



# The Ripple Effects of Delayed Graft Function

Yee Lu<sup>1</sup> · Kenneth J. Woodside<sup>2,3</sup>

Accepted: 26 February 2024 / Published online: 11 April 2024  
© The Author(s), under exclusive licence to Springer Nature Switzerland AG 2024

## Abstract

**Purpose of Review** The number of people with end-stage kidney disease requiring renal replacement therapy is growing at a faster rate than the number of kidneys available for transplant. Additional options for deceased donor kidney transplant will increase risk for delayed graft function, which has expansive clinical, performance, and financial implications. The purpose of this paper is to discuss how delayed graft function impacts different domains.

**Recent Findings** Given that most kidney transplants in the USA are performed with deceased donors, expanding the deceased donor pool is likely to be of the highest impact. The potential additional sources of deceased donors include increasing organ donation in general and willingness to change perspectives about acceptable kidneys for transplant. An important implication of expanding criteria for acceptable kidneys for transplant is the risk for delayed graft function, what is expected, and how do we manage a potential increase burden for patients, transplant centers, and organ procurement organizations. Given the directives of Advancing American Kidney Health policies, it is important that we are thorough and thoughtful about navigating the post-transplant experience for patients and providers. The breadth of impact ranges from exploring the additional resources patients require to manage the social and financial complications associated with delayed graft function to balancing transplant centers' challenge to provide excellent clinical care in a standard fashion against desire to transplant all eligible candidates.

**Summary** This paper summarizes the historical approach to delayed graft function and proposes a dynamic framework for an improved system to review impact to the multiple stakeholders.

**Keywords** Kidney transplant · Delayed graft function · Health inequity · Race · Outcome

## Introduction

In 2019, the Department of Health and Human Services (DHHS) proposed policy to double the number of kidneys available for transplant by 2030 [1]. Potential sources of additional kidneys for transplant include utilizing more of the deceased donor kidneys (DDK) recovered, but not transplanted, and increasing the number deceased donors. In 2022, 9416 additional kidneys were recovered by Organ Procurement Organizations (OPO) and offered to transplant centers, but ultimately not accepted for transplant [2].

Based on the 2021 Scientific Registry of Transplant Recipients (SRTR) report, the nonuse rate was 40–60%, highest in deceased donors aged 55 years or older, with a history of diabetes or hypertension, elevated BMI, or Kidney Donor Profile Index (KDPI) greater  $\geq$  85% [3].

## More Aggressive Utilization Likely Means More Delayed Graft Function

To increase the DDK pool, additional donors will need to be more aggressively recovered from donors from older age groups and those deceased after cardiac death (DCD). Many of the variables associated with kidneys that were procured and historically not transplanted are also at increased risk for delayed graft function (DGF) when they are actually engrafted. Such kidneys are progressively becoming more common and include donors with acute kidney injury, more advanced glomerular sclerosis on biopsy, higher KDPI

✉ Yee Lu  
yeel@umich.edu

<sup>1</sup> Division of Nephrology, Department of Internal Medicine, University of Michigan, 6689 UH South, 1500 E. Medical Center Drive, Ann Arbor, MI 48109-5296, USA

<sup>2</sup> Gift of Life Michigan Medicine, Ann Arbor, MI, USA

<sup>3</sup> Academic Invisus, LLC, Ann Arbor, MI, USA

score, poor pump numbers, prolonged cold ischemia time, surgical injury, and a combination of age and DCD status [4, 5]. The impact of DGF, defined most commonly as dialysis requirement within the first 7 days post kidney transplant, has different impacts on patients, patient support systems, transplant centers, and the healthcare system [6]. Currently, there are no mechanisms in place to assist patients navigating complications associated with DGF or offer flexibility in OPO and transplant center performance standards and payments if there is increased rates of DGF and primary nonfunction (PNF). There must be thoughtfulness crafting the national policies addressing the impact on multiple stakeholders in this conversation.

