

# Personalizing the Kidney Transplant Decision

## Who Doesn't Benefit from a Kidney Transplant?

Deirdre Sawinski<sup>1</sup> and David P. Foley<sup>2</sup>

CJASN 15: 279–281, 2020. doi: <https://doi.org/10.2215/CJN.04090419>

The transplant community has succeeded in clearly communicating the survival benefit generally associated with kidney transplantation in comparison to maintenance dialysis. However, although kidney transplantation is associated with survival gains on a population level, this is not universally true on an individual level. As a community we have also asserted that even if longevity is not enhanced by transplantation, quality of life usually is; the data supporting this claim are less robust. Despite the prevailing sentiment, individuals exist who do not benefit from transplantation and this must be acknowledged; the challenge lies in objectively identifying and counseling these candidates not to pursue transplantation.

The US Renal Data System Annual Report (1) compares projected remaining life years for the general population, individuals with ESKD, and kidney transplant recipients, consistently demonstrating across all age strata that transplantation is associated with longer life expectancy than dialysis. However, these data are not risk-adjusted and the magnitude of this difference decreases with increasing patient age. Despite an early increase in the risk of death, Wolfe *et al.* (2) found an equivalent mortality risk for transplantation compared with remaining on the waitlist at postoperative day 106, and a survival benefit from postoperative day 244 onward. Since this landmark publication, others have demonstrated a similar survival benefit associated with transplantation even in high-risk groups, including the elderly, those with long dialysis vintage, and those with prior kidney transplants. In the published literature it is hard to identify a population that does not have improved survival with transplantation over dialysis.

It therefore seems that all waitlisted patients benefit from kidney transplantation and justifies more inclusive listing practices. However, study methods require closer examination. Candidate selection practices have evolved over time, so the source population for many studies (patients from the 1990s and early 2000s) are not representative of those evaluated today. Contemporary transplant candidates often have significantly greater comorbidities and many would never have been listed in earlier eras. Listing practices vary significantly by center. Some members of the waiting list may

not actually be transplant candidates but are registered with minimal workup to accrue time in long wait-time areas. Most studies do not distinguish between active and inactive waitlist status, which introduces immortal time bias and inflates the waitlist mortality rate. Furthermore, survival benefit analyses may not be as reliable for longer-term outcomes, beyond the mandated 1- and 3-year follow-up, and the transplant registry data they are based upon do not report other outcomes that are meaningful to patients, such as quality of life. Additionally, there is the potential for confounding by indication in these analyses, where the treatment (transplantation) and outcome (survival) are closely related. Use of more advanced statistical techniques, such as marginal structural modeling, can overcome this limitation as well as address time varying confounding. A recent study from Cohen *et al.* (3) that incorporated organ offers, a contemporary waitlist/transplant cohort, and active/inactive status, as well as using marginal structural methods, still found a survival benefit associated with transplantation, but both the initial mortality risk and the long-term benefit compared with the waitlist were attenuated. Kidney transplantation may not actually be as universally beneficial as it previously seemed and population-based analyses do not guarantee individual patient results.

Despite the evidence supporting near-universal transplant benefit, there are scenarios where this does not apply, although the published literature is limited. Providers can all recall individual patients with poor posttransplant outcomes, but this is obscured in population-level data and transplantation should be practiced on the basis of evidence rather than anecdote. All survival analyses demonstrate an increase in mortality immediately after transplantation, and patients who die in the early postoperative period or in the first post-transplant year clearly do not benefit. This is a rare event, affecting <5% of recipients (4), and most deaths in the first 3 months are cardiac in nature (4). Older patient age, diabetes, preexisting cardiac disease, and longer dialysis vintage are all associated with a greater risk of early mortality (4). Likewise, patients who lose their allograft in the first year do not benefit from transplantation. Early graft loss affects only 3% of kidney recipients, with recipient death, thrombosis, acute rejection, and primary nonfunction being the

