Global Perspective on Kidney Transplantation: United States

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Introduction
Kidney transplantation is the gold standard treatment for ESKD, offering superior survival and quality of life compared with dialysis. The first successful kidney transplant in the United States was performed by Dr. Joseph Murray in 1954, and transplantation has expanded steadily in the United States after the Uniform Anatomic Gift Act passed in 1968 permitted US adults to donate their organs. The purpose of this review is to report on the current status of kidney transplantation in adults in the United States, with special emphasis on post-transplant outcomes and barriers to transplant.

Organ Allocation
Unlike other solid organ transplants, such as liver and heart, allocation of kidneys is primarily on the basis of waiting time rather than severity of illness. Candidates also receive points for prior living donation, higher calculated panel reactive antigen score, and degree of human leukocyte antigen-DR mismatch; the higher the allocation score, the higher the position is on the waitlist. Patients in the United States are eligible for waitlisting once their eGFR reaches ≥20 ml/min per 1.73 m². Allocation policies were significantly revised in December 2014, allowing patients to accrue waiting time either when they were listed or when they initiated dialysis, whichever is earliest, in an attempt to reduce disparities in early referral for kidney transplant, which disproportionately affected non-White patients (1). Deceased donor kidney allocation underwent an additional major change in March 2021 in an attempt to improve geographic disparities in access to transplant, moving from arbitrarily defined Donation Service Area boundaries to “proximity circles” from the deceased donor organ.

Recipient Evaluation
There are 256 kidney transplant programs in the United States. Candidates referred by their nephrologist for a transplant undergo a rigorous medical and psychosocial evaluation and, if approved, they are placed on a national waitlist regulated by the Organ Procurement and Transplantation Network. Currently, there are 92,751 patients waitlisted in the United States for a kidney alone or kidney-pancreas transplant, which represents only 18% of prevalent patients on dialysis (2). The average wait time for a deceased donor kidney transplant is 5 years but can vary greatly depending on listing region and blood type, and more than half of listed candidates die or are removed from the list before transplant.

Transplant Rates
As of December 2018, there were 229,887 patients in the United States with a functioning kidney transplant, or 678 recipients per million people, and representing 40% growth since 2008 (3). In 2019, a record 24,273 kidney transplants were performed in the United States (Figure 1) (4). Approximately 72% of these transplants were from a deceased donor. Transplant recipients were 61% men, and half had either diabetes mellitus (30%) or hypertension (20%) as the listed cause of ESKD, whereas GN (18%) and cystic kidney disease (13%) were less common (4). Non-Hispanic White patients comprised the largest proportion of transplant recipients (45%) followed by Black (27%), Hispanic (19%) and Asian (7%) participants (4). Continuing a trend seen since 2015, transplants in patients aged 50–64 years and ≥65 years continued to increase relative to other age groups, and the proportion of transplant recipients aged ≥50 in 2019 was 60%. Racial disparities in access to living donor kidney transplant have persisted, and worsened over the past two decades (5). In addition, although data on referrals are not systematically collected, available data suggest racial disparities also persist in referral and waitlisting (1).

Perioperative Care
In the United States, the kidney transplant surgery is performed by transplant surgeons who have completed transplant fellowship training. The average length of stay post-transplant is 6.7 days (range 4–7) (6). After discharge, care is provided in an outpatient setting by transplant nephrologists and surgeons.
depending on the institution, and clinical pharmacists, social workers, and transplant nurse coordinators. Given some patients live far from the transplant center, some recipients elect to return to their general nephrologist for primary transplant management after the immediate post-transplant period.

Nearly all kidney transplant recipients in the United States receive induction therapy. Use of T cell-depleting agents has increased in the past 10 years and are given to 74% of patients, whereas 21% receive an IL-2 receptor antagonist (4). A triple regimen of tacrolimus, mycophenolate mofetil, and corticosteroids are the predominant initial maintenance immunosuppression and are given to 65% of patients (4). Although a quarter of recipients receive steroid-free immunosuppressive regimens, this percentage has not increased over the past decade (4).

Kidney Transplantation Costs

In 2020, the average kidney transplant cost was US$442,500 (6). Charges for the transplant admission, which include the surgery itself, are the most expensive line item, accounting for 34% of the total cost. Despite the rising prices of medications, only 7% of the total costs are for immunosuppression and other transplant-related medications, such as prophylactic antibiotics (time of transplant to 6 months post-transplant) (6).