### DGF Takes Resources—but That Is Okay if the Patient Gets Off Dialysis

While the long-term kidney and patient survival for DGF is promising, recovering from DGF takes times and resources. Patients with DGF have longer hospitalization days, more frequent re-admissions, more clinic visits, and higher rates of rejection, sensitization, cardiac events, and infections [7, 8, 9•]. The increase in treatment burden adds to work and resources required for care, resulting in a different utilization pattern of healthcare resources and poorer quality of life [10•]. Patients with DGF are also accumulating financial complications, but this data is very limited. Compared to those without DGF, patients with DGF have longer admissions and more clinical follow-ups. This impacts the utilization of sick days, if available, ability to return to work, and caretaker availability. In terms of healthcare costs, care for patients with commercial insurance and DGF is almost \$20,000 higher, with some of that being out-of-pocket deductibles [11]. With the implementation of the Kidney Allocation System (KAS) on December 4, 2014, there was increased DGF for all races. However, the distribution of DGF was disparate among races. For non-Hispanic Black (NHB) and Hispanic patients, DGF increased by 5–6%, as compared to about 2% in non-Hispanic White (NHW) [12]. Practices that expand DDK pools and increase utilization of nonuse kidneys will increase incidence and prevalence of DGF, potentially resulting in disproportionate burden for certain vulnerable populations. Not only are the risk of DGF disproportionately higher in Hispanic and Black kidney transplant recipients, Black patients also bear the greatest economic burden for health disparities [13•]. Implementing Advancing American Kidney Health goals is an opportunity to design a system that incorporate diverse perspectives that are intentional in addressing inequalities in access to transplant, patient and graft outcome, and resource utilization.

Unfortunately, there is little guidance for conversation between healthcare providers and patients about DGF risks

and burden. Literature suggests patients want to participate in their end-stage kidney disease (ESKD) decision-making process, as opposed to deferring to medical providers. Regardless of the decision maker preference, patients want more information about their health management [14]. There is also some data about what patients want to prioritize for their health decisions. Howell et al. reported that transplant recipients view kidney rejection and function as the most important outcomes, more important than their own survival. Only 12% of participants in their study ranked death more important than kidney rejection or kidney dysfunction. In this study, there was also a time-dependent component of priorities. Participants were more concerned about the kidney function in the first year and risk for rejection after the first year [15]. DGF directly impacts a patient reported 1-year priority. With the change in policies and trend in DDK donor demographics and risk for DGF, more attention and research are needed to understand how these systematic decisions factor into patients' decision process and impact their lives.

### Impact of Metrics

There are many clinical variables that are used to estimate risk for DGF and can be helpful for decision-making conversations. The Kidney Donor Profile Index (KDPI), which is a derivative of Kidney Donor Risk Index (KDRI), is familiar to most and integrated into allocation. KDPI is a continuous metric calculated using donor characteristics: ethnicity, race, age, height, weight, history of hypertension, history of diabetes, cause of death, serum creatinine, HCV status, and DCD criteria. It has been observed that kidneys with  $KDPI \geq 85\%$ , a “high risk” label, are more likely to have DGF and be nonuse [16]. Just having a “high KDPI” label changes how transplant providers utilize a potential kidney and whether a patient will accept the organ for transplant.

Metrics can have impact disproportionate to their accuracy. Transplant regulatory metrics are also limited by what data is collected, which is notoriously incomplete. The Centers for Medicare and Medicaid Services (CMS) published the Final Rule and Conditions for Approval and Re-Approval of Transplant Centers that defines the threshold, using the observed to expected ratio for a given outcome, which triggers citation and review [17]. Donor and recipient variables are collected and included, but there are concerns about what is included and how it is used. The most glaring example is that DonorNet does not have a data field where it is specified *if a deceased donor who donates a kidney is on dialysis*. There is a current proposal to include such a field—which only then will allow it to be included in the risk adjustment—currently out for public comment [18]. In 2016, there was a 30-day period when there was a programming error

for the yearly KDPI adjustment. The result was a 1–21% increase in the KDPI score. Risk-adjusted model demonstrate a higher nonuse rate with no change in recipient characteristics. The nonuse rate was much higher for kidneys with inflated KDPI scores that crossed the 85% threshold, when compared to those that did not [12]. Even after adjusting for donor characteristics on multivariate analysis, they demonstrated that kidneys with a high KDPI label had at least a twofold increased likelihood for nonuse. Mohan et al. demonstrated the same “high KDPI” label bias [19]. There is also some concern about the dynamic nature of the KDPI score, as it is recalibrated annually based on the characteristics of the procured kidneys from the previous year. The result is that KDPI 85% threshold is adjusted with time. Crannell et al. demonstrated that, for the same kidney, the KDPI score gets lower over time. A kidney with KDPI score of > 85% in 2012 would have been recalibrated to 83% in 2020 [20]. It is imperative to account for the dynamic and continuous nature of the KDPI scale when crafting policies and standards that incorporate this score.

