

# Deceased-Donor Kidneys: Is Past Performance an Indicator of Future Transplant Success?



Divya Raghavan<sup>1</sup>, Isabelle Dominique V. Tomacruz<sup>2</sup> and Isaac E. Hall<sup>1</sup>

<sup>1</sup>Division of Nephrology & Hypertension, Department of Internal Medicine, University of Utah School of Medicine, Salt Lake City, Utah, USA; and <sup>2</sup>Division of Nephrology, Department of Medicine, Philippine General Hospital, University of the Philippines Manila, Metro Manila, Philippines

*Kidney Int Rep* (2021) 6, 2025–2027; <https://doi.org/10.1016/j.ekir.2021.06.009>

© 2021 International Society of Nephrology. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

[See Clinical Research on Page 2075](#)

There continues to be a disparity between the number of kidneys available for transplantation and the number of patients with end-stage kidney disease. Although kidney transplantation remains the best treatment option for most patients with end-stage kidney disease, the current demand still outpaces organ supply. Because of the mortality associated with remaining on the waitlist, higher-risk kidneys, such as those from donors with acute kidney injury, are increasingly being considered for transplantation. Such kidneys are usually used in recipients with shorter post-transplant life expectancies. Historically, kidney allocation systems have attempted to optimize organ use by incorporating donor factors in prediction models and risk scores. This has

helped health care professionals better stratify deceased-donor organs for allocation, while also facilitating clinical decision making and helping guide counseling of recipient candidates. As such, it is important to understand how donor kidney characteristics relate to recipient outcomes. Donor serum creatinine, in particular, continues to be the primary marker for determining donor kidney function and predicting recipient graft function, but which time point to use for the donor serum creatinine value remains an open question.

Prior to 2014, deceased-donor kidneys in the United States were classified as either “standard criteria” or “expanded criteria” donor kidneys based on 4 factors—age, “terminal” serum creatinine, history of hypertension, and cause of death.<sup>1</sup> Kayler *et al.*<sup>2</sup> evaluated recipient outcomes of kidneys from adult donors using US transplant registry data from 1995 to 2007. They found that standard criteria donor kidneys with elevated terminal serum creatinine values were

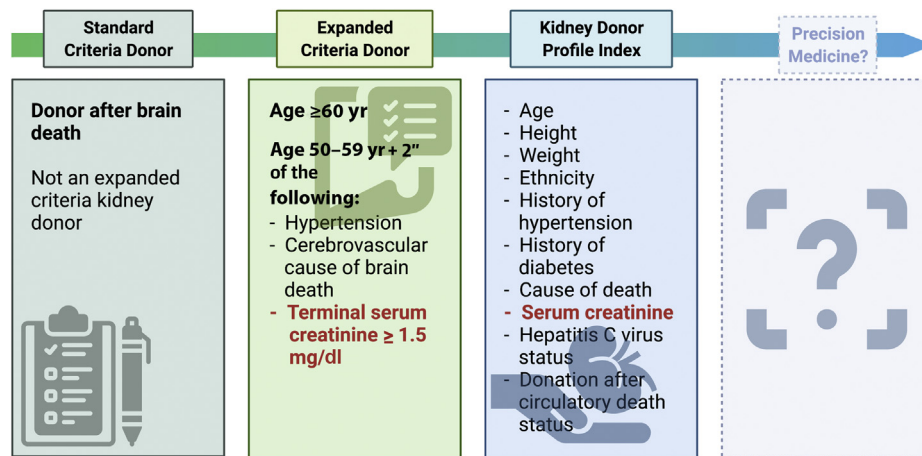
more likely to be discarded. However, when such organs were transplanted, the elevated terminal creatinine was not a significant risk factor for graft loss. On the other hand, in recipients of expanded criteria donor kidneys, higher terminal creatinine was associated with an increased risk of graft loss.

