Outcome of overseas commercial kidney transplantation: an Australian perspective

Sean E Kennedy, Yvonne Shen, John A Charlesworth, James D Mackie, John D Mahony, John J P Kelly and Bruce A Pussell

ABSTRACT

- Lack of donors has led to a worldwide increase in commercial kidney transplantation programs where recipients acquire kidneys either from executed prisoners or live non-related donors.
- Commercial transplantation is prohibited by legislation in Australia.
- Our centres have had 16 patients who have travelled overseas to receive a commercial kidney transplant; five have subsequently died.
- As has been found previously, patients who received commercial transplants were more likely to develop infections such as HIV, hepatitis B virus, cytomegalovirus and fungal infections.
- Previous reports have found that patient and graft survival were comparable to local results, whereas we found that patient and graft survival were worse than transplantation within Australia.
- Patients considering the option of overseas commercial donation should be advised that heightened risks to life and graft survival exist.

MJA 2005; 182: 224–227

Kidney transplantation is accepted as a better treatment for patients with endstage kidney disease (ESKD) than long-term dialysis. Mortality, morbidity and cost comparisons are significantly better than dialysis regimens.[1-3] The major factor limiting transplantation rates is availability of donor kidneys. About 520 kidney transplants are performed each year in Australia,[4] and this number has remained relatively stable over recent years, despite a steady increase in the number of patients receiving dialysis treatment. There are about 2000 Australians awaiting kidney transplantation.

The deceased donor (DD) rate has diminished over the past 10 years, but there has been a corresponding increase in living donor (LD) transplants. In Australia, these now contribute 35%–40% of kidney transplants. LD kidneys have traditionally been from related donors (usually parents or siblings), but there has been a recent rise in the number of living unrelated donors (LURD).[4] LURD kidneys are from spouses (69%), with other "emotionally related" donors making up most of the remainder. A small number of kidneys are transplanted from donors who have no direct genetic or emotional relationship with the recipient, and increasing the frequency of this type of donation is seen as a potential way of reducing the waiting list for transplantation. Most Australian states have enacted laws that forbid payment for organs and tissues for transplantation. Protocols enabling altruistic donor procedures are currently under consideration by health authorities.

The lack of transplantable organs is a universal problem in developed countries, and has led to the growth of commercial programs or renal transplantation in which donors are financially compensated. The main centres for these practices were initially in India; although the practices are now illegal in India, an estimated 60% of kidney donations are still paid donations.[5] More recently, programs have developed in Iraq, Iran, Eastern Europe, South America, South Africa and the Philippines.[6] Large commercial transplantation programs have also been established in China, attracting recipients from around the world. The source of these commercially acquired kidneys is not always apparent; some reports claim that up to 90% of transplanted kidneys in China are retrieved from executed prisoners.[7] South Korea is notable for having developed an organ donation registry supporting both altruistic LURD and "paired-exchange" donations.[8] A paired exchange occurs when two patients have incompatible potential donors and kidneys are exchanged. Paired exchanges are presently illegal in Australia.

A small percentage of Australian patients with ESKD have availed themselves of overseas commercial kidney transplantation. We reviewed the literature about outcome of overseas commercial kidney transplantation and report the experience of four Australian centres.

FOR EDITORIAL COMMENT, SEE PAGE 204

East Coast Renal Services, Prince of Wales Hospital, Royal North Shore Hospital, St George Hospital, Sydney, NSW, and Illawarra Regional Hospital, Wollongong, NSW.
Sean E Kennedy, FRACP, Renal Registrar, Prince of Wales Hospital;
Yvonne Shen, FRACP, Renal Registrar, Prince of Wales Hospital;
John A Charlesworth, MD, FRACP, Professor of Renal Medicine, Prince of Wales Hospital;
James D Mackie, FRACP, Renal Physician, Prince of Wales Hospital and Illawarra Regional Hospital;
John D Mahony, FRACP, Renal Physician, Royal North Shore Hospital;
John J P Kelly, MD, FRACP, Renal Physician, St George Hospital;
Bruce A Pussell, PhD, FRACP, Professor of Medicine, Prince of Wales Hospital.
Reprints will not be available from the authors.
Correspondence: Professor Bruce A Pussell, Department of Nephrology, Prince of Wales Hospital, Sydney NSW 2031. b.pussell@unsw.edu.au

Literature review

We reviewed the literature using the MEDLINE database 1966 to June 2003. Primary search terms were "kidney transplantation" and "commerce", followed by a second search using "kidney transplantation" and "living donors" and "unrelated". The phrase "commercial transplantation" was used as a separate keyword. The abstracts of retrieved articles were reviewed, and those that focused on outcome of commercial transplantation were obtained in full, and their reference lists were searched for further articles. Four articles, each reviewing the outcome of more than 100 cases of commercial transplantation (1301 cases in total), were published between 1990 and 2001 (Box 1). These are discussed below.