There is concern about the inclusion of race in the KDPI score, specifically how “race” contributes to the score, impacts organ utilization, and predicts risk for DGF and graft failure. Historically, DDK from Black donors have been described as associated with lower graft and patient survival [21]. With the recognition of the weak association between reported race and biological outcomes, including graft function, and efforts for transparency regarding structural racism, there is growing literature comparing the current KDPI score to a race-free KDPI score. Using a race-free KDPI calculator would reclassify up to 50% of these donors from KDPI > 85% to KDPI ≤ 85% [22, 23•, 24•]. Chong et al.’s model demonstrated that 73% of Black donors with KDPI > 85% would be scored to ≤ 85%. In their study, kidneys reclassified to a lower KDPI score had better allograft survival than those that did not get reclassified. A reduction in the number of nonuse kidneys from Black donors might benefit Black recipients due to improved blood type and HLA matching [25]. To optimize resource utilization and address bias, removing race from KDPI may improve access and equity without compromising outcome.

Another potential source of DDK that has increased risk for DGF is procured, but not transplanted, kidneys. The number of nonuse kidneys has been growing steadily [3]. From 2000 to 2015, the number of nonuse deceased donor kidneys increased by almost 90%, with the rate of nonuse kidneys outpacing the rate of total kidney recovered [19]. The characteristics associated with the nonuse kidneys are related to concern for poor patient and graft outcomes, increased healthcare cost, and logistical limitations. Organs from donors with multiple concerning variables have a higher probability of not being transplanted. The nonuse kidneys were associated with older donors, death due to a

stroke, higher terminal creatinine, higher KDPI, increased likelihood of a biopsy, and comorbidities such as hypertension, diabetes, or hepatitis C [19]. However, there is also significant overlap in nonuse rate for KDPI ≥ 85 and KDPI 21–85%, 40–50%, and 30–50%, respectively [19, 20]. This is concerning for potential loss of kidneys that could have provided better quality of life and graft and patient survival.

There are many potential contributors to the wide overlap for nonuse. One observation is different UNOS regions have varying rates of nonuse. After adjusting for donor demographics, clinical factors, and social histories, the likelihood for nonuse ranged from UNOS region 1 having 27% lower likelihood to UNOS region 10 having 28% higher likelihood [19]. In addition to different transplant center practices, regulatory metrics might incentivize transplant centers to be risk averse and selective about donors and recipients who are higher risk. Among programs with on-going CMS compliance concerns CMS, transplant volumes usually decrease by about 40%, compared to 6% increase for those without compliance concerns [26]. Schold et al. demonstrated a mean decline of about 22 transplants in centers with low-performance program specific reports, compared to an expected annual increase of 8 transplants [27•]. In response to scrutiny, it has been observed that transplant centers also change the candidate selection criteria, resulting in limited access for more high-risk patients and utilization of more high-risk donors [28].

In addition to concern about patient outcome and access, there are also financial implications. Insurance companies also review performance metrics to determine contractual relationships with transplant centers. Outcome can affect whether insurance companies allow their patients access to a transplant center. DGF also cost more for the transplant centers, about \$20,000 higher index hospitalization cost and \$40,000 higher cost over the first year when compared to non-DGF transplants [11, 29•].

As practice patterns and policies move towards metrics to promote expanding the donor pool, outcomes should be interpreted in the context of potential unintended impact on transplant center practices and patient access. Performance and outcome metrics, to be reasonably applicable, have to be relatively short term (e.g., 1 year outcome); otherwise, transplant programs, and for that matter the entire transplant system, will have changed such that the metrics are no longer applicable to the current conditions. Additionally, just like every other aspect regulated behavior, Goodhart’s Law applies: When a metric becomes a target, it ceases to be a good metric because behavior changes in response to the new metric (formally stated as “Any observed statistical regularity will tend to collapse once pressure is placed upon it for control purposes.”) [30]. However, it is those very long-term outcomes that the short-term metrics try to reflect. There is no easy mechanism to institute change

in response to outcomes from practices from a decade ago when the practices have already changed. While this will be a continual struggle with the inevitable corruption of any given metric, all aspects of the transplant system, from regulators to transplant centers to patients, must keep the actual important outcome—long-term patient survival and quality of life. Given the current organ supply, increased DGF is to be expected, coupled with increased resource utilization and cost, but as long as the greater transplant community prioritizes long-term patient and graft outcomes, there will be all benefit to the patients.