As a part of the ongoing quest to better predict the future performance of deceased-donor kidneys, the new kidney allocation system in 2014 replaced the standard or expanded criteria donor classification with the kidney donor profile index (KDPI), which provides an estimate of the risk of post-transplant graft loss compared with deceased-donor kidneys from the previous year. As a continuous marker, the KDPI was thought to be a better indicator than the binary standard or expanded criteria donor classification.<sup>1</sup> The KDPI is derived from the kidney donor risk index, which incorporates 10 donor factors, some of which were also used in the previous standard or expanded criteria donor classification. Interestingly, though the KDPI and kidney donor risk index scores are US-centric, they may have utility in other countries as well.<sup>3,4</sup> Clayton *et al.*<sup>4</sup> found that the US kidney donor risk index score was a moderately good predictor of death-censored and overall graft survival in the Australian and New Zealand populations. Although the kidney donor risk index is not used for allocation in Australia, it is reported to clinicians and has implications for decisions about organ acceptance.

Subsequent research has focused on further improving the predictive power of the KDPI score by more carefully examining the role of the individual factors that comprise the score. Chiles *et al.*<sup>5</sup> explored the relationship between

**Correspondence:** Isaac E. Hall, University of Utah School of Medicine, 30 N 1900 E, Room 4R312, Salt Lake City, Utah 84132, USA. E-mail: [isaac.hall@hcs.utah.edu](mailto:isaac.hall@hcs.utah.edu)

**Received 7 June 2021; accepted 7 June 2021**



**Figure 1.** Evolution of kidney donor risk scoring.

initial versus terminal donor creatinine and its impact on KDPI for predicting graft outcomes in the United States. They used data from the Organ Procurement and Transplantation Network to perform a retrospective cohort study of 104,510 kidney transplants (20% of which came from donors with acute kidney injury), and found that 55% of the kidneys changed KDPI categories when the initial serum creatinine was used instead of the terminal serum creatinine (35% changed to a worse KDPI category). They found no consequential differences in graft loss or death-censored graft failure at 1 and 3 years after transplant. Their results were similar when the analysis was limited to kidneys from donors with acute kidney injury. Although this was ultimately a negative study, a more nuanced understanding of the individual KDPI factors could lead to better predictions of post-transplant outcomes.

In this edition of *KI Reports*, Irish *et al.*<sup>6</sup> investigate whether donor admission, terminal, or highest estimated glomerular filtration rate (eGFR) best predicted post-transplant outcomes. It is important to note that only admission and last recorded serum creatinine are collected in the

registry, and “highest” eGFR is simply the higher of the 2 values. Data were obtained from the Australian and New Zealand organ donation dialysis and transplant registries (ANZDATA) between 2003 and 2019.

The authors first focus on delayed graft function. An important finding was that higher terminal eGFR for both male and female donors was associated with lower risk of delayed graft function. For male donors, every 10–ml/min per 1.73 m<sup>2</sup> increase in terminal eGFR corresponded to a 10% decrease in the likelihood of delayed graft function; for female donors, the same increase in terminal eGFR was associated with a 15% decrease in the likelihood of delayed graft function. Similar associations were observed using highest eGFR. Notably, admission eGFR did not appear to have as strong an association (4% for male donors and 10% for female donors).

Next, the authors studied the impact of donor eGFR on 6-month and 12-month recipient eGFR. The same 10–ml/min per 1.73 m<sup>2</sup> increase in terminal eGFR was associated with only a 0.69–ml/min per 1.73 m<sup>2</sup> increase in 6-month recipient eGFR and a 0.62–ml/min per 1.73 m<sup>2</sup> increase in 12-month recipient eGFR. The corresponding increases in

recipient eGFR based on the highest donor eGFR were 0.8 ml/min per 1.73 m<sup>2</sup> for 6-month and 0.83 ml/min per 1.73 m<sup>2</sup> for 12-month recipient eGFR. In contrast, for the donor admission eGFR, these increases were 0.58 and 0.63 ml/min per 1.73 m<sup>2</sup> for the 6-month and 12-month values, respectively. It is important to note that though the correlations are strong, the effect sizes for the 6-month and 12-month eGFRs are small in comparison to the effect sizes observed for delayed graft function. Similar small effect sizes were observed for graft loss and death-censored graft failure. Donor eGFR was a predictor for graft survival across all models, and the association was strongest for terminal eGFR.

