



Patient-Centered Outcomes with Second Kidney Transplant

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CJASN 14: 1131–1132, 2019. doi: <https://doi.org/10.2215/CJN.07400619>

Kidney transplantation is the treatment of choice for patients with ESKD, yet the underutilization of transplantation in the United States suggests that these advantages are not adequately recognized (1). The proportion of the prevalent dialysis population currently waitlisted is low (15.5% in 2016), decreasing, and plagued with significant disparities (1,2). Although the recent decline in waitlisting may be partially related to the loss of a sense of urgency for waitlisting in the new Kidney Allocation System, the increasingly selective process being applied by transplant centers in determining which patients are eventually waitlisted and which patients should be removed from the waitlist is a significant contributing factor (1,3). As a result, thousands of potentially eligible patients never get the opportunity to receive this life-saving treatment.

Much of the transplant community has been focused on the 1-year quality measures that transplant centers are evaluated on and how these metrics potentially influence center-level behavior to the detriment of patients (4,5). Given that effective quality metrics are those that identify and measure areas of meaningful improvement and stimulate increases in desired behaviors and outcomes, these concerns may be appropriate. The rate of improvement in unadjusted 1-year graft survival in the period before the introduction of the current 1-year graft survival metric (1999–2006: 86.8%–89.6%; total relative increase 3.2%; annualized 0.46%) was almost threefold higher than the rate of improvement in the period after the introduction of the current program specific reports (2007–2015: 90.5%–92.7%; total relative increase 2.4%; annualized 0.15%), calling into question the positive effect, if any, of the current outcomes metrics on short-term outcomes (6). Notably, unadjusted 10-year graft survival rates are also improving (1999–2006: 43.7%–48.3%; total relative increase 10.5%; annualized 1.5%) but remain dismal, and therefore, it comes as no surprise that patients are frequently in need of a second transplant and in the case of our younger recipients, potentially a third transplant as well (6).

Given the continued scarcity of deceased donor organs, improving long-term outcomes after kidney transplants and reducing the need for subsequent transplants need to be part of any strategy to close the gap between the supply and demand for organs. However, until such time that we start to see dramatic improvements in the

long-term outcomes for kidney transplant recipients, there is likely to be a steady stream of individuals with failing allografts that exacerbate the shortage of organs available for transplantation and thus a pressing need to better understand this group of patients.

In this issue of CJASN, Clark *et al.* (7) report on access to second transplants and the outcomes after transplantation for a cohort of individuals whose initial allografts functioned for 3 or more years. Although the authors, not surprisingly, find that second transplants do not fare quite as well as first transplants, they continue to provide a large and significant reduction in mortality compared with remaining on dialysis, underscoring the value of repeat transplantation for individuals with a failed allograft. The authors should be commended for using a comprehensive approach to measure the effect of a transplant, demonstrating a reduction in mortality with a second transplant and the differences between patient survival and death-censored allograft survival, absolute allograft survival, and the duration of additional kidney replacement therapy needed within 10 years.

However, their analysis prompts several additional questions—especially ones that would be of interest to patients and policy makers. For example, are there differences between centers in access to transplantation for individuals with failed allografts that are driving observed disparities in access to retransplantation (8)? Are there specific causes of allograft failure, such as disease recurrence or nonadherence to immunosuppression, that are particularly prone to differential treatment across centers that could inadvertently exacerbate disparities? Given the authors' finding that PRA did not adversely affect the longevity of second transplants, were the inferior outcomes associated instead with longer cumulative dialysis vintage? If the inferior outcomes are, in fact, a function of cumulative dialysis vintage, perhaps the current methods of calculating estimated post-transplant survival (and thus, access to the best quality kidneys) need to be reconsidered, especially given the relatively young age of many individuals needing a second transplant.

