Personalizing Donor Kidney Selection  
Choosing the Right Donor for the Right Recipient

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The selection of the optimal living or deceased donor for the patient with ESKD remains a critical decision point for kidney transplant programs. Kidney transplant candidates are routinely counseled on the relative benefits of both living and deceased donor kidney transplantation during their initial transplant evaluation. Living donor kidney transplantation is the preferred option for multiple reasons, including a timelier transplant, reduction of dialysis time, higher rates of immediate kidney function, and improved graft survival compared with a deceased donor. However, for most patients with ESKD without a living donor, deceased donor kidney transplantation remains the better option for prolonged survival compared with dialysis.

Personalizing the selection of a given donor kidney for a specific recipient can yield significant long-term benefits for the recipient, especially when there are multiple donor options. Consideration should be given to immunologic, chronologic, and anatomic issues when identifying the "best" donor.

Immunologic matching remains the cornerstone of personalization in kidney transplantation. When a recipient has multiple medically cleared living donors, assessment for donor-specific antibodies and HLA class I and class II matching can guide donor selection; "unused" donors can be given the option to serve as altruistic, nondirected donors. ABO compatibility, the absence of preformed donor-specific antibodies, and increased HLA matching are preferred for a given donor. In patients with donor-specific antibody, transplantation after desensitization is possible but leads to increased cost; increased rates of rejection, infection, and readmission; and graft loss. ABO-incompatible transplantation after desensitization is an option if the patient has low antibody titers. However, we believe that entering incompatible donor-recipient pairs into a local or national paired kidney exchange program to identify an HLA- or ABO-compatible match is the preferred approach. On the basis of a large database analysis, HLA matching may be more favorable to receiving a younger kidney (1). Although not previously considered a risk factor in kidney transplant outcomes, HLA DQ mismatching leads to increased rates of acute cellular and antibody-mediated rejection (2), and it is to be avoided if possible.

We know that the development of de novo donor-specific antibody is an independent risk factor for premature allograft failure. Any donor-recipient matching that can decrease the development of de novo donor-specific antibody is favorable. Matching can also be optimized at the epitope level (3). In one analysis, amino acid mismatches at peptide binding sites of the HLA-DRB1 led to an increase risk of graft loss in deceased donor and living donor kidney transplants (4). Algorithms have been developed to predict the presence of donor-derived HLA epitopes and subsequent development of de novo donor-specific antibody. These signatures may be better predictors of histocompatibility for kidney transplants (5). However, before epitope matching can become widely accepted in clinical practice, more data are required to determine epitope compatibility and the role of epitope matching in kidney allocation algorithms (6).

Other nonimmunologic factors that contribute to a better donor to recipient matching include age, nephron mass (on the basis of donor and recipient weights), and computed tomography scan assessment of kidney volume. If a large discrepancy (>10%) exists between a living donor’s two kidneys and differential kidney function is confirmed with additional testing, then the smaller kidney is usually considered for donation. Donor to recipient size matching in conjunction with HLA matching is critical in obtaining optimal patient and graft survival outcomes (7).

Anatomy of the donor kidney is also a consideration. If a right donor kidney is preferred on the basis of volumetric analysis, a short right kidney vein may preclude the use of the kidney, especially if the recipient has a high body mass index (BMI) or there is a significant amount of iliac arterial calcification that limits surgical options. Finding the right combination of kidney size and favorable vascular anatomy are critical nonimmunologic factors contributing to optimal donor-recipient matching.

Personalizing the optimal deceased donor kidney for a given recipient poses additional challenges. The current system allocates deceased donor kidneys on the basis of time from the initiation of dialysis or waitlist time for those not on dialysis, panel reactive antibody, and blood type. Donor factors are used to calculate the kidney donor risk index, which maps to the kidney donor profile index (KDPI). High KDPI kidneys are predictive of inferior graft survival compared with lower KDPI kidneys. Although kidney transplantation provides the option of multiple donor options, a living donor is usually better for clinical benefit.
a survival benefit compared with dialysis in most instances, the allograft needs to function for a duration of time such that the benefit of transplant outweighs the risk of surgery. This time point varies depending on the quality of the donor allograft (8).

