



ADVOCACY

Uniquely South African: Time to consider offering HIV-positive donor kidneys to HIV-infected renal failure patients?

W D Francois Venter, Sarala Naicker, Ames Dhai, June Fabian, Shoyab Wadee, Russel Britz, Graham Paget, Graeme Meintjes

Kidney transplantation has been established as the most effective form of renal replacement therapy from a cost and quality of life perspective in the developed world. The first year after the transplant can be more expensive and may have a slightly higher mortality, but after the first year, expected survival is 10 - 15 years longer than in patients on dialysis, and the intervention is significantly cheaper.¹⁻³ While cost-effectiveness in the developing world is less well described, the renal transplant programme in South Africa has a long history, with expansion in the last decade driven from the private sector.

HIV infection was an absolute contraindication to organ transplantation throughout the world before the advent of antiretroviral therapy (ART). In recent years, encouraging immunological and clinical outcomes with ART have meant that in some international centres renal transplantation has been performed on HIV-infected patients with end-stage renal failure who fulfilled specific pre-transplant criteria. One- and 3 - 5-year survival data have shown that both graft and patient survival in HIV-infected patients is comparable to that in the HIV-negative transplant population, in spite of a higher number of acute rejections.^{4,5} The transplant guidelines of the National Department of Health in South Africa have subsequently removed HIV as a contraindication to organ transplantation. ART adherence is onerous, at least as demanding as adherence to transplant drugs. HIV patients on successful ART, a precondition for transplant, are theoretically ideal transplant patients, with objectively demonstrated medication adherence pre-transplant. Furthermore, they are

already in a system of monitored health care, and are generally younger than other chronic renal failure patients, making them better surgical candidates. This change in the guidelines, while expanding health care access, has created additional demand for dialysis and transplantation, as HIV is in itself a common cause of end-stage renal failure. However, anecdotal reports suggest that the new guidelines are not yet being implemented in South Africa, owing to concerns about already limited dialysis and transplant resources.

The number of donated organs is the primary limiting factor in meeting transplantation needs in South Africa, as in most countries. This is compounded by the fact that the cadaver donor pool has a very high HIV infection rate. These HIV-infected kidneys would almost certainly infect any HIV-negative recipient, and are not harvested. In well-resourced countries, HIV infection in the general population is very low, and few organs are lost. This unharvested pool represents 28.1% of deceased donors reviewed at one Wits University-affiliated hospital in Johannesburg in the past year.

South Africa is therefore unique – it provides transplant services, including to HIV-positive people, yet loses a large proportion of the donor pool. Could HIV-positive kidneys be transplanted into HIV-positive recipients? The idea is enticing – a significant number of patients could receive transplants, and donor kidney supply could be maximised. Dialysis slots, currently at a premium in the state sector, would be freed. Patients in ART programmes could receive screening for kidney disease, monitoring and early intervention, and those progressing to end-stage renal disease could be rapidly transferred for renal replacement therapy.

There are several theoretical considerations before HIV-infected cadaveric donor kidneys are used in this way.

1. Transmission of different strains of HIV from the infected kidney to the recipient may occur. There is concern that superinfection with a different clade or subtype of virus may have negative consequences.⁶ However, ART is very effective in suppressing all clades of virus, and will probably suppress any acquired drug-sensitive superinfection.
2. Transmission of drug-resistant virus to the recipient may occur. This is plausible, although drug-resistant virus in the community, and even among those on ART, is still unusual in South Africa.

The authors are all academics concerned with improving access to health care. Francois Venter works on state HIV programmes for the Reproductive Health and HIV Research Unit, and lectures at the Steve Biko Centre for Bioethics at Wits, of which Ames Dhai is Director. Sarala Naicker (Head), June Fabian, Shoyab Wadee and Graham Paget represent the Wits Division of Nephrology (Department of Medicine), and Russel Britz, a transplant surgeon, the Department of Surgery. Graeme Meintjes is an HIV and TB expert in the Department of Medicine, University of Cape Town, at G F Jooste Hospital.

Corresponding author: F Venter (f.venter@rhrujhbc.co.za)



3. Inoculation with opportunistic infections present within the donor kidney, especially tuberculosis, may occur. Again this is very plausible, and may be significant in the context of additional immunosuppression. Having said this, routine chemoprophylaxis against infections such as tuberculosis and pneumocystis pneumonia is standard practice after a transplant. In addition, biopsies at implantation should be standard of care.

4. Donated HIV-positive kidneys may have HIV-linked lesions, and may not be as robust as HIV-negative kidneys. This again is possible, although in some studies HIV-infected patients have been allocated 'marginal' kidneys and graft survival was not compromised.⁷ Simple tests such as screening for proteinuria and renal biopsy at the time of transplantation may alert clinicians to underlying renal disease in the donor. Transplanting kidneys from other 'high-risk' groups, such as hypertensive and diabetic donors, is more accepted by the renal transplant community now than in the past.⁸ All HIV-infected recipients would continue to receive ART after transplantation, which effectively prevents opportunistic illness and progression of HIV-related kidney disease.