Overall, these findings support continued access to transplantation for patients with a failed prior transplant. Additionally, the success of transplantation in patients with prior transplant failure provides additional evidence against the limited access to transplantation for other subgroups at higher risk for graft

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failure. Second transplant candidates are unique compared with other groups with regard to their access to transplantation, but there is reason to believe that patients with other comorbidities that limit access to transplantation would similarly benefit from transplantation. Patient-centered metrics that encourage broader access to transplantation may improve waitlisting rates among such patients.

The authors also examined access to transplantation and found that, although patients with failed allografts were not more likely to get a transplant once on the waitlist, they did have a higher adjusted likelihood of making it onto the waitlist. This significant advantage with respect to access to the waitlist is not surprising, and is likely related to having successfully navigated the process the first time and having an established ongoing relationship with a transplant center. First-hand experience of the improved quality of life associated with transplantation is also likely to be a strong motivator for these patients.

Interestingly, these results cast doubt on the dogma around the 1-year outcome metrics being the primary driver of transplant center behavior that adversely affects access to transplantation. Considering that recipients of second transplants are currently excluded from regulatory transplant center metrics, these individuals might be expected to have had a higher likelihood of transplantation if center reluctance to use certain organs was being driven primarily by the concerns related to the scrutiny of 1-year outcomes. Although the authors did not specifically look to see whether the kidney donor profile index of kidneys used for second transplants was similar to those used for initial transplants, the lack of a difference in the likelihood of transplantation suggests an absence of any meaningful difference. This, in turn, would imply that the mere proposed elimination of these regulatory metrics will not be sufficient to change center-level behavior related to organ offer acceptance. Although the proposed withdrawal of the 1-year transplant center metrics from the regulatory framework in the United States is a welcome change, well designed quality metrics that focus on patient-preferred measures are needed to encourage transplant centers to continue to focus on patient-centered outcomes. Candidates and recipients of second transplants could also benefit from their own specific patient-centered measures if chosen carefully.

Patients are primarily interested in the amount of time that they have to spend waiting for their transplants, and individuals with failing allografts are not likely to be any different (9). For patients with failing allografts, an awareness of a center's willingness to relist them in a timely manner—especially in the context of the cause of failure of the first allograft (e.g., recurrent disease, nonadherence, sensitization, or BK infection) or specific clinical characteristics (e.g., age or obesity)—and their probability of being transplanted after waitlisted could all be used to empower patients to advocate for relisting and retransplantation (10). These individuals may also be uniquely positioned to view the risk/benefit balance of marginal organs more positively, and clear documentation of these preferences ahead of time could positively affect center-level acceptance patterns and the current high discard rate nationally. Patient-level organ offer acceptance/decline rates specific for this subset of patients should also be considered as part of any new potential patient-centered measures panel.

The careful identification and adoption of meaningful patient-centered metrics from the time that the initial allograft is deemed to be failing (eGFR or measured GFR <20 ml/min)

to the second transplant would improve care for this important subset of patients. These metrics must incentivize improved access to transplantation across the spectrum of care to optimize transplantation rates and improve patient-level outcomes for previous transplant recipients. Broad adaptation of such patient-centered transplant metrics for the wider ESKD community can help ensure greater access for all patients who would benefit from transplantation.

Disclosures

Dr. Mohan reports personal and other fees from Angion Pharmaceuticals; personal fees from HSAG, Jazz Pharmaceuticals, and Kidney International Reports; and other fees from Bravado Health, outside the submitted work.

Funding

Dr. Mohan is supported by National Institutes of Health, grants R01 DK114893 and U01 DK116066. Dr. Husain is supported by NIH (National Center for Advancing Translational Sciences) grant KL2 TR001874 and reports grants from the National Kidney Foundation, outside the submitted work.

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Published online ahead of print. Publication date available at www.cjasn.org.

See related article, "Access to Kidney Transplantation after a Failed First Kidney Transplant and Associations with Patient and Allograft Survival: An Analysis of National Data to Inform Allocation Policy," on pages 1228–1237.