

# Association of Admission, Nadir, and Terminal Donor Creatinine With Kidney Transplantation Outcomes



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**Introduction:** When assessing deceased kidney donors, a key factor in organ acceptance and allocation is donor kidney function. It is unclear whether terminal, admission, or the highest of terminal and admission donor estimated glomerular filtration rate (eGFR) most predicts recipient outcomes.

**Methods:** We examined which measurement best predicts outcomes. Using data from the Australia and New Zealand Organ Donation and Dialysis and Transplant Registries, we included adult recipients of deceased donor kidney-only transplants over 2003 to 2019. We compared the 3 different exposure variables of admission, terminal, or highest eGFR. We created logistic regression models for delayed graft function (DGF), multilinear regression models for 6- and 12-month eGFR, and Cox proportional hazards models for graft loss, death censored graft failure and patient death.

**Results:** A total of 8971 transplant recipients were included. There was strong evidence of an association between terminal, admission, and highest donor eGFR and DGF and recipient eGFR at 6 and 12 months. The eGFR was a strong predictor of graft and death censored graft failure, but not patient death. Terminal was a better predictor than admission and highest eGFR particularly for more contemporaneous outcomes.

**Conclusion:** In assessing kidney donors, terminal eGFR were marginally better than admission and highest at predicting outcomes. Terminal eGFR should be used in risk equations to predict hard clinical endpoints.

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KEYWORDS: delayed graft function; epidemiology; graft function; graft survival; survival analysis

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## See Commentary on Page 2025

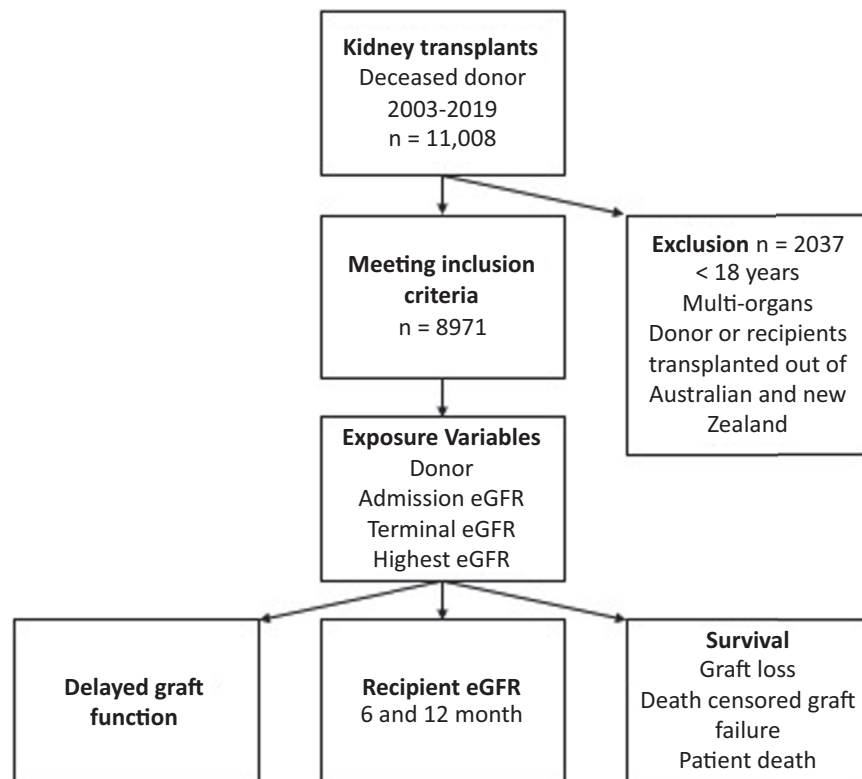
Kidney transplantation is the best treatment for most patients with end-stage kidney disease, providing improved quality of life and survival while using fewer resources.<sup>1–4</sup> Deceased donor kidneys are a scarce resource, with an imbalance between the number of people who would benefit from a kidney transplant and the number of available organs. This necessitates attempts to increase the number of kidneys for transplantation, while maximizing the use of reasonable-quality organs. Several deceased donor factors affect recipient outcomes.<sup>5–9</sup> These donor factors are incorporated into risk scores to help clinicians

and patients make decisions about stratifying the risk of using particular organs, accepting organ offers, and counselling patients on these risks.<sup>10–13</sup> These scores are also included in formal transplantation allocation algorithms in some countries.<sup>11,14</sup>

A key factor when making decision about kidney allocation is the donor's kidney function.<sup>15</sup> This is estimated by the so-called "terminal" or last recorded pre-donation serum creatinine (SCr) or estimated glomerular filtration rate (eGFR). This value is incorporated into risk scores.<sup>10</sup> Elevated SCr occurs commonly in deceased kidney donors.<sup>16,17</sup> In the general population, acute kidney injury (AKI) is associated with the development of chronic kidney disease.<sup>18</sup> In kidney transplantation, although acutely elevated donor creatinine is associated with delayed graft function (DGF), there are conflicting reports in the literature about its impact on graft failure.<sup>16</sup> It is hypothesized that the AKI seen in the peri-transplantation period is likely to have a degree of reversibility, so