1 Summary of commercial transplantation case reports

First author	Country of origin of patients	Country of transplant	Years	No.	Patient survival at 1 year	New HIV infection	New HBV infection
Salahudeen[9]	UAE and Oman	India	1984–1988	131	81.5%	3.8%	2.3%
Living Non-Related Renal Transplant Study Group[10]	Saudi Arabia	India	1978–1993	540	96%	4.6%	8.1%
Sever[11]	Turkey	India, Iraq, Iran	1992–1999	115	90% (2 years)	nr	6%
Morad[12]	Malaysia	nr	1990–1996	515	92%	nr	12%
Onwubalili[13]	Saudi Arabia	India	1985–1991	16	nr	6.25%	6.25%
Ivanovski[14]	Macedonia	India	1993–1997	14	78%	nr	nr

UAE = United Arab Emirates; HIV = human immunodeficiency virus; HBV = hepatitis B virus; nr = not reported

Renal outcomes

Salahudeen et al reported the outcome of 131 transplants in patients from the United Arab Emirates and Oman who received commercial transplants in India.[9] All patients had arranged their own transplants in Bombay through brokers and without reference to their treating nephrologists. Eight patients died during the perioperative period, a further eight within the first 3 months and another eight before 12 months (patient survival rate, 81.5% at 1 year). Infections were the major cause of death (56%). One patient developed AIDS and died within 3 months of transplantation; HIV infection in the recipient had been suspected pre-transplantation. A further four patients became HIV-positive. Other fatal infections included pneumonia, septicaemia, tuberculosis, viral hepatitis and fungaemia. Most patients returned from India without adequate documentation (50 had no record or knowledge of their antirejection regimen) and many were sick or undergoing rejection on arrival home.

The pooled experience of several Saudi Arabian centres was reported in 1997.[10] The outcomes of 540 patients who had received commercial transplants in India between 1978 and 1993 were compared with patients transplanted at their own centres with LD kidneys. After adjusting for several variables, the 1-year,

2 Pretransplant and transplant details and outcomes for the 16 patients seen in our Australian centres

Patient No.	Age	Sex	Primary disease	Time on dialysis	Previous transplant	Year and country of transplant	Rejection episodes	Graft survival	Outcome
1	53	M	Glomerulonephritis	2 years	No	1990, India	0	13 years†	Well with good function
2	75	M	Interstitial nephritis	5 months	No	1993, China	1	12 months (death with functioning graft)	CMV disease at 3 months; HBV hepatitis at 9 months; death at 12 months with fulminant hepatitis
3	43	M	Diabetic nephropathy	12 months	No	1994, India	1	12 months (renal infarction)	Death after 13 months; ischaemic infarct
4	54	M	Hypertension	12 months	No	1994, India	1	1 month (acute rejection)	Death after 4.5 years; sepsis
5	56	M	Glomerulonephritis	4 years	No	1998, Iraq	0	4 years†	Well with good function
6	31	M	Glomerulonephritis	2 years	No	1999, China	0	5 years†	Well with good function
7	65	M	Diabetic nephropathy	2 years	No	1999, Philippines	0	5 years†	Well with good function
8	66	F	Glomerulonephritis	2 years	Yes	2000, ? Eastern Europe	0	3 years†	Systemic CMV infection on return
9	52	M	Glomerulonephritis	12 months	No	2000, China	1	3 years†	Well with good function
10	55	F	Glomerulonephritis	10 months	No	2002, China	0	2 years†	Well with good function
11	43	M	Glomerulonephritis	12 months	No	2002, China	0	2 years†	Disseminated herpes zoster
12	49	F	Reflux nephropathy	0	No	2002, Lebanon	Multiple	1 month (aspergillosis)	Aspergillosis; septicaemia; dialysis required
13	41	M	Glomerulonephritis	10 months	No	2004, China	0	4 months†	CMV pneumonitis
14	54	M	Glomerulonephritis	6 weeks	No	Nil,* Lebanon	na	na	Dialysis
15	70	M	Diabetic nephropathy	5 years	No	Nil,* China	na	na	Death
16	52	M	Glomerulonephritis	3 years	No	Nil,* India	na	na	HBV;‡ death

HBV = hepatitis B virus; CMV = cytomegalovirus; na = not applicable.
* Travelled overseas for transplant but not transplanted. † Ongoing graft function. ‡ Acquired hepatitis (positive for HBV e antigen) while on dialysis awaiting transplant.