## Conclusions

The number of patients with ESKD is growing at a faster rate than the availability of deceased donor kidneys. A more aggressive organ acceptance approach is a reasonable, given published practice patterns and outcomes in other regions [31]. There is evidence that the variables used to define standard of practice and risk adjustments, with direct impact on patient access to transplant, outcomes, program performance metrics, and payment, form an evolving continuum. Performance metrics for a single center and clinical decisions for an individual patient are based on large population studies. While that is not an unreasonable approach most of the time, we must always bear in mind the unmeasured and unknown factors that result in unexpected outcomes inherent to patient care. Scientific research is constantly changing, sometimes incremental additions to current models and other times surging to replace previous models. Given the evolving unknowns, it is not realistic for a given model to include all relevant variables and anticipate all potential changes and impact. While the goals are reasonable and well-intentioned, sometimes the weight given to certain variables in statistical models is out of proportion, in both directions, to their clinical significance.

An example of perhaps too much leniency is peripheral vascular disease. The data variable lacks nuance, meaning the same weight is given to a toe amputation as an above-knee amputation or limb-threatening ischemia, despite the two having very different clinical impacts. Additionally, societal understanding of how demographics are defined and reported is progressing. Our understanding of gender, for example, is undergoing rapid development. Self-reported gender versus sex assigned at birth is something that has not been incorporated into current models for risk adjustment—and remains inadequately captured by current data collection approaches, further extending limitations on future analysis. This collection bias determines how this particular variable is defined and weighed for clinical impact without being accounted for in the models for performance and outcomes.

It is irresponsible to build an infrastructure that ignores incremental deviations due to perspectives that are unaccounted for in statistical models with devastating impacts on program performance and patient access.

The transplant community should be held to a higher standard when our decisions directly impact patient access to care, patient and system outcomes, as well as the allocation of resources for healthcare delivery. At the same time, those holding us to the standards must understand both the usefulness and limitations of the models we measure ourselves against. Both medical science and society itself continually evolve. This requires shorter review cycles to update the models and review the breadth of intended and unintended impact, as well as the appreciation that the next generation will find limitations and issues with the current statistical models. These ongoing evaluations and conversations about the transplant system should include a diverse panel, including a variety of stakeholders and people who have different priorities, perspectives, and experiences. While this might be tedious and uncomfortable, given the impact of the transplant centers and regulatory bodies on people's destinies, it is our responsibility to invest in thoughtful solutions.

**Acknowledgements** The editors would like to thank Dr. Aparna Padiyar for handling the review of this manuscript.

**Author Contributions** Y.L. wrote the main manuscript text. All authors reviewed and edited the manuscript.

**Data Availability** No datasets were generated or analysed during the current study.

## Declarations

**Conflict of Interest** The authors declare that they have no conflict of interest.

## References

Papers of particular interest, published recently, have been highlighted as:

### • Of importance

1. Advancing American Kidney Health. DHHS; 2019.
2. Massa, B., High rate of donated organs going unused is costing lives. In: *Nephrology news and issues*. 2023.
3. OPTN/SRTR 2021 annual data report. Organ Procurement and Transplantation Network (OPTN) and Scientific Registry of Transplant Recipients (SRTR). 2023.
4. Woodside KJ, et al. Utilization of kidneys with similar kidney donor risk index values from standard versus expanded criteria donors. *Am J Transplant*. 2012;12(8):2106–14.
5. Kayler LK, et al. Outcomes and utilization of kidneys from deceased donors with acute kidney injury. *Am J Transplant*. 2009;9(2):367–73.