Overall, Irish *et al.* have produced a comprehensive study of donor kidney function at different time points showing strong evidence of association with clinically relevant outcomes; however, the strengths of association were more pronounced for the earlier post-transplant outcome (i.e., delayed graft function) rather than longer-term outcomes. Donor eGFR based on serum creatinine showed no evidence of association with patient survival, which is consistent with the idea that recipient factors are more likely to be influential at later time points.

When analyzing the cumulative hazard for death-censored graft failure, donor terminal eGFR performed better than highest or admission eGFR. The authors acknowledge the small effect sizes across the board and recognize the marginal benefit of using terminal eGFR over admission and highest eGFR. They also note that calculating eGFR during the donor's hospitalization limits its accuracy as the serum creatinine values may not be at a steady state during critical illness. Despite the aforementioned limitations, these findings appear to lend support to the current practice of using terminal eGFR/serum creatinine to predict early transplant outcomes.

Moving forward, as we enter the era of precision medicine (Figure 1), investigators will likely further explore the relationship between other donor kidney variables, such as biomarkers or predisposing genetic variations, for their utility in risk prediction and organ allocation. For instance, Julian *et al.*<sup>7</sup> showed that using APOL1 genotypes instead of race in donors of recent African ancestry as part of a refined kidney donor risk index could improve allocation by providing these good-quality kidneys to recipients with longer estimated post-transplant survival. Comparing donor and recipient HLA epitopes, which are antigenically important subunits critical for antibody

binding, may also make certain antigen mismatches acceptable and provide additional information for decision making around kidney allocation and induction immunosuppression to improve transplant outcomes. However, these advances may pose challenges to health care professionals and policy makers seeking to balance utility and equity.<sup>8</sup>

The findings in this article constitute a small but important step in the endeavor to better understand the predictive power of deceased-donor score-based systems for recipient outcomes. Such score-based systems will likely help make better decisions in terms of organ discard and facilitate improved matching of donor kidneys with appropriate recipient profiles. This work not only has implications for patients from Australia and New Zealand but could help refine the interpretation of KDPI scores for patients in other countries as well. More evidence quantifying these effect sizes is needed, however, before large-scale re-evaluations of existing scoring systems are undertaken.

## DISCLOSURE

All the authors declared no competing interests.

## REFERENCES

1. Organ Procurement and Transplantation Network Policy 8: Allocation of Kidneys. Published 2021. Updated April 1, 2021. Accessed May 5, 2021 <https://optn.transplant.hrsa.gov/governance/policies/>.
2. Kayler LK, Garzon P, Magliocca J, et al. Outcomes and utilization of kidneys from deceased donors with acute kidney injury. *Am J Transplant.* 2009;9:367–373.
3. Dahmen M, Becker F, Pavenstadt H, Suwelack B, Schutte-Nutgen K, Reuter S. Validation of the Kidney Donor Profile Index (KDPI) to assess a deceased donor's kidneys' outcome in a European cohort. *Sci Rep.* 2019;9:11234.
4. Clayton PA, Dansie K, Sypek MP, et al. External validation of the US and UK kidney donor risk indices for deceased donor kidney transplant survival in the Australian and New Zealand population. *Nephrol Dial Transplant.* 2019;34:2127–2131.
5. 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.
6. Irish GL, Coates PT, Clayton PA. Association of admission, nadir, and terminal donor creatinine with kidney transplantation outcomes. *Kidney Int Rep.* 2021;6:2075–2083.
7. Julian BA, Gaston RS, Brown WM, et al. Effect of replacing race with apolipoprotein L1 genotype in calculation of kidney donor risk index. *Am J Transplant.* 2017;17:1540–1548.
8. Caulfield T, Murdoch B, Sapir-Pichhadze R, Keown P. Policy challenges for organ allocation in an era of "precision medicine.". *Can J Kidney Health Dis.* 2020;7:2054358120912655.