Risk Assessment for HIV+ Organ Donors: Is the CD4 T Cell Count a Marker of Increased Risk of Transmissible Diseases?

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Effective combined antiretroviral therapy (cART) has dramatically changed the survival of people living with human immunodeficiency virus (HIV) infection.¹

Many HIV-positive patients now have life expectancies similar to those of the general population; however, certain chronic diseases are more prevalent and, when present, these conditions appear to progress more rapidly. Coinfection with hepatitis C virus (HCV) can result in liver failure, which is a major cause of death among people with HIV. Kidney disease is also common, with HIV-associated nephropathy being a leading cause of renal failure.²

Until recently, HIV infection has been considered to be a contraindication to organ transplantation, nevertheless, during the past few years, the role of liver, kidney, pancreas, heart and lung transplantation among HIV-infected individuals with end-stage organ disease has been revisited in the context of improved outcome.^{3,4}

With organ transplantation now becoming increasingly recognized as the standard of care for many HIV-infected patients with end-stage renal disease or end-stage liver disease, an already existing shortage of available organs, that affects all transplant candidates has been exacerbated globally. To expand the availability of transplantable organs for HIV-positive patients, successful transplantation of healthy kidneys from HIV-positive donors into selected HIV-positive recipients was reported for the first time by the Groote Schuur Hospital program in Cape Town, South Africa.⁵ More recently, liver transplantation from HIV-positive donor to HIV-positive recipient has been reported by a Swiss group.⁶

With the aim to generate evidence-based, research-driven data to put forth criteria that would facilitate the feasibility of HIV-to-HIV transplantation in the United States, the US Congress approved the HIV Organ Policy Equity Act (HOPE) Act (42 U.S.C. § 274f-5(b)) in November 2013, mandating a revision to the National Organ Transplant Act of 1988 prohibition of transplanting organs from HIV+

donors. The US Department of Health and Human Services was charged with developing guidelines for clinical research involving HIV-positive organs. On November 25, 2015, the final human HOPE Act safeguards and research criteria were published.⁷ The Johns Hopkins University School of Medicine, Baltimore, Maryland, opened the first clinical trial under these criteria and in March 2016 a liver and kidney transplantation using organs from a deceased HIV-positive donor were successfully performed in the United States.⁸

In addition, the group of Birmingham (UK) has recently reported 5-year survival of an HIV-HCV coinfecting liver transplant recipient of an organ from an HIV-HCV co-infected donor.⁹

In a recent study examining patient-specific data from HIV infected patients dying in care, it was extrapolated that in the United States, approximately 356 potential HIV-Infected deceased donors (HIVDD) yielding 192 kidneys and 247 livers could be procured annually and that 196 to 285 of these potential HIVDD would get authorization for donation depending on their demographics.

The discrepancy between kidneys and livers yield is due to the fact that many of the potential HIVDD currently in care in the United States have suboptimal kidneys as a result of older age and the presence of substantial comorbidities (diabetes, hypertension, HIV associated nephropathy, high prevalence of HCVAb+, African American race). In contrast to kidneys, livers from potential HIVDD are of better quality.¹⁰

Although the HOPE Act Research Criteria does not explicitly set a CD4 count requirement, it urges transplant teams to assess donors with CD4 counts of 200 cells/ μ L or less with special caution for potential disease transmission.

This recommendation is based on the well-known increased risk of opportunistic infection or malignancies in HIV-infected individuals with a CD4+ T cell count of 200/ μ L or less. However, what is the CD4+ T cell count in HIV-negative brain dead donors is currently unknown.

Serrano et al¹¹ reported the results of an interesting study aimed at evaluating the circulating T lymphocyte subset profiles in 20 conventional HIV-negative brain dead donors. The most relevant finding is that 80% of the subjects had a CD4 count less than 441 cells/ μ L and 55% had a CD4 count less than 200 cells/ μ L. CD4/CD8 ratio was below normal in 3 patients. The authors conclude that CD4 absolute numbers are an inconsistent metric for assessing organ donor risk, irrespective of HIV status.