6. Mallon DH, et al. Defining delayed graft function after renal transplantation: simplest is best. *Transplantation*. 2013;96(10):885–9.
7. Yarlagadda SG, Klein CL, Jani A. Long-term renal outcomes after delayed graft function. *Adv Chronic Kidney Dis*. 2008;15(3):248–56.
8. Tapiawala SN, et al. Delayed graft function and the risk for death with a functioning graft. *J Am Soc Nephrol*. 2010;21(1):153–61.
- 9.● Vasilj M, et al. *SP757* The burden of delayed graft function on kidney transplant recipients and impact on long-term outcomes. *Nephrol Dial Transplant*. 2019;34(Supplement\_1). **Retrospective study exploring delayed graft function's burden on patients and health care system.**
- 10.● Lorenz EC, et al. Patient experience after kidney transplant: a conceptual framework of treatment burden. *J Patient Rep Outcomes*. 2019;3(1):8. **Patient survey to determine patient treatment burden after kidney transplant.**
11. Mayne T, CF, Dillon A, Wang W, Mohan S. The 1-year incremental costs of delayed graft function (DGF) in commercially insured kidney transplant patients under 65 [abstract]. *Am J Transplant*. 2020;20
12. Stewart DE, et al. Changes in deceased donor kidney transplantation one year after KAS implementation. *Am J Transplant*. 2016;16(6):1834–47.
- 13.● LaVeist TA, et al. The economic burden of racial, ethnic, and educational health inequities in the US. *JAMA*. 2023;329(19):1682–1692. **Racial and ethnic minorities are subject to significant health inequities.**
14. Orsino A, et al. Medical decision-making and information needs in end-stage renal disease patients. *Gen Hosp Psychiatry*. 2003;25(5):324–31.
15. Howell M, et al. Important outcomes for kidney transplant recipients: a nominal group and qualitative study. *Am J Kidney Dis*. 2012;60(2):186–96.
16. Zens TJ, et al. The impact of kidney donor profile index on delayed graft function and transplant outcomes: a single-center analysis. *Clin Transplant*. 2018;32(3):e13190.
17. Centers for, M. and H.H.S. Medicaid Services, Medicare program; hospital conditions of participation: requirements for approval and re-approval of transplant centers to perform organ transplants. Final rule. *Fed Regist*. 2007;72(61):15197–280.
18. OPTN Operations and Safety Committee. Public comment proposal: deceased donor support therapy data collection. 2023.
19. Mohan S, et al. Factors leading to the discard of deceased donor kidneys in the United States. *Kidney Int*. 2018;94(1):187–98.
20. Crannell WC, et al. Deceased donor kidneys are discarded at higher rates when labeled as high kidney donor profile index. *Am J Transplant*. 2022;22(12):3087–92.
21. Swanson SJ, et al. Effect of donor factors on early graft survival in adult cadaveric renal transplantation. *Am J Transplant*. 2002;2(1):68–75.
22. Chong K, et al. Reconsidering donor race in predicting allograft and patient survival among kidney transplant recipients. *Kidney360*. 2021;2(11):1831–5.
- 23.● Doshi MD, et al. Clinical utility in adopting race-free kidney donor risk index. *Transplant Direct*. 2022;8(7): e1343. **Race free KDRI does not impact graft failure and might lower discard of kidneys from Black donors.**
- 24.● Callender CO, et al. Blacks as donors for transplantation: suboptimal outcomes overcome by transplantation into other minorities. *Transplant Proc*. 2008;40(4):995–1000. **This study examines donor ethnicity on graft survival rates and mortality.**
25. Roberts JP, et al. Effect of changing the priority for HLA matching on the rates and outcomes of kidney transplantation in minority groups. *N Engl J Med*. 2004;350(6):545–51.
26. White SL, et al. Patient selection and volume in the era surrounding implementation of Medicare conditions of participation for transplant programs. *Health Serv Res*. 2015;50(2):330–50.
- 27.● Schold JD, et al. The association of center performance evaluations and kidney transplant volume in the United States. *Am J Transplant*. 2013;13(1):67–75. **There is significant association between reduced kidney transplant volume and low performance evaluation.**
28. Schold JD, Arrington CJ, Levine G. Significant alterations in reported clinical practice associated with increased oversight of organ transplant center performance. *Prog Transplant*. 2010;20(3):279–87.
- 29.● Kim DW, et al. Financial impact of delayed graft function in kidney transplantation. *Clin Transplant*. 2020;34(10):e14022. **Delayed graft function result in increased financial cost and resource utilization.**
30. Goodhart C. Problems of monetary management: the U.K. experience, in Inflation, depression, and economic policy in the West. In: Courakis A, editors. Barnes and Noble Books: Totowa, New Jersey; 1975. pp. 116.
31. Aubert O, et al. Disparities in acceptance of deceased donor kidneys between the United States and France and estimated effects of increased US acceptance. *JAMA Intern Med*. 2019;179(10):1365–74.

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.