Allocating Deceased Donor Kidneys to Sensitized Candidates

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In this edition of the Clinical Journal of the American Society of Nephrology, Gebel et al. (1) present simulation data showing that the new kidney allocation system (KAS) increases the offer rate for highly sensitized kidney transplant candidates. This is counter to the previously held belief that the only possibility of transplanting a highly sensitized patient is with an HLA-identical kidney. The modeling by Gebel et al. (1) shows that even a candidate with calculated panel-reactive antibody (cPRA) of 100% has multiple potential donors. This is consistent with European data and the early results of the KAS that went into effect on December 4, 2014 (2,3). This observation is notable, and it is valuable for the general nephrologist to understand both how and why this new approach to the highly sensitized patient was developed as well as the consequences that stem from it.

Among the many changes to kidney allocation is a new sliding-scale point system and larger geographic sharing of kidneys for highly sensitized candidates. Such patients are those who formed anti-HLA antibodies through events, such as prior solid organ transplantation, blood transfusion, or prior pregnancy, and are unable to receive transplants from some or most organ donors because of immunologic incompatibility. There are many myths about these highly sensitized patients. It is often assumed that all of these patients have already received a kidney transplant and are now seeking a second, third, etc. However, the reality is that nearly 40% of them are being waitlisted for their first transplant and require additional priority in allocation to receive a transplant (D. Stewart, personal communication). The intent of this change was to provide improved access to transplantation for these patients.

To develop a sliding-scale point system for degree of sensitization, the Organ Transplantation Network (OPTN)/United Network for Organ Sharing (UNOS) Kidney Transplantation Committee studied the time to next offer (how long a patient would be expected to wait for a second offer if the first offer was declined) for sensitized patients. The intent was to determine the value for cPRA at which a recipient becomes truly become disadvantaged. The time to next offer analysis results were unexpected and dramatic. The median time for a patient with cPRA at 0% is 11.7 days. The effect of sensitization level escalates as cPRA increases into the 60%–69% decile, with the median time more than doubling to 31.2 days. It nearly doubles again to 55.2 days when cPRA reaches 75%–79%. As the cPRA increases to >90%, there are large increases in the time to next offer. An increase from 95% to 97% results in a near doubling of the estimated median time from 175 to 330 days, and increasing cPRA by an additional two points to 99% triples the time to 993 days. Most striking is the observation that, for a patient with cPRA of 100%, the median time to next offer increases to 4969 days or >13 years. The allocation system in existence before December 4, 2014 allocated a lump sum of four allocation points to individuals with a cPRA of >80%. Therefore, in this system, a patient with cPRA of 80% and one with cPRA of 100% are treated exactly the same. The additional four points resulted in individuals with cPRA between 80% and 95% receiving an increased access to transplantation, whereas for those candidates with cPRA of >95%, these four additional allocation points did nothing to change the rate of transplantation (4).

To correct this imbalance in access to kidney transplantation caused by sensitization, the KAS uses both a sliding-scale point system and a tiered system of larger geographic sharing. The sliding-scale point system exponentially assigns additional allocation points beginning at a cPRA of 20%, when a candidate receives an additional 0.08 points up to a maximum of 202.10 points for a candidate with cPRA of 100%. The tiered geographic sharing allows candidates with cPRA of 100% access to all kidneys recovered nationally; those with cPRA of 99% have access to kidneys recovered regionally, and for individuals with cPRA of 98%, the additional 24.4 points that they are allotted place them first on the local (donor service area) list (5). The intention of this combined approach is to ensure from the time of listing that these candidates are placed at the top of their respective allocation pools so that they will immediately start receiving offers.

The results of this approach are consistent with the modeling done by Gebel et al. (1). In the first few months of the KAS, the transplant rate for patients with 98%–100% cPRA increased dramatically, whereas the transplant rates for candidates with cPRAs of 80%–96% fell back to be proportional with their representation on the waiting list, thus both improving access for those truly in need and undoing the unintended advantage given to others. This bolus effect was predicted, and in the months since the KAS was initiated, the percentage of these highly sensitized candidates being transplanted...
has declined. Coincident with this decline in transplant rate has been a decrease in the number of these candidates on the transplant waiting list, suggesting that, with the passage of time, this bolus of transplants occurring in this group will subside and mirror their representation on the waiting list (6).

There are legitimate concerns about this approach to allocating kidneys to highly sensitized candidates. The first is that the increased shipping of organs imposed by the sharing over a larger geographic area will increase cold ischemic time and result in a higher rates of delayed graft function and discards. The initial 6-month data does indicate that cold ischemic time has increased slightly and that delayed graft function has increased from 24.5% to 31%. Additionally, the discard rate, especially for kidneys in the higher kidney donor profile index range (0.86–100), has increased. However, it is not certain whether this is because of larger geographic sharing (6). Additionally, in recent months, the discard rate has returned to its pre-KAS baseline (7). Another concern is that transplant centers will use highly sensitized patients to draw in kidneys that will be crossmatch positive with the intended candidate and then, allocate them to another patient on the list. Because of national sharing, the total number of kidneys being offered for nonlocal sensitized patients has increased proportionately more than offers for local patients. This has resulted in the weighted average of kidneys being placed into the unintended recipient to increase. However, when only nonlocal offers are considered, although the total number of offers going to the unintended recipient has increased, the percentage has decreased (OPTN/UNOS Kidney Transplantation Committee, unpublished data). Thus, it seems that the system is functioning more efficiently. Additionally, in June of 2015, the OPTN/UNOS Board of Directors voted to include HLA-DQε and –DPβ typing into the required HLA types that must be entered into a candidate’s record. This should further decrease the number of unexpected positive crossmatches that occur after allocation and improve system efficacy.

It is possible that the outcome of kidneys transplanted into highly sensitized candidates will be worse than if transplanted into candidates with potentially lower immunologic risk. Because the expected half-life of a deceased donor kidney is between 5 and 11 years, the final answer to this question will be some years in the future (8). Finally, the shipping of organs for highly sensitized candidates has imposed new logistic challenges to the allocation of kidneys that are still being resolved: when to send samples for crossmatching, how many centers to send them to, and how to allocate to another candidate if the intended candidate has positive crossmatch. Although these challenges should not be diminished, they also offer the opportunity to test and evaluate how best to share kidneys over a larger geographic area in preparation for the next iteration of kidney allocation that will seek to reduce the glaring geographic disparities that currently exist in access to kidney transplantation (9,10).

There is no doubt that this component of the KAS has challenged the transplant community and placed stress on both the organ procurement organization system and transplant centers. However, it has allowed patients to be transplanted who, in the past system, had little chance. Moreover, this stress has necessitated development of improved systems for sharing and shipping deceased donor kidneys. These improvements will form the basis for larger geographic sharing of kidneys in the future. Additionally, these changes have caused transplant centers to reconsider how they manage their waiting lists, because candidates must be kept up to date on their anti–HLA antibody screening and medically ready for the kidney offer that may come. Therefore, although admittedly this change has caused the transplant community to think creatively and work harder, the net result has been improved patient care and better access to transplantation for a disadvantaged group of patients, and ultimately, the benefit justifies the increased effort.

Disclosures
None.

References
4. Stewart DE; OPTN/UNOS Kidney Transplantation Committee: Time-to-Offer Analysis for Adult Kidney Candidates; Estimating the Average Time between Deceased Donor Kidney Offers for Adults on the Waitlist, by Level of Allosensitization, Richmond, VA, CPRA, 2011

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