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**Figure 1.** Histograms for donor estimated glomerular filtration rate (eGFR). Indication of distributions of the different exposure variables.

elevated donor creatinine may not predict medium- to long-term graft function. Elevated terminal creatinine does increase the rate of organ discard, and thus reduces the organ pool.<sup>15,17</sup>

Although terminal creatinine is the most commonly used marker of kidney function in donors, given the rate of AKI in the intensive care population,<sup>18</sup> the initial or admission creatinine may be a better predictor of long-term graft function. Acknowledging the fluctuations in serum creatinine, the “best” recorded kidney function might better represent long-term function. Conversely, pre-hospitalization events such as out-of-hospital cardiac arrest might make the admission creatinine higher than the true baseline, and this may settle during hospital admission, with terminal creatinine being a better marker of baseline function. In our study, we examined whether terminal, initial, or highest eGFR best predicted a number of kidney transplantation–related outcomes including DGF, 6- and 12-month eGFR, and graft loss, death censored graft failure, and patient death, to determine which measurement should be used for risk prediction and organ allocation.

## MATERIALS AND METHODS

### Study Population

We extracted data from the Australia and New Zealand Organ Donation (ANZOD) and Dialysis and Transplant

(ANZDATA) Registries. We included adult recipients of deceased-donor kidney-only transplants in Australia and New Zealand over 2003 to 2019. Recipients were excluded if they were <18 years old at the time of transplantation, if their donors were <18 years of age, if they received multiple types of organs, or if their donors were from outside of Australia and New Zealand (Figure 1). Recipients were also excluded if inadequate information was available to calculate any of the donor eGFR timepoints. Implausible values were excluded, as they appeared to be due to data entry errors (ischemic time >40 hours, donor body mass index [BMI] <10 or >80 kg/m<sup>2</sup>, donor height <100 cm, recipient BMI >50 kg/m<sup>2</sup>, terminal or admission creatinine <15 μmol/l, terminal or admission eGFR >200 μmol/l; total n = 157, 1.7%). Few data were missing (<5%), so listwise deletion was used to handle this rather than other statistical techniques.

### Definitions

The original Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was used to calculate eGFR.<sup>19</sup> Admission eGFR was calculated using the first creatinine recorded on admission to hospital. Terminal eGFR was calculated using the last creatinine prior to organ procurement. Best eGFR was the highest of these 2 values. No other creatinine measurements are collected in the registry. Delayed graft function was

defined as the need for dialysis within the first 7 days of transplantation or prior to 2015 if there was no spontaneous fall (>10%) in SCr and dialysis was required within 72 hours. Historically, this had been recorded differently in the registry prior to 2015. Oliguria was defined as a urine output <500 ml in the preceding 24 hours.

### Outcome Measures

Six different outcomes were analyzed based on the exposure of donor eGFR: delayed graft function, recipient eGFR (at 6 months and 12 months), and survival (graft loss, death censored graft failure, and patient death).

Overall graft loss was defined as time from transplantation to return to dialysis, death with a functioning graft, or re-transplantation. Death censored graft failure was the same apart from censoring those who died with a functioning graft. Patient death was defined as the time from date of transplantation to patient death, not censored at graft failure. Follow-up was until 31 December 2019, and all survival times were censored at the end of follow-up or loss to follow-up. Exposure eGFR results were presented as 10 ml/min per 1.73 m<sup>2</sup> for ease of interpretation.

### Covariates

The donor variables age, sex, ethnicity, BMI, cause of death, diabetes, hypertension, smoking status, donation after circulatory death status, and oliguria were all analyzed as potential covariates. The following recipient variables were examined; age, sex, ethnicity, BMI, primary renal disease, number of previous transplantations, diabetes, hypertension, chronic lung disease, ischemic heart disease, peripheral vascular disease, cerebrovascular disease, and smoking. In addition, the transplant factors total ischemia time, peak panel reactive antibody, and human leukocyte antigen mismatches at A, B, DR were considered as potential covariates. The registry does not collect procurement biopsy results, and thus this could be not included in the analysis. Australia and New Zealand do not routinely use machine perfusion and these data are not collected in the registry, and thus this was not a part of the analysis.

### Data Analysis

The baseline characteristics of the study cohort were expressed either as mean (SD) or as median (interquartile range [IQR]), depending on the variable distribution. We created logistic regression models for the outcome of delayed graft function adjusting for covariates. Collinearity was assessed using variance inflation factor. The linearity assumption was assessed through categorization of continuous variables. Age at transplantation was found not to be linear and was dealt

with by using a restricted cubic spline. We checked for interaction terms using forward elimination. Nonsignificant variables were removed from the model using backward elimination with a cutoff of  $P < 0.05$ . Variables were also considered confounders if they changed the coefficient of the explanatory variable by >10%. The different exposure variables were inserted into the model. We compared the models using  $F$  test, adjusted  $R^2$ , and the Hosmer–Lemeshow goodness of fit and the  $C$  statistic (Supplementary Table S22).

Two multilinear regression models for the outcomes of recipient eGFR at 6 and 12 months were created, adjusting for covariates. Collinearity of different variables was assessed using the variance inflation factor. The linearity assumption was assessed using scatter plots of residual values for each continuous variable. Effect modification was assessed for using the forward elimination method. Nonsignificant variables were removed from the model using backward elimination. The different exposure variables were then assessed in the different models. The Wald test was used to assess the significance of exposure variable plus any interaction terms. We then compared the variables of interest for the different models using the  $F$  test and adjusted  $R^2$ .