<sup>1</sup>Renal Electrolyte, and Hypertension Division, Department of Medicine, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania; and <sup>2</sup>Division of Transplantation, Department of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin

**Correspondence:**

Dr. Deirdre Sawinski, Renal Electrolyte and Hypertension Division, Department of Medicine, University of Pennsylvania, 3400 Spruce Street, Philadelphia, PA 19104. Email: [Deirdre.sawinski@uphs.upenn.edu](mailto:Deirdre.sawinski@uphs.upenn.edu)

most common causes (5). Donor factors are the main contributors (5). This “no benefit” phenotype overlaps significantly with patients identified as being at greatest risk of premature death on dialysis, perceived to have the greatest urgency for transplantation and often offered marginal kidneys.

Patients are often counseled that transplant is worthwhile even without a significant extension in longevity, because of the enhanced quality of life. However, improved posttransplant quality of life is not universal and patients may not experience gains in all measured domains. Furthermore, quality of life improvement is significantly modified by age, comorbidities, allograft function, and complications (including hospitalizations and medication side effects) (6). Marginal candidates are at increased risk for complications, which can negate any potential survival or quality-of-life benefit.

Another rationale for inclusive transplant candidacy practices has been the cost-savings traditionally associated with transplantation. However, contemporary economic analysis (7,8) of kidney transplantation has demonstrated that use of high-scoring Kidney Donor Profile Index kidneys is only cost-effective, and the median overall cost of transplantation increases with recipient estimated post-transplant survival (EPTS) (8). Thus, the financial benefit of transplantation risks erosion by acceptance of higher-risk donors and recipients. Even if 3 years of graft survival (or less) remains the financial break-even point, is that really an outcome providers or patients should deem acceptable?

In light of our limited organ supply, it bears consideration if survival benefit should be incorporated into kidney allocation decisions. To some extent it already is, as the EPTS score determines access to the lowest-scoring Kidney Donor Profile Index organs, which are presumed to be of the best quality. Simply prioritizing patients for transplantation on the basis of EPTS would significantly penalize older candidates, patients with diabetes, and patients on dialysis. Instead, as proposed by Wolfe *et al.* (9), we suggest that greater weight should be given to projected post-transplant survival, in addition to waiting time and degree of allosensitization, when calculating a candidate's allocation score, to promote maximal utility of all available organs and avoid futile transplants.

Helping an individual patient determine if he or she will benefit from transplantation is difficult on the basis of the available data. How, then, to achieve personalization? More comprehensive and granular data and studies that reflect the current clinical reality in which we practice are required to accurately prognosticate individual outcomes. In the absence of objective and universally agreed upon criteria for kidney transplant candidacy, most providers use the “eyeball test,” which is not only unscientific but subject to provider and transplant program biases, and results in unequal opportunity for transplantation. As an alternative, we would propose incorporation of a scoring system (10) into the evaluation process. This tool (10), which assigns mortality risk according to comorbidities, when paired with a relative threshold beyond which kidney transplantation would be considered futile and a candidate should not proceed, could enhance clinical decision

making and inject greater objectivity and transparency into the evaluation process. Frailty assessments can also provide a quantifiable, trackable, and objective metric for transplant candidacy. Use of these types of assessments can help guide difficult conversations with patients regarding candidacy. Prospective validation and study of any metric are required before broad application to clinical practice, but this more scientific and uniform approach is the direction in which patient evaluation practices need to move.

