

Wanted: kidneys and livers

PWAs try to break open the organ bank

by Paula Braitstein

Historically, being HIV-positive was considered an “absolute contra-indication” to getting an organ transplant. Consequently, there has yet to be a person in Canada living with HIV/AIDS to receive a transplant. Initially, it was thought that people would die of AIDS before they were able to get any real benefit from having a new organ such as a liver. It was also believed that the immune suppressive drugs that a transplant recipient must take to avoid rejection of the organ would aggravate the HIV disease. These issues, combined with the relative rarity of organs available for transplantation, meant that in the pre-HAART era it just didn’t make sense for most HIV-positive people to get transplants.

Things are different today. Treatments such as highly active antiretroviral therapy (HAART) can extend a person’s life for many years. At the same time, people living with HIV often have any one of a number of complicating conditions: hepatitis B or C, which can cause serious liver damage; diabetes, which can often result in needing a kidney transplant; and toxic side effects of antiretrovirals, which over time can interfere with organ function. However, not only are people living with HIV/AIDS for much longer and with better health, but because they are living longer, they are increasingly in need of organ transplantation in order to continue to survive.



HIV and transplantation, pre-HAART

Several pre-HAART era reports on individuals who were either infected with HIV at the time of the transplant (peri-operatively), or were retrospectively found to have HIV, suggested that the progression to AIDS in these individuals was extremely rapid. However, cases were also reported of HIV-positive people who received transplants and maintained normal graft function for at least eight years following the transplant.

Reports also show long-term graft survival in the presence of immune-suppression with variable rates of disease progression and death. The importance of these reports is that they concluded that AIDS progression was the most common cause of death in HIV-positive transplant recipients during this pre-HAART period.

“All published reports of transplantation in HIV-positive patients who are receiving multi-drug antiretroviral regimens have concluded that, in most cases, HIV infection does not affect the outcome of the transplantation.” – *New England Journal of Medicine*, July 2002

HIV and transplantation, post-HAART

Since 1996 and the use of HAART, the situation has changed substantially for HIV-positive individuals requiring transplantation. Reports from the United States, the United Kingdom, Japan, and elsewhere all suggest that liver transplantation is a viable option in terms of both overall survival and graft survival for people living with HIV/AIDS. The reports of these transplants show that there is variation in terms of survival rates and other outcomes among the HIV-positive individuals.

The largest group of HIV-positive people to have received transplants shows that their rate of survival at one year is roughly equivalent to the rate among HIV-negative people, at just over 90%. The variability in the other reports is due to a number of factors:

- many of the patients also have or had hemophilia;
- some had hepatitis C and some didn't;
- some were treated for hepatitis C and some were not;
- some were treated for hepatitis C with Rebetron (ribavirin and recombinant interferon alfa-2b) and some with pegylated interferon;
- patients were immune-suppressed with a variety of agents which may have influenced their survival;
- some had histories of AIDS-defining illnesses, while others did not.

In general, the data suggest that although not uniformly successful—nor are transplants in HIV-negative individuals

uniformly successful—transplantation offers an intervention resulting in increased survival, where otherwise death would be imminent.

Hepatitis C co-infection

Most of the deaths among HIV-infected individuals in the post-HAART reports were among those who were co-infected with hepatitis C, and the causes of death were not HIV-related. Causes of death in the HIV-negative, hepatitis C-positive populations were reported as infection, cardiac complications, graft failure, and multi-organ failure. These reported causes were not different from the causes of death of transplant recipients who did not have hepatitis C. As well, these causes of death are not substantially different from the causes of death in the HIV-positive recipients.

It is important to consider that novel and more effective drugs for hepatitis C are in development. A liver transplant may provide many people with the extra time needed until these improved drugs are available. Even though hepatitis may be the major complicating factor for an HIV-positive person needing a transplant, hepatitis C is also the leading cause of liver transplants in the United States and elsewhere.

HIV management issues

The literature indicates a number of important post-surgery issues specific to people living with HIV/AIDS. These include antiretroviral management and avoiding drug interactions with immune suppressants. Important references show that many positive and negative interactions occur between immune-suppressive drugs (exogenous immune suppressants) and antiretrovirals.