Three separate multivariable Cox proportional hazards models were created to assess the outcomes of graft loss, death censored graft failure, and patient death. Nonlinear continuous variables were made categorical. Interaction terms were assessed. The nonsignificant variables were removed from the model using backward elimination. We used scaled Schoenfeld residuals to assess the proportional hazards assumption. Wald statistics were used to assess the significance of exposure variables. The models were assessed using the Harrell  $C$  statistic and Akaike Information Criterion (AIC). The cumulative incidence curves were presented with the eGFR variable stratified into equal quartiles to visually represent the difference in outcomes for the different levels of eGFR.

### Sensitivity Analysis

We undertook sensitivity analyses using serum creatinine instead of eGFR. There is no record in the ANZOD registry as to whether donors received dialysis prior to donation, and in this situation their SCr may be falsely low. To try to account for this, we undertook a sensitivity analysis by restricting the cohort to individuals without oliguria using oliguria as a surrogate marker of those requiring dialysis.

### Statistical Analysis

All analyses were conducted in Stata/IC 16.1 (StataCorp, College Station TX). The somersd package (Statistical Software Components, Boston College Department of

**Table 1.** Demonstrating baseline characteristics for transplant donors and recipients (N = 8971)

| Characteristic   | Value        |
|--|--------------|
| <b>Donor factors</b>                                     |              |
| Donor age, yr, median (IQR)                              | 50 (38, 60)  |
| Donor sex, male  | 5020 (56.0%) |
| Donor ethnicity  |              |
| Caucasian  | 8083 (90.2%) |
| Aboriginal/Torres Strait Islander                        | 147 (1.6%)   |
| Maori  | 119 (1.3%)   |
| Pacific  | 54 (0.6%)    |
| Asian  | 431 (4.8%)   |
| Other  | 128 (1.4%)   |
| Donor body mass index, kg/m <sup>2</sup> , mean (SD)     | 28 (6)       |
| Donor hypertension                                       | 2334 (26.3%) |
| Donor diabetes mellitus                                  | 522 (5.9%)   |
| Donor smoker   | 5816 (64.8%) |
| Donation after brain death                               | 7063 (78.7%) |
| Donor cause of death                                     |              |
| Stroke   | 4470 (49.8%) |
| Road trauma  | 877 (9.8%)   |
| Other trauma   | 798 (8.9%)   |
| Hypoxia/anoxia   | 1716 (19.1%) |
| Cerebral tumor   | 64 (0.7%)    |
| Other  | 1046 (11.7%) |
| Donor oliguria   | 976 (10.9%)  |
| Donor eGFR, admission, mean (SD)                         | 84 (26)      |
| Donor eGFR, terminal, mean (SD)                          | 89 (31)      |
| Donor eGFR, highest, mean (SD)                           | 97 (26)      |
| Donor creatinine, admission, mean (SD)                   | 90 (44)      |
| Donor creatinine, terminal, mean (SD)                    | 93 (76)      |
| Donor creatinine, lowest, mean (SD)                      | 75 (34)      |
| KDRI, raw score, median (IQR)                            | 1 (1, 2)     |
| <b>Recipient factors</b>                                 |              |
| Recipient age at transplantation, yr, median (IQR)       | 54 (45, 61)  |
| Recipient sex (male)                                     | 5722 (63.8%) |
| Recipient ethnicity                                      |              |
| Caucasian  | 5970 (72.4%) |
| Aboriginal/Torres Strait Islander                        | 381 (4.6%)   |
| Maori  | 214 (2.6%)   |
| Pacific  | 303 (3.7%)   |
| Asian  | 1113 (13.5%) |
| Other  | 266 (3.2%)   |
| Primary renal disease                                    |              |
| Glomerulonephritis                                       | 3756 (42.0%) |
| Polycystic disease                                       | 1249 (14.0%) |
| Reflux nephropathy                                       | 609 (6.8%)   |
| Hypertensive nephropathy                                 | 633 (7.1%)   |
| Diabetic nephropathy                                     | 1367 (15.3%) |
| Other  | 1320 (14.8%) |
| Recipient body mass index, kg/m <sup>2</sup> , mean (SD) | 27 (5)       |
| Recipient smoker   | 4161 (47.0%) |
| Recipient diabetes mellitus                              | 2047 (22.9%) |
| Recipient ischemic heart disease                         | 1967 (22.0%) |
| Recipient peripheral vascular disease                    | 1034 (11.5%) |
| Recipient cerebrovascular disease                        | 589 (6.6%)   |
| Recipient chronic lung disease                           | 843 (9.4%)   |
| Graft number >1 (kidney)                                 | 1003 (11.2%) |
| <b>Transplant factors</b>                                |              |
| HLA-A mismatch   |              |

(Continued)