3-year, and 5-year patient survival rates in the Indian group were similar to those of the locally transplanted group (95%, 91%, 91% and 97%, 94%, 92%, respectively; $P = 0.4921$), as were the graft survival rates. There was a higher incidence of HIV infection (4.6% v 0), and hepatitis B virus infection (8.1% v 1.4%) in the cohort transplanted in India.

Sever et al reported the experience of 115 Turkish patients who were transplanted in India (106 patients), Iraq (7) and Iran (2) between 1992 and 1999.[11] There was a high incidence of early surgical complications, as well as three cases of primary non-functioning grafts. The non-surgical infectious complications included 10 patients who developed malaria, 8 who developed serious fungal infection (5 fatal) and six cases of atypical pneumonia. Six patients became positive for hepatitis B. The patient survival rates at 2 years (90%), 5 years (80%) and 7 years (74%) were not significantly different from LD transplants performed in Istanbul (90%, 85% and 80%, repectively; $P = 0.53$). Graft survival rates for commercial transplants were 84%, 66% and 53% v 86%, 78% and 73% for Turkish LD transplants ($P = 0.036$) at these endpoints.

A comparison of 515 Malaysian patients who had received overseas commercial kidneys with 258 patients who had received LD kidneys in Malaysia showed that patient and graft survival, as well as infectious complications, were comparable between all groups.[12] The analysis did not include all patients who went overseas for commercial transplants — only those who returned.

Other, smaller reviews have also been published, with similar high rates of infectious complications (see Box 1).[13,14]

Local experience

We surveyed four renal units in the East Coast Renal Services of New South Wales and identified 16 patients who had travelled overseas for commercial kidney transplantation. Patient details and outcomes are shown in Box 2. Three patients who travelled overseas did not receive a kidney graft, but received haemodialysis therapy while abroad. Two have subsequently died. Patient 15 travelled to China twice for transplantation. During his first visit urological surgery was performed in preparation for transplantation, but on his return visit he was considered too unwell for further surgery and has subsequently died. Patient 16 contracted hepatitis B virus while undergoing dialysis in India and died of liver failure.

Patient survival

Overall 1-year patient survival in this small series was 85%, with long-term outcomes possibly worse. Seven of the patients were transplanted more than 5 years ago. Three of these have since died, all within 5 years. Two deaths followed graft failure and one was the result of HBV infection. All eight patients transplanted in the past 5 years have survived, but with an increased incidence of infectious complications.

Graft survival

Four grafts failed within 12 months, giving a 1-year graft survival rate of 66% compared with the Australian survival rate of 90% at one year. Kidneys that survived beyond 12 months generally continued to function well.

Acute rejection

Early acute rejection or delayed graft function was documented in four cases. In one instance this was the result of the patient being given an inadequate supply of medications before returning home.

Infectious complications

Patients 2 and 16 contracted HBV in China and India, which led to death. Three patients were admitted to hospital soon after their return to Sydney with serious cytomegalovirus infections. Patient 12 returned from Lebanon with aspergillus infection of the kidney graft and required nephrectomy. Her surgical wounds were also infected by multiresistant *Pseudomonas aeruginosa*. There have been no instances of HIV seroconversion in this group of patients.

Documentation and correspondence

Documentation of transplantation procedure, patient progress and medication doses was variable. In at least three instances, no documentation was available. All correspondence from China was in Chinese. Donor details were generally not available, although it was known that at least two kidneys were from executed Chinese prisoners.

Discussion

Kidney transplantation has significant survival advantages over dialysis therapy,[1] and the quality of life of kidney transplant recipients is significantly better than that of similar patients maintained on dialysis.[15] It is therefore not surprising that some dialysis patients are prepared to seek alternatives to the uncertain waiting period associated with a DD transplant. Similarly, patients who, for reasons of comorbid disease or advanced age, are not offered the option of DD transplantation may seek transplant donors from other sources.

Our case series highlights some areas of concern about overseas commercial kidney transplantation. As illustrated in previously published series, the early postoperative mortality rate was high. The 1-year patient survival rate of overseas commercial transplants may be between 80% and 96%, compared with greater than 95% for Australian LD transplants.[4] Although the early survival rate was good in our relatively small series, two patients died 1 year after transplant and the 5-year patient survival rate was 60%. This is a marked survival disadvantage compared with the Australian DD kidney transplant recipients' 5-year survival rate of 82% or greater.[4] Survival rates for Australian dialysis patients placed on the transplant waiting list in Australia at 1 year (from time of joining the list) are also above 95%.[1] The 3-year survival rate for all dialysis patients in Australia is greater than 60%.