Much debate surrounds the use of cyclosporine to treat HIV. Researchers have noted that many of the HIV-positive transplant recipients who survived long-term prior to HAART were immune-suppressed with cyclosporine. While cyclosporine may be beneficial to HIV-positive patients, other exogenous immune suppressants may be harmful. The required amount of exogenous immune suppression in HIV-positive liver transplant recipients is unknown, but it is believed to be similar to non-HIV-infected transplantation recipients.

The use of antibiotic prophylaxis for opportunistic infections is an important consideration for both HIV-infected and non-infected transplant recipients. While the issue of preventing opportunistic infections is important for both groups, drug interactions with antiretroviral medication is a further complication among HIV-infected patients.

The ethics of transplantation

Several ethical issues arise about whether HIV-positive people should receive transplants. Transplantable organs are scarce; therefore, determining the most ethical system

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of allocation requires simultaneous consideration of efficacy, urgency, and equity. The number of HIV-infected patients to have received transplants is still small enough that a direct comparison of efficacy is not yet possible. However, preliminary data do suggest that the rates of favourable outcomes between HIV-positive and HIV-negative recipients are similar.

Even if HIV-positive individuals have somewhat poorer outcomes, relative efficacy should not be the sole ethical criterion for determining eligibility. Patients with hepatitis C, diabetes, older patients, women, and African-American and Asian patients have more post-transplantation complications and diminished survival. These patient groups are nonetheless eligible for transplantation.

Medical urgency is the primary criterion for determining patient eligibility in the United Network for Organ Sharing (UNOS), and their policy regarding HIV/AIDS states clearly that HIV-seropositivity shall not automatically exclude individuals from receiving a transplant. The notion of medical urgency helps explain why patients who require retransplantation routinely receive it, even though the probability of survival in these people is substantially diminished.

A proposal is circulating to provide HIV-positive individuals with so-called marginal organs, such as organs from older individuals or other HIV-positive individuals. However, the outcomes for recipients of marginal organs are typically worse than outcomes for recipients of healthy organs. Furthermore, if an individual is medically recognized to require an organ transplant and meets the criteria for transplantation (such as medical urgency), no ethical justification can exist for providing this individual with anything but an ideal organ. It should be noted, however, that people with hepatitis C requiring liver transplants do receive HCV-positive donor organs in about 2–3% of cases. These livers are considered marginal, although they are only used when there is no fibrosis found on liver biopsy.

“The BC Transplant Society believes that the health-restoring benefits of organ transplant services should be available to those individuals who meet the suitability and eligibility criteria for transplantation in British Columbia.” – www.transplant.bc.ca

Conclusions

Sufficient evidence now indicates that, thanks to HAART, HIV-positive individuals can be the successful recipients of liver transplants. Regarding HIV as an absolute contra-indication to transplantation is a historical artifact and a practice

not based on current medical evidence. Ethical considerations regarding HIV-infected individuals are now on a par with other chronic illnesses, such as hepatitis C mono-infection, diabetes, or hemophilia.

The factors that will increase the probability of successful transplants in HIV-positive people include the following:

- The ability to suppress HIV replication using combination antiretroviral medication.
- A high CD4 count. It is more likely that the patient will survive if s/he is healthy at the time of transplant.
- Access to a multidisciplinary team of healthcare providers. In addition to hepatologists, clinical immunologists, and transplantation surgeons, this team must include a knowledgeable pharmacist, an HIV specialist, and a strong psychosocial support component.

While hepatitis C co-infection is an important negative prognostic factor, it is a leading cause of liver transplantation in the HIV-negative population, and with appropriate therapeutic management with the most effective anti-viral agents available (such as pegylated interferon combined with ribavirin), the probability of aggressive hepatitis C reinfection of the graft is minimized.

Transplanting the organ of an individual who is dying of AIDS would be an inefficient use of valuable resources in the same way that transplanting someone with metastatic liver cancer would be inappropriate. Both individuals would probably die of their respective illnesses before receiving any significant benefit from the new organ. However, in the era of HAART, people are *living* with HIV/AIDS—people are returning back to work, to school, and to life. ⊕



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