**Table 1.** (Continued)

| Characteristic                            | Value        |
|---|--------------|
| 0   | 1652 (18.5%) |
| 1   | 4126 (46.1%) |
| 2   | 3172 (35.4%) |
| HLA-B mismatch                            |              |
| 0   | 1248 (13.9%) |
| 1   | 3394 (37.9%) |
| 2   | 4307 (48.1%) |
| HLA-DR mismatch                           |              |
| 0   | 2806 (31.4%) |
| 1   | 3166 (35.4%) |
| 2   | 2964 (33.2%) |
| Total ischemia to nearest hour, mean (SD) | 12 (5)       |
| Delayed graft function                    | 2800 (31.8%) |

Economics, Newton, MA) was used to calculate C statistics and their 95% confidence intervals.<sup>20</sup>

### Ethical Approval

This research was conducted with approval from the Royal Adelaide Hospital Human Research Ethics Committee HREC Reference number, HREC/17/RAH/408 and the Central Adelaide Local Health Network Reference number, R20170927.

## RESULTS

### Demographics

A total of 8971 transplant recipients were included in the analysis. The demographic details of recipients and donors are displayed in [Table 1](#). In all, 1585 patients died (17.7%), and 2307 (25.7%) had graft loss. A total of 72 patients were lost to follow-up (0.8%). Of the donors, 74 (0.82%) were excluded, as their eGFR could not be calculated because of missing data.

### Exposure Measurement

The mean terminal eGFR was 89 ml/min per 1.73 m<sup>2</sup> (SD = 31), the mean admission eGFR was 84 ml/min per 1.73 m<sup>2</sup> (SD = 26), and the mean highest eGFR was 97 ml/min per 1.73 m<sup>2</sup> (SD = 26). Terminal eGFR was higher than admission eGFR for 5222 values, equal to admission eGFR for 375 values, and less than admission eGFR for 3374 values. The results comparing the prediction of the different exposures are in the supplementary material ([Supplementary Table S1](#)). The unadjusted models are included in the supplementary material ([Supplementary Tables S2–S4](#)). The variables included in the multivariable model are detailed in the supplementary material ([Supplementary Tables S5–S22](#)).

### Delayed Graft Function

There was strong evidence of an association between DGF and terminal donor eGFR when adjusting for covariates ([Table 2](#)). The terminal and highest eGFR

**Table 2.** Model test statistics, aORs, and values for different adjusted eGFR models for DGF

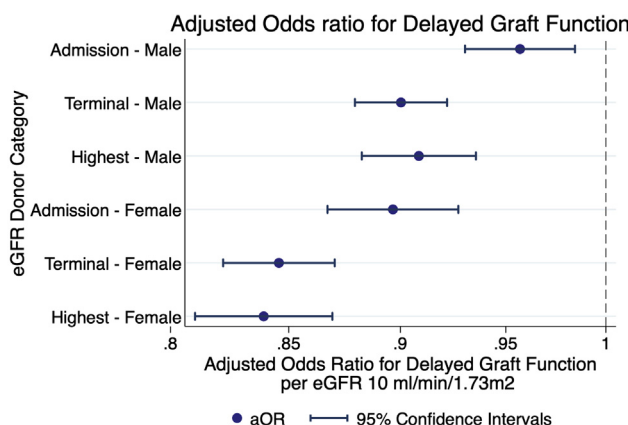
|                        | Admission eGFR per 10 ml/min per 1.73 m <sup>2</sup> | Terminal eGFR per 10 ml/min pr 1.73 m <sup>2</sup> | Highest eGFR per 10 ml/min per 1.73m <sup>2</sup> |
|------------------------|--|--|---|
| Delayed graft function |  |  |   |
| aOR for male donors    | 0.96   | 0.90   | 0.91  |
| (95% CI)               | (0.93–0.98)  | (0.87–0.92)  | (0.88–0.94)                                       |
| aOR for female donors  | 0.90   | 0.85   | 0.84  |
| (95% CI)               | (0.87–0.93)  | (0.82–0.87)  | (0.81–0.87)                                       |
| χ <sup>2</sup> Test    | 49   | 198  | 129   |
| P value                | <0.0001  | <0.0001  | <0.0001   |
| C statistic            | 0.75   | 0.76   | 0.75  |
| (95% CI)               | (0.74–0.76)  | (0.72–0.75)  | (0.73–0.76)                                       |

aOR, adjusted odds ratio; CI, confidence interval; DGF, delayed graft failure; eGFR, estimated glomerular filtration rate.

had lower odds of having delayed graft function compared to admission eGFR (Figure 2). An interaction term between donor sex and donor eGFR was included. Because of the interaction term between donor sex and donor eGFR, we presented the odds ratios (OR) for the different models stratified by donor sex. Interestingly, women had a lower risk of delayed graft function compared to men. The models had moderate discrimination and were similar across all models (C statistics: terminal C = 0.76 [95% confidence interval {CI} = 0.72–0.75], admission C = 0.75 [95% CI = 0.74–0.76], highest C = 0.75 [95% CI = 0.73–0.76]). The models were well calibrated (Supplementary Table S23).

### Recipient Kidney Function at 6 and 12 Months

There was strong evidence of an association between 6- and 12-month recipient eGFR and donor eGFR at different time points (Table 3). Terminal and highest eGFR were better predictors of 6- and 12-month eGFR compared to admission eGFR based on the test statistics, although the degree of difference was not marked.