In the case of HIV-positive living donors wanting to donate to an HIV-positive family member the issue is also complex, as the 'natural history' of HIV has been so changed with ART, and the impact of HIV and ART on kidney function over decades is unknown.

All these risks are unquantifiable at present. The dilemma that ensues is whether, in the face of the dire shortage of donor kidneys, HIV-positive patients requiring transplants should be exposed to these unquantifiable risks. Would receiving a kidney quickly from an HIV-positive donor outweigh the present harm associated with delayed transplantation? Should HIV-positive patients be involved in making these determinations, or should this be limited to health practitioners and policy makers only? And when health practitioners deny patients these kidneys, on the basis of perceived unknown risks, are they then not guilty of unjust paternalism?

This approach is fraught with ethical complexities, particularly in the context of justice. In the case of renal transplantation, the concept of justice hinges around fair distribution and equity. It would be unethical to insist that HIV-positive recipients be limited to receiving organs from HIV-positive donors, with the level of medical uncertainty described above. Theoretically, HIV-positive potential recipients could be asked whether, if they were offered a HIV-positive donation

listing them on a separate allocation programme dealing with HIV-positive donors only, they would be willing to accept this uncertainty or possible risk. This approach could be viewed as a double-edged sword: They are offered the opportunity to receive a transplant at an earlier date than they would otherwise receive on dialysis. This in itself could represent a significant survival advantage, but then they could be exposed to the unknown medical risks listed above. As long as the patient makes an informed decision with all the facts and uncertainties clearly explained, the principle of autonomy and informed consent would be fulfilled. Paradoxically, too, this approach may mean that HIV-positive recipients would initially enjoy more access to organs than those who are uninfected. This in itself would not be problematic in terms of utilitarian considerations whereby utility would be maximised for the HIV-positive group. Health care to HIV-positive patients has, in the main, taken back stage in this country. These patients have suffered discrimination, stigmatisation and stereotyping. Justice may require a remediation of these past injustices by according new opportunities to this group that has been so unfairly treated. While offering equal opportunity to HIV patients, this approach is still limited by the number of donors.

These issues deserve serious scrutiny – it is unlikely that any other large country is in the same position, offering a transplant service in the midst of a generalised HIV epidemic. Research is needed, and probably a good starting point would be to ask potential HIV-positive transplant recipients whether they would accept an HIV-infected kidney with the unknown level of risk described above. Exploration of transplanting kidneys from HIV-infected donors must be done within a tightly controlled research setting.

1. Oniscu GC, Brown H, Forsythe JL. Impact of cadaveric renal transplantation on survival in patients listed for transplantation. *J Am Soc Nephrol* 2005; 16(6): 1859-1865.
2. Kontodimopoulos N, Niakas D. An estimate of lifelong costs and QALYs in renal replacement therapy based on patients' life expectancy. *Health Policy* 2007; 8 Nov. http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6V8X-4R3BW4J-1&_user=10&_rdoc=1&_fmt=&orig=search&_sort=d&view=c&_acct=C000050221&_version=1&_urlVersion=0&_userid=10&m5=88ab15913628660b0fb8da6e8f2658ee (accessed 30 January 2008).
3. Schippers HM, Kalff MW. Cost comparison haemodialysis and renal transplantation. *Tissue Antigens* 1976; 7(2): 86-90.
4. Qiu J, Terasaki PI, Waki K, Cai J, Gjertson DW. HIV-positive renal recipients can achieve survival rates similar to those of HIV-negative patients. *Transplantation* 2006; 81(12): 1658-1661.
5. Roland ME, Barin B, Carlson L, et al. HIV-infected liver and kidney transplant recipients: 1- and 3-year outcomes. *Am J Transplant* 2007/2008; 8(2): 355-365 (epublication). <http://www.blackwell-synergy.com/doi/abs/10.1111/j.1600-6143.2007.02052.x> (accessed 30 January 2008).
6. van der Kuyl AC, Cornelissen M. Identifying HIV-1 dual infections. *Retrovirology* 2007; 4: 67. <http://www.retrovirology.com/content/4/1/67> (accessed 30 January 2008).
7. Kumar MS, Sierka DR, Damask AM, et al. Safety and success of kidney transplantation and concomitant immunosuppression in HIV-positive patients. *Kidney Int* 2005; 67(4): 1622-1629.
8. Michelon T, Piovesan F, Castilho C, et al. Marginal cadaveric kidney donors: an attractive way to expand the donor pool. *Transplant Proc* 2002; 34(7): 2515-2517.