Even if the supply of kidneys were unlimited, there would still be patients for whom a transplant is inappropriate, despite the dwindling number of absolute contraindications to kidney transplantation. Careful patient selection would still be necessary to avoid unacceptable outcomes such as “premature” death or worse quality of life compared with remaining on dialysis. Age and overall life expectancy would be less of a consideration with a nonscarce resource, although overall societal cost and the effect on individual program outcomes would still factor in for some insurers and transplant centers. Therefore, an individual patient's ability to survive the surgery and recover would predominate patient selection concerns. Individuals with significant frailty, a prohibitive burden of cardiovascular or peripheral vascular disease, active malignancy, or other end-organ failure, would still not be operative candidates. Social and economic contraindications to transplant would still exist; medical insurance and immunosuppressive coverage are essential to maintaining a transplant as is the ability to comply with treatment. Although less expensive than dialysis, transplantation is still costly to society and resources devoted to futile transplants are funds that cannot be used to promote other health efforts. Defining futility in kidney transplantation is a discussion the transplant community must have, as with the nearing possibility of xenotransplantation, organ scarcity will not dominate the conversation forever.

Kidney transplantation is associated with a multitude of benefits for many but not all recipients. It is important that transplant professionals are honest with patients and themselves when having candidacy discussions. Better-quality data, objective assessments, and a scientific approach are needed to inform the conversation and limit personal biases in candidate selection.

#### Acknowledgments

The authors would like to thank Dr. Kimberly Brown for her thoughtful discussion of the “eyeball technique” for patient selection at the American Society of Transplantation's Cutting Edge of Transplantation Meeting, held in Phoenix, Arizona.

The content of this article does not reflect the views or opinions of the American Society of Nephrology (ASN) or the *CJASN*. Responsibility for the information and views expressed therein lies entirely with the author(s).

#### Disclosures

Dr. Sawinski reports other funding from Veloxis and Merck outside the submitted work. Dr. Foley has nothing to disclose. Dr. Sawinski has received other support from Merck and Veloxis and a travel grant from CareDx.

## References

1. US Renal Data System: *2018 USRDS Annual Data Report: Epidemiology of Kidney Disease in the United States*, Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2018
2. Wolfe RA, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LY, Held PJ, Port FK: Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med* 341: 1725–1730, 1999
3. Cohen JB, Potluri V, Porrett PM, Chen R, Roselli M, Shults J, Sawinski DL, Reese PP: Leveraging marginal structural modeling with Cox regression to assess the survival benefit of accepting vs declining kidney allograft offers [published online ahead of print February 6, 2019]. *Am J Transplant* doi:10.1111/ajt.15290
4. Farrugia D, Cheshire J, Begaj I, Khosla S, Ray D, Sharif A: Death within the first year after kidney transplantation--an observational cohort study. *Transpl Int* 27: 262–270, 2014
5. Hamed MO, Chen Y, Pasea L, Watson CJ, Torpey N, Bradley JA, Pettigrew G, Saeb-Parsy K: Early graft loss after kidney transplantation: Risk factors and consequences. *Am J Transplant* 15: 1632–1643, 2015
6. Gentile S, Beauger D, Speyer E, Jouve E, Dussol B, Jacquelinet C, Briançon S: Factors associated with health-related quality of life in renal transplant recipients: Results of a national survey in France. *Health Qual Life Outcomes* 11: 88, 2013
7. Axelrod DA, Schnitzler MA, Xiao H, Irish W, Tuttle-Newhall E, Chang SH, Kasiske BL, Alhamad T, Lentine KL: An economic assessment of contemporary kidney transplant practice. *Am J Transplant* 18: 1168–1176, 2018
8. Axelrod DA, Schnitzler MA, Xiao H, Naik AS, Segev DL, Dharnidharka VR, Brennan DC, Lentine KL: The changing financial landscape of renal transplant practice: A national cohort analysis. *Am J Transplant* 17: 377–389, 2017
9. Wolfe RA, McCullough KP, Leichtman AB: Predictability of survival models for waiting list and transplant patients: Calculating LYFT. *Am J Transplant* 9: 1523–1527, 2009
10. Dusseux E, Albano L, Fafin C, Hourmant M, Guérin O, Couchoud C, Moranne O: A simple clinical tool to inform the decision-making process to refer elderly incident dialysis patients for kidney transplant evaluation. *Kidney Int* 88: 121–129, 2015

Published online ahead of print. Publication date available at [www.cjasn.org](http://www.cjasn.org).