**Figure 2.** Scatter plot for donor terminal compared to admission estimated glomerular filtration rate (eGFR).

**Table 3.** Model test statistics and values for adjusted eGFR models for 6- and 12-month eGFR

|                        | Admission eGFR per 10 ml/min per 1.73 m <sup>2</sup> | Terminal eGFR per 10 ml/min per 1.73 m <sup>2</sup> | Highest eGFR per 10 ml/min per 1.73 m <sup>2</sup> |
|------------------------|--|---|--|
| 6-mo eGFR              |  |   |  |
| Adjusted β coefficient | 0.58   | 0.69  | 0.80   |
| (95% CI)               | (0.39–0.77)  | (0.53–0.85)   | (0.61–0.99)  |
| F test statistic       | 10.8   | 21.4  | 20.1   |
| P value                | <0.0001  | <0.0001   | <0.0001  |
| 12-mo eGFR             |  |   |  |
| Adjusted β coefficient | 0.63   | 0.62  | 0.83   |
| (95% CI)               | (0.43–0.83)  | (0.46–0.78)   | (0.63–1.03)  |
| F test statistic       | 10.4   | 14.7  | 16.75  |
| P value                | <0.0001  | <0.0001   | <0.0001  |

eGFR, estimated glomerular filtration rate.

Interaction terms were created between donor eGFR and donor age, donor diabetic status, and donor smoking status. The models performed similarly, although adjusted R<sup>2</sup> values were worse for donor admission eGFR compared to terminal or highest GFR.

### Graft Loss and Patient Death

Cox proportional hazard models showed that eGFR was a predictor of graft survival across all models, although the evidence was strongest for terminal donor eGFR compared to both admission or highest eGFR (Table 4).

For death censored graft failure, Cox proportional hazard models showed that eGFR had strong evidence of an association across all models. Figure 3 shows the different cumulative incidence curves for the different donor eGFR variables. For terminal donor eGFR, there is clear delineation between the cumulative incidence curves for the different levels of eGFR. For the admission donor eGFR, the lower 2 groups' cumulative incidence curves converge. For the highest donor eGFR, the lower 2 categories of eGFR groups cross. For patient survival, there was no evidence of an association between donor eGFR and survival, with no statistically significant P values and confidence intervals that crossed 1.

For graft loss and patient death, there was an interaction between donor eGFR and donor age. For death censored graft failure, there was an interaction between donor eGFR and age and between donor eGFR and donor BMI. For all the Cox models, the C statistics showed moderate discrimination, and the AIC demonstrated similar model performance.

### Sensitivity Analyses

Sensitivity analyses were undertaken for all outcomes using Scr instead of eGFR. These did not change any of the conclusions (Supplementary Table S24). In a restricted cohort that excluded individuals with oliguria, there was little change in the model's performance (Supplementary Table S25).

**Table 4.** Model test statistics and values for adjusted eGFR models for survival outcomes

|                                     | Admission eGFR per 10 ml/min per 1.73 m <sup>2</sup> | Terminal eGFR per 10 ml/min per 1.73 m <sup>2</sup> | Highest eGFR per 10 ml/min per 1.73 m <sup>2</sup> |
|-------------------------------------|--|---|--|
| <b>Graft loss</b>                   |  |   |  |
| Adjusted HR                         | 0.98   | 0.97  | 0.96   |
| (95% CI)                            | (0.96–0.99)  | (0.95–0.98)   | (0.94–0.98)  |
| Wald statistic                      | 6.37   | 19.7  | 15.22  |
| P value                             | 0.04   | <0.0001   | 0.0005   |
| <b>Death censored graft failure</b> |  |   |  |
| Adjusted HR                         | 0.95   | 0.94  | 0.94   |
| (95% CI)                            | (0.93–0.98)  | (0.92–0.96)   | (0.92–0.97)  |
| Wald statistic                      | 13.1   | 33.5  | 21.6   |
| P value                             | 0.01   | <0.0001   | 0.0002   |
| <b>Patient death</b>                |  |   |  |
| Adjusted HR                         | 0.99   | 0.98  | 0.98   |
| (95% CI)                            | (0.97–1.01)  | (0.96–1.00)   | (0.96–1.00)  |
| Wald statistic                      | 0.85   | 4.61  | 3.12   |
| P value                             | 0.6  | 0.09  | 0.2  |

CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio.

