of graft failure using 12-month eGFR stratified by recipient race, deceased donor cohort (N=25,118).

Supplemental Figure 1. Minimum increase in mean 12-month eGFR associated with reductions in graft failure hazard.

Supplemental Figure 2. Regression results: relative subdistribution hazard ratio by 6-month eGFR post transplantation in the deceased donor cohort (N=25,950).

Supplemental Figure 3. Regression results: relative subdistribution hazard ratio by 6-month eGFR post transplantation, living donor cohort (N=7645).

Supplemental Figure 4. Regression results: relative subdistribution hazard ratio by 12-month eGFR post transplantation stratified by recipient race, deceased donor cohort (N=25,118).

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