Opportunities and Challenges for Kidney Donation from and to HIV-Positive Individuals

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As of November of 2014, there were 955,081 persons living in the United States diagnosed with HIV infection (1). Despite and to some extent, as a consequence of advances in the treatment of HIV, there is an increasing prevalence of ESRD in patients who are HIV-positive (HIV+) (2,3). Mortality in this population is high, particularly in black patients with HIV-associated nephropathy (HIVAN) and those with inadequate viral suppression (4). Multiple studies have shown favorable patient and graft outcomes after kidney transplantation in carefully selected HIV-infected patients (5). In the National Institutes of Health (NIH) multicenter trial of solid organ transplantation in HIV+ recipients, 3-year survival among 150 kidney transplant recipients was 88% compared with 90% in HIV-uninfected (HIV−) recipients (6). Unfortunately, as Locke et al. (7) show in this issue of the Clinical Journal of the American Society of Nephrology in their analysis of Scientific Registry of Transplant Recipients data comparing 1636 HIV+ candidates with 72,297 HIV− candidates on the kidney transplant waitlist from 2001 to 2012, those with HIV and ESRD waited longer to be approved for transplantation and even longer to receive a kidney. The difference was most acutely observed in living donor transplants, with HIV infection conferring a 47% lower likelihood of a living donor kidney transplant.

Although the reasons for this disparity need to be explored further, it is possible that the challenges associated with renal transplantation in patients who are HIV+ have acted as a deterrent to transplant providers and centers. One unexpected challenge was the two- to threefold higher rate of acute rejection (5,6,8). This has been attributed to both HIV-related immune dysregulation and a preferential reconstitution of memory T cells in the setting of combination antiretroviral therapy (cART) (9,10) as well as suboptimal dosing of immunosuppression due to strong pharmacokinetic interactions with protease inhibitors (PIs). Although early outcomes were not affected, the long-term effect of these rejection episodes on graft function and graft survival is likely to be detrimental. For this reason, many transplant centers switch HIV+ candidates to cART regimens that avoid PIs before transplant. In fact, trials that avoided PIs and managed transplant recipients on integrase-based cART have reported significantly lower rates of acute rejection (11,12).

Recurrence of HIVAN after transplantation is another challenge. Although observed in only three of 150 HIV+ kidney recipients in the United States study (10), a French study reported the presence of HIV-RNA in 12 of 19 transplanted kidneys (9). If localized predominantly in the podocytes (five of 12 patients), the result was progressive HIVAN and graft loss. The reasons for the disparity between the United States and French studies are currently being explored and may relate to genetic polymorphisms in the APOL-1 gene.

The most anticipated challenge in transplanting HIV+ recipients was the potential for exacerbation of HIV with immunosuppression and progression to AIDS. Confounding expectations, the 5-year data from the NIH multicenter trial showed excellent control of HIV infection in the recipients and even longer to receive a kidney. The difference was most acutely observed in living donor transplants, with HIV infection conferring a 47% lower likelihood of a living donor kidney transplant.

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from both living and deceased HIV+ individuals is permitted under the HOPE Act criteria, transplant centers have been slow to embrace HIV+ living kidney donation due to the known risk of ESRD and the lack of data on the effect of uninephrectomy on renal outcome in HIV+ donors. However, the effect on deceased donation is likely to be substantial (18,19). Boyarsky et al. (18) used data from two national registries, the Nationwide Inpatient Sample (which included 8600 inpatient deaths per year from 2005 to 2008) and the HIV Research Network (which included 3798 deaths from 2000 to 2008), to estimate that approximately 500 potential donors would be added per year to the donor pool. Another study identified 13 potential organ donors among 508 HIV-infected patients dying in care in six urban medical centers (19), which they extrapolated nationally to arrive at an estimate of 356 HIV+ deceased donors per year, yielding 192 kidneys.

This approach is not without its own challenges. The kidney is a known reservoir for HIV, even in apparently nonviremic patients on cART (9,20). Superinfection, which occurs uncommonly through more conventional modes of transmission when the recipient is on antiretroviral therapy (21,22), may occur more frequently due to the large dose of virus that is delivered with the organ and be exacerbated by the immunosuppression required post-transplant. The prevalence of drug resistance among HIV strains in the United States is estimated to be 10%–18%; however, resistance to all three classes of antiretroviral therapy is extremely rare (23,24). Furthermore, it remains unclear whether the fitness of a mutated virus would be greater than the recipients’ established virus. The South African experience is not helpful in this regard, because the majority of HIV infection there is caused by the wild-type virus, all donors except one were treatment naive, and viral sequencing was not obtained in donors (16). On the basis of the increasing number of effective antiretroviral agents that are able to control resistant strains, the risk of superinfection with a multidrug-resistant strain seems likely to remain a theoretical one.

Another concern relates to the quality of the donor kidney. Of the 13 potential deceased donors identified in a study of urban patients who are HIV+ dying in care, two had ESRD, and nine had a kidney donor profile index ≥90% (19). The high kidney donor profile index resulted from a combination of age, high terminal creatinine, hepatitis C, black race, hypertension, and diabetes. Some of these characteristics may not generalizable to the United States HIV+ population as a whole. However, given the high prevalence of CKD in patients who are HIV+, the HOPE Act Safeguards and Research Criteria require that all HIV+ kidneys be biopsied before implantation (17) to ensure that the quality of the organ has not been compromised. Kidneys with subtle tubular dysfunction, seen in 12%–25% of nonviremic patients on cART (particularly those on tenofovir), will still be transplanted in this scenario, because such abnormalities are not easily picked up on standard clinical tests or renal pathology (25). Of note, routine post-transplant biopsies in the South African patients revealed early changes of HIVAN (not present in baseline biopsy specimens) in three recipients, despite undetectable viremia (16). As noted previously, similar findings have been observed to occur de novo in kidneys transplanted from HIV− donors (9), and therefore, it is not clear that they are necessarily related to the donor’s HIV infection, particularly in the absence of sequencing data. A urinary assay for HIV RNA, which has been correlated with the presence of HIV in the kidney (9), may be used in the future to identify/exclude potential donors with renal involvement by HIV as well as allow post-transplant monitoring of the recipient.

The gulf between the prospect and the reality of renal transplantation stretches even wider in patients who are HIV++, as discovered by Locke et al. (7) in their timely analysis. The specific risks of receiving an HIV+ kidney need to be balanced against the moral imperative to provide lifesaving organs to patients with ESRD. These risks are less well defined and exist along the continuum of risk from any/all deceased donors. An independent advocate not part of the research team is required (17) to protect the rights of the potential recipient and ensure that the patient makes an educated and voluntary decision. Data from transplants conducted within the framework of the HOPE Act will increase knowledge about the safety and efficacy of HIV+ to HIV+ kidney transplants in the United States, including possibly from living donors, and help define the future role of this strategy in improving equity and redressing disparities in transplantation for patients who are HIV+.

Disclosures
None.

References