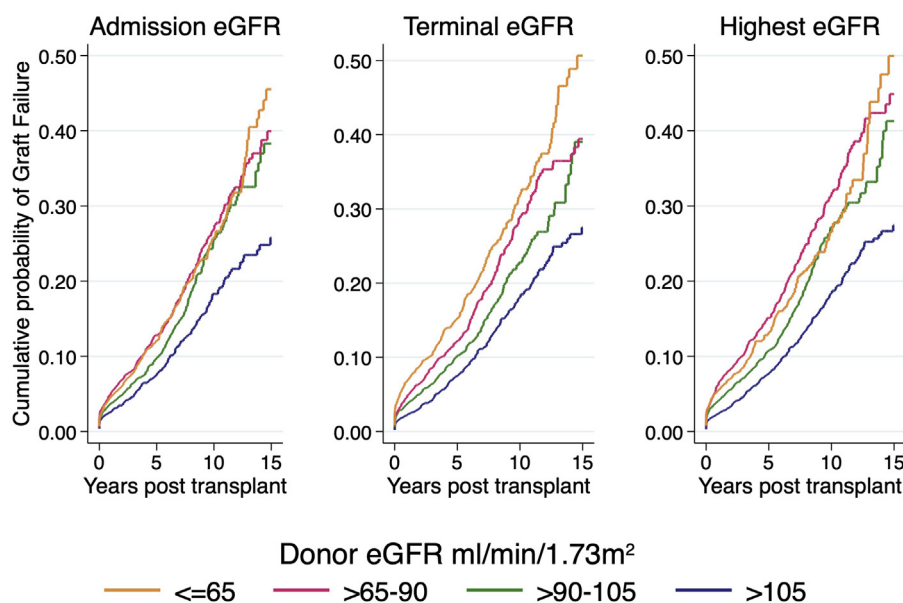
## DISCUSSION

We present a detailed prediction study assessing donor kidney function at different time points prior to organ procurement to predict clinically relevant outcomes. This study confirms a number of expected findings, particularly that donor kidney function was strong evidence of an association with recipient outcomes. The evidence of this association was stronger for outcomes that occurred earlier posttransplantation. For the short-term outcome of DGF, there was strong evidence of associations between terminal, admission, and highest

donor eGFR. Terminal donor eGFR, however, best predicted DGF followed by highest and then the admission donor eGFR. For the outcome of recipient 6- and 12-month eGFR, all donor eGFR time points had strong evidence of an association. Both terminal and highest donor eGFR had stronger evidence of an association than admission eGFR for 6 and 12-month recipient eGFR. For longer terminal outcomes, donor eGFR had stronger evidence of an association with death censored graft failure. This too, had the greatest evidence of an association with terminal followed by highest donor eGFR. This was also seen for the outcome of graft loss; however, evidence of an association was not as strong. There was no evidence of an association between donor eGFR and patient death. The strength of the associated effect was more pronounced for events than for earlier posttransplantation. This is an anticipated finding, because for long-term outcomes such as graft loss and patient death, they are more likely to be affected by recipient factors.

The absolute difference in mean eGFR between terminal and highest was 12.2 ml/min per 1.73 m<sup>2</sup> (mean eGFR: terminal 89 [SD = 31], admission 84 [SD = 26], highest 97 [SD = 26] ml/min per 1.73 m<sup>2</sup>). There was strong evidence for a difference in prediction when using terminal compared to admission eGFR to predict DGF. For longer-term outcomes, there was no difference in predicting outcomes when using the different donor eGFR measurements. For terminal donor eGFR, there was clear delineation between the cumulative incidence curves for the different levels of eGFR, suggesting that this exposure variable may be helpful for

## Cumulative Hazard function for Death Censored Graft Failure

**Figure 3.** Cumulative hazard function for death censored graft failure.

predicting outcome from all levels of eGFR. For highest and admission eGFR, for the lower categories of eGFR, the cumulative incidence curves crossed or joined. It could be argued that for the lower categories of eGFR, it is more important to be able to predict the outcomes than for higher levels of eGFR when there will more clearly be a survival advantage. There is a greater association between donor eGFR and early post-transplantation outcomes. For example, terminal eGFR compared to admission eGFR is better at predicting DGF that is the earlier posttransplantation outcome.

In certain instances with high-risk recipients, it may be particularly important to avoid DGF. For these circumstances, the use of terminal (rather than admission or highest) donor eGFR in conjunction with the other donor, recipient, and transplantation risk factors may aid in clinical decision making

The main study that has previously examined the timing of kidney function in donors to predict recipients outcomes was a study by Chiles *et al.*<sup>21</sup> They used the Organ Procurement and Transplantation Network /United Network for Organ Sharing data to assess whether admission or terminal creatinine was better able for discriminating the outcomes of graft or death censored failure at 1 and 3 years, using receiver operator characteristic curves.<sup>21</sup> They were unable to find a clinically meaningful difference in C statistics at either the 1- or 3-year time point (1 year:  $C = 0.6090$  vs.  $0.6058$ ,  $P = 0.001$ ; 3 years:  $C = 0.5985$  vs.  $0.5957$ ,  $P = 0.001$ ). This study suggested that either admission or terminal creatinine could be used to assess donor kidney function.

Overall, in our study, when assessing the different exposure variables for the different outcomes, terminal eGFR and highest eGFR performed slightly better than admission eGFR, although the difference between these outcomes were minimal. We assessed a number of different outcome measurements and found that the exposure variables performed similarly in the models for the different outcomes. This reinforces that current transplantation practice, in which terminal eGFR is most commonly used for risk assessment, is sound.

There are a number of strengths to our study. It is a comprehensive assessment of a number of different outcome variables that have not been previously examined. The study also included a large number of patients. There were few missing data, and the study captured most kidney transplantations performed in Australia and New Zealand over this time period. In addition, we undertook sensitivity analyses to assess whether eGFR or SCr was a better explanatory variable.