In 2019, more transplant recipients had public Medicare coverage (60%) compared with private insurance (32%) (4). A minority of patients had Medicaid (6%), a state-run program for low-income individuals, or other government (2%) insurance. Although Medicare is generally only available to individuals aged ≥65 years, patients with ESKD in the United States are automatically eligible (4). Medicare coverage includes the pretransplant workup, perioperative inpatient care, provider professional fees, and immunosuppression. However, Medicare typically only covers 80% of costs, so most recipients must obtain a secondary policy to cover the remainder. In addition, Medicare eligibility ends at 3 years post-transplant, unless the recipient is aged ≥65 years or disabled. Recognizing that inability to access immunosuppression was resulting in an estimated 375 allograft failures each year, the US Congress passed the Comprehensive Immunosuppressive Drug Coverage for Kidney Transplant Patients Act in December 2020 (7). This law will take effect in 2023 and extends Medicare immunosuppression coverage for the life of the transplant.

Outcomes

Both short- and long-term allograft and patient survival in the United States are excellent and have steadily improved over the past decade (Figure 2) (4). Unadjusted death-censored allograft survival rates in deceased donor kidney transplant recipients were 97%, 90%, and 77% at 1, 5, and 10 years, respectively (4). Not surprisingly, living donor transplant recipients have better unadjusted death-censored allograft survival rates compared with their deceased donor counterparts with 1, 5, and 10-year rates of 99%, 94%, and 84%, respectively (4). A similar trend was seen in patient survival. For patients transplanted in 2013, the unadjusted 1, 5, and 10-year patient survival rates in living donor recipients were 99%, 94%, and 85%, respectively, compared with 99%, 89%, and 75%, respectively, in deceased donor recipients (4).

Future Challenges

The Advancing American Kidney Health initiative unveiled in July 2019 set forth a number of goals to improve the care of patients with CKD in the United States. One of the three arms of the initiative was improving access to kidney transplantation, specifically by: (1) doubling the number of kidneys available for transplant by 2030, (2) increasing procurement and reducing discards of deceased donor organs, and (3) reducing disincentives and providing financial incentives to living organ donation (8).

A shortage of donors remains the primary obstacle to achieving these goals. Although the number of kidney transplants performed in the United States was 30% higher in 2019 compared with 2015, this was still insufficient to meet demand, as evidenced by the roughly 90,000 patients currently waitlisted for transplant (4). As a result, wait times in the United States are getting longer, especially for those with O or B blood type, and many waitlisted candidates will die or become too sick to undergo transplant. In an attempt to reduce the deceased donor organ discard rate, the transplant community is discussing how to incentivize the transplantation of “nonstandard” kidneys (e.g., kidney donor profile index ≥85%) when the survival benefits outweigh the risk of remaining on dialysis. In addition, direct acting antivirals for hepatitis C have led to a marked decreased in the discard rate of hepatitis C antibody–positive kidneys procured for transplant, from 56% in 2013 to 26% in 2019 (4). Approximately 29% of US centers transplant kidneys from hepatitis C nucleic acid–positive donors into hepatitis C–seronegative recipients (9).
Improved utilization of deceased donor kidneys will not be enough to address the need to expand the donor pool. Despite a slight upward trend since 2018, the number of living donor transplants performed annually has remained stagnant over the past decade, highlighting the need to intensify strategies to encourage living donation especially among non-White candidates. Living donors often incur significant donation-related expenses that are not covered by the recipient’s health insurance, and financial burdens are frequently listed as a barrier. Encouragingly, as of October 22, 2020, the US Department of Health and Human Services now allows living donors to be reimbursed for lost wages, child care expenses, and elder care expenses (10). Previously, the only reimbursable expenses were travel to the transplant center, lodging, and meals.

Life-saving kidney transplantation has been widely available in the United States for many decades and allograft and patient post-transplant outcomes are improving. Despite this, several challenges remain. Finding solutions to increase living donation, shorten the wait time to transplant, and eliminate racial disparities in access to transplant are all future priorities for the US transplant community.

Figure 2. | Unadjusted death-censored allograft survival among living donor (A) and deceased donor (B) United States adult kidney transplant recipients; unadjusted patient survival by donor type (C).

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