One of the biggest challenges is deciding when to transplant a high KDPI kidney for a given recipient versus waiting for the next offer. Data suggest that patients over 50 years of age with ≥33 months of waitlist time who receive a kidney with KDPI >85% gain a greater survival benefit compared with waiting for a lower KDPI kidney offer (9). In a recent analysis among candidates who declined a kidney transplant offer, only 43% ultimately received a kidney transplant. Recipients who later underwent kidney transplant after declining the first offer had longer waitlist times, and in 56% of the patients, they received kidneys that were either similar or of lower quality than the initial offer (10). There are clearly significant risks in declining a kidney offer.

However, not all deceased donors are suitable for all recipients. A high-KDPI kidney recovered from a woman with a low BMI and thus, low eGFR may not be the best option for a candidate who is a man with a BMI >35. This donor-recipient pair may lead to suboptimal kidney function and poor long-term outcome. Similarly, when pediatric en bloc kidneys from smaller donors (<15 kg) are allocated to adults, smaller recipients are often chosen to maximize kidney function and avoid hyperfiltration seen with larger adult recipients. Alternatively, some centers may choose larger adult recipients due to the potential of increased growth of the kidneys to adult size. More studies are necessary to identify the optimal recipient for these kidneys.

High-KDPI kidneys with mild to moderate histologic damage on the basis of fibrosis, glomerulosclerosis, or arteriolar sclerosis may be better used together as dual- as opposed to single-kidney transplant. Dual-kidney transplantation of two “marginal” kidneys increases nephron mass and can lead to better outcomes than transplanting the kidneys separately. However, one needs to select the optimal recipient carefully. Patients with severe iliac atherosclerotic disease may not be the best recipients for dual-kidney transplantation due to the need for greater length of nondiseased artery for successful implantation of multiple kidney arteries. Dual-kidney transplantation prolongs the surgical procedure and the duration of anesthesia. Therefore, because of increased surgical risk, patients with significant or noncorrectable coronary artery disease may not be the best candidates. Ideal recipients of dual-kidney transplantation may include larger patients with sufficient space in the retroperitoneum for the placement of two kidneys, patients with noncalcified iliac arteries, and patients with sufficient cardiac function and reserve to tolerate delayed graft function.

Some have suggested that high-KDPI kidneys should be preferentially allocated to patients on dialysis with limited wait time accrued who have an anticipated prolonged waitlist time. These patients would avoid the physiologic insults of prolonged dialysis and mitigate the negative effect that dialysis time has on post-transplant allograft function. These benefits may counterbalance the limited longevity of receiving a high-KDPI kidney. More studies need to be performed before formally incorporating these factors into the allocation process.

Patients with significant burden of coronary artery disease or marginal BPs may not tolerate a deceased donor kidney with high risk of delayed graft function. For patients ≥65 years old with significant heart disease, living donor kidney transplant results in lower early postoperative mortality rate compared with receiving a deceased donor kidney (8). Some have suggested that older recipients with significant coronary artery disease should only be eligible for a living donor kidney transplant. This approach must be applied carefully. The expected survival rate of living donor transplants is high, and therefore, an increased number of graft losses or deaths due to recipient risk factors could result in a high observed to expected ratio in the Scientific Registry of Transplant Recipients program-specific reports, placing a center at risk for flagging by the regulatory agencies. Reflecting these concerns, others take the opposite approach, where marginal candidates will only be offered a deceased donor predicated on their ability to survive long enough on the waiting list to receive an offer.

Identifying the optimal donor kidney for a given recipient is complex and challenging. A risk in personalizing the allocation of a given deceased donor kidney to a specific recipient is the potential for another patient to be skipped on the match run, potentially increasing individual wait time and mortality. However, flexibility to match a higher-risk kidney with the optimal recipient could result in increased utilization of high-risk organs and reduced organ discard. New kidney allocation systems should incorporate flexibility at the transplant center level to allow for improved donor-recipient matching so as to increase kidney transplant rates while obtaining the best possible outcomes.

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