Our study had the limitations associated with using registry data. Also, analysing only those individuals who have already undergone transplantation means

that patients who had a lower terminal eGFR may have been excluded from the study, which may have contributed to selection bias. We used eGFR rather than SCr, as eGFR accounts for demographic and clinical variables in providing an estimate of filtration rate. GFR is ideally measured, however, during a steady state of creatinine,<sup>22</sup> and during intensive care admission and intercurrent illness this may not be the case.<sup>23</sup> Because of a lag in creatinine accumulation when the glomerular filtration rate changes, this will also be an issue when using creatinine as a marker of kidney function. This was demonstrated when there was no difference in outcome when SCr was used for the sensitivity analyses. In addition, using creatinine as a marker of kidney function does not account for the impact on creatinine production from muscle wasting states, diet, or medications.<sup>22</sup> Perhaps further research could be considered regarding whether measuring donor glomerular filtration rate by either traditional or novel methods would provide better predictive ability than SCr or eGFR.

In conclusion, this analysis suggests that terminal eGFR is a better predictor of a number of clinically important transplantation outcomes, although the differences were not large. Given this, as a component of prediction of graft outcomes, we support the use of terminal eGFR to assess donor kidney function.

## DISCLOSURE

All the authors declare no competing interests.

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## SUPPLEMENTARY MATERIAL

[Supplementary File \(PDF\)](#)

**Supplementary Methods**

**Supplementary Results**

**Table S1.** Table comparing prediction for different donor eGFR

**Table S2.** Test statistics and model values for 3 exposure variables of terminal, admission and highest eGFR different unadjusted models, for outcome of DGF

**Table S3.** Test statistics and model values for 3 exposure variables of terminal, admission and highest eGFR different unadjusted models, for outcome of 6 and 12 month eGFR. Assessment of model fit included in table

**Table S4.** Test statistics and model values for 3 exposure variables of terminal, admission and highest eGFR different unadjusted models, for survival outcomes

**Table S5.** Coefficients, 95% confidence intervals, and *P* values for exposure of admission eGFR per 10 ml/min per 1.73 m<sup>2</sup> outcome of delayed graft function

**Table S6.** Coefficients, 95% confidence intervals, and *P* values for exposure of terminal eGFR per 10 ml/min per 1.73 m<sup>2</sup> outcome of delayed graft function

**Table S7.** Coefficients, 95% confidence intervals and *P* values for exposure of highest eGFR per 10 ml/min per 1.73 m<sup>2</sup> outcome of delayed graft function

**Table S8.** Coefficients, 95% confidence intervals, and *P* values for exposure of admission eGFR per 10 ml/min per 1.73 m<sup>2</sup> outcome of recipient 6-month eGFR

**Table S9.** Coefficients, 95% confidence intervals, and *P* values for exposure of terminal eGFR per 10 ml/min per 1.73 m<sup>2</sup> outcome of recipient 6-month eGFR

**Table S10.** Coefficients, 95% confidence intervals and *P* values for exposure of highest eGFR per 10 ml/min per 1.73 m<sup>2</sup> outcome of recipient 6-month eGFR

**Table S11.** Coefficients, 95% confidence intervals, and *P* values for exposure of admission eGFR per 10 ml/min per 1.73 m<sup>2</sup> outcome of recipient 12-month eGFR

**Table S12.** Coefficients, 95% confidence intervals, and *P* values for exposure of terminal eGFR per 10 ml/min per 1.73 m<sup>2</sup> outcome of recipient 12-month eGFR

**Table S13.** Coefficients, 95% confidence intervals, and *P* values for exposure of highest eGFR per 10 ml/min per 1.73 m<sup>2</sup> outcome of recipient 12-month eGFR

**Table S14.** Coefficient, 95% confidence intervals, and *P* values for exposure of admission eGFR per 10 ml/min per 1.73m<sup>2</sup> outcome graft loss

**Table S15.** Coefficient, 95% confidence intervals, and *P* values for exposure of terminal eGFR per 10 ml/min per 1.73 m<sup>2</sup> outcome graft loss

**Table S16.** Coefficient, 95% confidence intervals, and *P* values for exposure of highest eGFR per 10 ml/min per 1.73 m<sup>2</sup> outcome graft loss

**Table S17.** Coefficient, 95% confidence intervals, and *P* values for exposure of admission eGFR per 10 ml/min per 1.73 m<sup>2</sup> outcome death censored graft failure

**Table S18.** Coefficient, 95% confidence intervals, and *P* values for exposure of terminal eGFR per 10 ml/min per 1.73 m<sup>2</sup> outcome death censored graft failure

**Table S19.** Coefficient, 95% confidence intervals, and *P* values for exposure of highest eGFR per 10 ml/min per 1.73 m<sup>2</sup> outcome death censored graft failure

**Table S20.** Coefficient, 95% confidence intervals, and *P* values for exposure of admission eGFR per 10 ml/min per 1.73 m<sup>2</sup> outcome patient death

**Table S21.** Coefficient, 95% confidence intervals, and *P* values for exposure of terminal eGFR per 10 ml/min per 1.73m<sup>2</sup> outcome patient death

**Table S22.** Coefficient, 95% confidence intervals, and *P* values for exposure of highest eGFR per 10 ml/min per 1.73 m<sup>2</sup> outcome patient death