Absolute prevention of the transmission of donor-derived infections in organ transplantation is not possible. However, improvements in screening technologies will potentially enhance the safety of transplantation in the future.¹²

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Organ transplantation using organ from HIV-positive donors poses further challenges. In addition to the risk of transmitting opportunistic infections or malignancies, there is the potential risk of HIV superinfection in the recipient, that is, transmission of HIV strain with resistance to antiretrovirals that may preclude HIV suppression after transplantation. However, in the UK case, despite the transmission of a different strain, responsible for an HIV viral load rebound on day 2 after transplantation, resuppression of the recipient's viral load occurred within the first 7 postoperative weeks without a change in the cART regimen. His viral load has subsequently remained undetectable throughout the first 5 years after transplantation.⁹

Based on the data generated by the study of Serrano et al,¹¹ assessing the CD4+ cell count in the donor does not seem by itself to be able to identify the donors with increased risk of disease transmission. As a consequence, transplant safety using organs from HIV-positive donors should not rely exclusively on a specific test like the CD4 cell count but on the availability of the most accurate documentation of all comorbidities and HIV related events at the time of organ donation, including treatment regimen(s) (unusual cART that may suggest resistance), HIV viral load, virologic rebound episodes, genotypic resistance patterns, opportunistic infection(s), and/or oncologic diagnoses. For this reason, it is recommended to consider as potential HIVDD only patients dying in care, because the retrieval of these information may be otherwise challenging in the limited time of organ donation. The donor's history of HIV genotypes and antiviral therapies should guide the recipient's antiretroviral management.

CONCLUSIONS

Although HIV-positive-to-HIV-positive transplantation is promising, it remains unclear whether patients will be inadvertently harmed. Accordingly, as experience will increase, ethical practice demands taking measures to ensure that risks are identified and minimized.¹³

For these reasons, the HOPE Act mandates that, for the time being, transplantation using HIV-positive organs occur exclusively within research protocols that are approved by institutional review boards and follow published NIH guidelines.

REFERENCES

1. Costagliola D, May M. Survival in individuals living with HIV. *Curr Opin HIV AIDS*. 2016;11:451–454.
2. Antiretroviral Therapy Cohort Collaboration. Causes of death in HIV-1-infected patients treated with antiretroviral therapy, 1996–2006: collaborative analysis of 13 HIV cohort studies. *Clin Infect Dis*. 2010;50:1387–1396.
3. Grossi PA. Update in HIV infection in organ transplantation. *Curr Opin Organ Transplant*. 2012;17:586–93.
4. Chin-Hong P, Beatty G, Stock P. Perspectives on liver and kidney transplantation in the human immunodeficiency virus-infected patient. *Infect Dis Clin North Am*. 2013;27:459–71.
5. Muller E, Barday Z, Kahn D. HIV-positive-to-HIV-positive kidney transplantation. *N Engl J Med*. 2015;372:2070–2071.
6. Calmy A, van Delden C, Giostra E, et al. HIV-Positive-to-HIV-Positive Liver Transplantation. *Am J Transplant*. 2016;16:2473–8.
7. Health Resources and Services Administration. Final Human Immunodeficiency Virus (HIV) Organ Policy Equity (HOPE) Act Safeguards and Research Criteria for Transplantation of Organs Infected with HIV. Department of Health and Human Services, National Institutes of Health. *Fed Register*. 2015;80:34912–21. <https://www.federalregister.gov/documents/2015/11/25/2015-30172/final-human-immunodeficiency-virus-hiv-organ-policy-equity-hope-act-safeguards-and-research-criteria>.
8. Malani P. HIV and transplantation: new reasons for HOPE. *JAMA*. 2016;316:136–8.
9. Hathorn E, Smit E, Elsharkawy AM, et al. HIV-positive-to-HIV-positive liver transplantation. *N Engl J Med*. 2016;375:1807–1809.
10. Richterman A, Sawinski D, Reese PP, et al. An assessment of HIV-infected patients dying in care for deceased organ donation in a United States urban center. *Am J Transplant*. 2015;15:2105–16.
11. Serrano OK, Kerwin S, Payne WD, et al. CD4 count in HIV– brain dead donors: insight into donor risk assessment for HIV+ donors. *Transplantation*. 2017;101:830–834.
12. Fishman JA, Grossi PA. Donor-derived infection—the challenge for transplant safety. *Nat Rev Nephrol*. 2014;10:663–72.
13. Durand CM, Segev D, Sugarman J. Realizing HOPE: the ethics of organ transplantation from HIV-positive donors. *Ann Intern Med*. 2016;165:138–42.