Our series covers a period of 14 years. The three patients who died were transplanted in the early 1990s. More recent overseas transplants appear to have better outcomes, but even in this small group there has been a high incidence of serious infection. It is also important to note that we (as in previously published series) reported only the outcomes of patients who have returned from overseas, which means early mortality and complications may be under-reported.

Infectious complications were notable. Cytomegalovirus infection is a common occurrence in the first 6 months after transplant, and, to reduce the risk of CMV disease, most Australian centres have instituted routine use of prophylactic therapy. Details of CMV screening of overseas donors were scarce. HIV and viral hepatitis

could both be contracted during the transplant period, either from an infected donor organ or blood products. Prospective Australian organ donors and blood donors are screened for CMV, HIV, HBV and hepatitis C virus. The screening procedures of commercial transplant programs are not evident, despite a generally high incidence of these infections in the populations of the countries performing commercial transplantation.

An area of concern identified in our patients is the lack of communication between the transplantation team and the unit caring for the patient in Australia. Our experience is similar to that reported by others. An obstacle in at least one instance was reluctance on behalf of the patient to disclose information.

Conclusions

As physicians caring for patients with ESKD, we should be able to offer informed advice about commercial transplantation. Ethical reasons, in particular concerning the rights and well-being of donors, are enough to prevent us from recommending overseas commercial transplantation (in its current form) as a treatment for ESKD.[16]

We suggest that patients considering commercial organ donation should be advised that heightened risks to life and graft survival exist. If they decide to proceed with commercial transplantation, they should specifically seek assurances about screening for HIV and viral hepatitis before departure. They should also be aware that a donor kidney may not be available and that haemodialysis overseas may further expose them to blood-borne viruses. All attempts should be made to ensure adequate documentation and communication.

Competing interests

None identified.

References

1 McDonald SP, Russ GR. Survival of recipients of cadaveric kidney transplants compared with those receiving dialysis treatment in Australia and New Zealand 1991–2001. *Nephrol Dial Transplant* 2002; 17: 2212-2219.

2 Winkelmayer WC, Weinstein MC, Mittleman MA, et al. Health economic evaluations: the special case of end-stage renal disease treatment. *Med Decis Making* 2002; 22: 417-430.

3 Wolfe RA, Ashby VB, Milford EL, et al Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med* 1999; 341: 1725-1730.

4 Australia and New Zealand Dialysis and Transplant Registry. Available at: www.anzdata.org.au (accessed April 2004).

5 Phadke KD, Anandh U. Ethics of paid organ donation. *Pediatr Nephrol* 2002; 17: 309-311.

6 Scheper-Hughes N. Keeping an eye on the global traffic in human organs. *Lancet* 2003; 361: 1645-1648.

7 Briggs JD. The use of organs from executed prisoners in China. *Nephrol Dial Transplant* 1996; 11: 238-240.

8 Kim ST, Kim JH. Organ donation — third party donation: expanding the living-donor pool. *Transplant Proc* 2000; 32: 1489-1491.

9 Salahudeen AK, Woods HF, Pingle A, Nur-El-Huda, et al. High mortality among recipients of bought living-unrelated donor kidneys. *Lancet* 1990; 336: 725-728.

10 The Living Non-Related Renal Transplant Study Group. Commercially motivated renal transplantation: results in 540 patients transplanted in India. *Clin Transplant* 1997; 11: 536-544.

11 Sever MS, Kazancioglu R, Yildiz A, et al. Outcome of living unrelated (commercial) renal transplantation. *Kidney Int* 2001; 60: 1477-1483.

12 Morad Z, Lim TO. Outcome of overseas kidney transplantation in Malaysia. *Transplant Proc* 2000; 32: 1485-1486.

13 Onwubalili JK, Obineche EN, Assuhaimi S, Bassiouni M. Outcome of bought living non-related donor kidneys followed up at a single centre. *Transplant Int* 1994; 7: 27-32.

14 Ivanovski N, Stojkovski L, Cakalaroski K, et al. Renal transplantation from paid, unrelated donors in India — it is not only unethical, it is also medically unsafe. *Nephrol Dial Transplant* 1997; 12: 2028-2029.

15 Valderrabano F, Jofre R, Lopez-Gomez JM. Quality of life in end-stage renal disease patients. *Am J Kidney Dis* 2001; 38: 443-464.

16 Zargooshi J. Quality of life of Iranian kidney "donors". *J Urol* 2001; 166: 1790-1799.

(Received 15 Jan 2004, accepted 30 Sep 2004) ❑