**Table S23.** Test statistics and model values for 3 exposure variables of terminal, admission, and highest eGFR different adjusted models, for 3 different outcomes DGF, 6- and 12-month eGFR, and graft loss, death censored graft failure, and patient death (complete table for all outcomes and exposure variables including test statistics and assessment of model performance)

**Table S24.** Sensitivity analysis: terminal, admission, and lowest serum creatinine used instead of eGFR to predict outcomes. Test statistics and models values for 3 exposure variables of terminal, admission, and highest eGFR different models, for 3 different outcomes DGF, 6- and 12-month eGFR, and graft loss, death censored graft failure, and patient death

**Table S25.** Sensitivity analysis: restricted to those without oliguria. Test statistics and model values for 3 exposure variables of terminal, admission, and highest eGFR different models, for 3 different outcomes DGF, 6- and 12-month eGFR, and graft loss, death censored graft failure, and patient death

## REFERENCES

1. Wolfe RA, Ashby VB, Milford EL, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med.* 1999;341:1725–1730.
2. Tonelli M, Wiebe N, Knoll G, et al. Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes. *Am J Transplant.* 2011;11:2093–2109.
3. Laupacis A, Keown P, Pus N, et al. A study of the quality of life and cost-utility of renal transplantation. *Kidney Int.* 1996;50:235–242.
4. Meier-Kriesche HU, Ojo AO, Port FK, et al. Survival improvement among patients with end-stage renal disease: trends over time for transplant recipients and wait-listed patients. *J Am Soc Nephrol.* 2001;12:1293–1296.
5. Keith DS, Demattos A, Golconda M, et al. Effect of donor recipient age match on survival after first deceased donor renal transplantation. *J Am Soc Nephrol.* 2004;15:1086–1091.
6. Nyberg SL, Matas AJ, Kremers WK, et al. Improved scoring system to assess adult donors for cadaver renal transplantation. *Am J Transplant.* 2003;3:715–721.
7. Nyberg SL, Matas AJ, Rogers M, et al. Donor scoring system for cadaveric renal transplantation. *Am J Transplant.* 2001;1:162–170.



8. Port FK, Bragg-Gresham JL, Metzger RA, et al. Donor characteristics associated with reduced graft survival: an approach to expanding the pool of kidney donors. *Transplantation*. 2002;74:1281–1286.
9. Schold JD, Kaplan B, Baliga RS, Meier-Kriesche HU. The broad spectrum of quality in deceased donor kidneys. *Am J Transplant*. 2005;5:757–765.
10. Rao PS, Schaubel DE, Guidinger MK, et al. A comprehensive risk quantification score for deceased donor kidneys: the Kidney Donor Risk Index. *Transplantation*. 2009;88:231–236.
11. Organ Procurement and Transplantation Network Policies (OPTN). 2017. Available at: [https://optntransplanthrsagov/media/1200/optn\\_policiespdf#nameddest=Policy\\_08](https://optntransplanthrsagov/media/1200/optn_policiespdf#nameddest=Policy_08). Accessed August 5, 2020.
12. Massie AB, Luo X, Chow EK, et al. Survival benefit of primary deceased donor transplantation with high-KDPI kidneys. *Am J Transplant*. 2014;14:2310–2316.
13. Bae S, Massie AB, Thomas AG, et al. Who can tolerate a marginal kidney? Predicting survival after deceased donor kidney transplant by donor-recipient combination. *Am J Transplant*. 2019;19:425–433.
14. NHS Blood and Transplant. Kidney Transplantation: Deceased Donor Organ Allocation. 2019. <https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/16915/kidney-allocation-policy-pol186.pdf>. Accessed August 5, 2020.
15. Dahmane D, Audard V, Hiesse C, et al. Retrospective follow-up of transplantation of kidneys from 'marginal' donors. *Kidney Int*. 2006;69:546–552.
16. Zheng YT, Chen CB, Yuan XP, Wang CX. Impact of acute kidney injury in donors on renal graft survival: a systematic review and Meta-Analysis. *Ren Fail*. 2018;40:649–656.
17. Hall IE, Schroppel B, Doshi MD, et al. Associations of deceased donor kidney injury with kidney discard and function after transplantation. *Am J Transplant*. 2015;15:1623–1631.
18. Hoste EA, Bagshaw SM, Bellomo R, et al. Epidemiology of acute kidney injury in critically ill patients: the multinational AKI-EPI study. *Intensive Care Med*. 2015;41:1411–1423.
19. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150:604–612.
20. Newson R. *SOMERSD*: Stata module to calculate Kendall's tau-a, Somers' D and median differences. *Statistical Software Components*. Newton, MA: Boston College Department of Economics; 1998.
21. Chiles MC, Husain SA, Skillen W, et al. Predictive value of using initial versus terminal deceased donor creatinine to calculate the Kidney Donor Risk Index. *Am J Kidney Dis*. 2017;70:153–154.
22. Stevens LA, Levey AS. Measured GFR as a confirmatory test for estimated GFR. *J Am Soc Nephrol*. 2009;20:2305–2313.
23. Coca SG, Yusuf B, Shlipak MG, et al. Long-term risk of mortality and other adverse outcomes after acute kidney injury: a systematic review and meta-analysis. *Am J Kidney Dis*. 2009;53:961–973.