Commercial renal transplantation: A risky venture? A single Canadian centre experience

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Cite as: *Can Urol Assoc J* 2011;5(5):335-40; DOI:10.5489/cuaj.11018

Abstract

Background: Canada, akin to other developed nations, faces the growing challenges of end-stage renal disease (ESRD). Even with expanded donor criteria for renal transplantation (the treatment of choice for ESRD), the supply of kidneys is outpaced by the escalating demand. Remuneration for kidney donation is proscribed in Canada. Without an option of living-related transplantation (biological or emotional donors), patients often struggle with long waiting lists for deceased donor transplantation. Accordingly, many patients are now opting for more expedient avenues to obtaining a renal transplant. Through commercial organ retrieval programs, from living and deceased donors, patients are travelling outside Canada to have the procedure performed.

Methods: Between September 2001 and July 2007, 10 patients (7 males, 3 females) underwent commercial renal transplantation outside Canada. We describe the clinical outcomes of these patients managed postoperatively at our single Canadian transplant centre.

Results: Six living unrelated and 4 deceased donor renal transplantations were performed on these 10 patients (mean age 49.5 years). All procedures were performed in developing countries and the postoperative complications were subsequently treated at our centre. The mean post-transplant serum creatinine was 142 μmol/L. The average follow-up time was 29.8 months (range: 3 to 73 months). One patient required a transplant nephrectomy secondary to fungemia and subsequently died. One patient had a failed transplant and has currently resumed hemodialysis. Acute rejection was seen in 5 patients with 3 of these patients requiring re-initiation of hemodialysis. Only 1 patient had an uncomplicated course after surgery.

Discussion: Despite the kidney trade being a milieu of corruption and commercialization, and the high risk of unconventional complications, patients returning to Canada after commercial renal transplantation are the new reality. Patients are often arriving without any documentation; therefore, timely, goal-directed therapy for surgical and infectious complications is frequently delayed because of the time taken to establish an accurate diagnosis. Refuting the existence of commercial renal transplantation may not be a practical solution; more consistent communication and documentation with transplant teams may be more pragmatic. In the current climate, patients considering the option of overseas commercial renal transplantation should be advised of the potential increased risks.

Introduction

The burden of kidney failure worldwide is momentous and escalating. Kidney transplantation is the treatment of choice for end-stage renal disease (ESRD).[1] It has been well-established that renal transplantation improves quality of life and reduces mortality for most patients compared to those maintained on dialysis.[2,3] However, the major factor limiting transplantation rates is the availability of donor kidneys. The paucity of transplantable organs is a universal problem in the developed world. To address this shortage of donor kidneys, acceptance of what previously have been "marginal" kidneys are now termed "expanded criteria donors." These kidneys from geriatric, hypertensive, renal insufficiency and even proteinuric donors have increased progressively.[4] Even so, the widening gap between increased demand for transplantable kidneys and the lacking corresponding supply has been the impetus for the growth of the commercial kidney market.

In developed countries, the availability of cadaveric organ donations has reached a plateau. Numerous options have been examined by various jurisdictions around the world to offset the disproportionate rise in demand compared to transplants being performed annually. At the time of writing this manuscript, there are 1199 patients waiting for kidney transplants in Ontario alone.[5] Despite a steady rise in the number of transplants performed over the last 10 years in Ontario, with the increase mainly from a greater number of living donors, the number of patients remaining on the waiting list has remained stable over the same period. Currently, 3 provinces in Canada, including Ontario, are focusing on increasing the number of living-related renal transplantations by offering a reimbursement program. This program supports the principle that living organ donors should not personally bear the financial costs of organ donation. The United

Kingdom reimburses costs ranging from travel and accommodation to lost wages, while France covers travel and accommodation. In contrast, certain countries, like China, have responded to the shortage of organs by allocating the kidneys of death penalty outlaws for kidney transplants.[6] This practice has been questioned on the international forum, yet the procedures still continue.

Commercial renal transplantation has emerged as an available outlet for expedited kidney transplantation for those who would rather not wait for a deceased donor kidney. It is without a doubt that the international black market for human kidneys is thriving. While the sale of human organs is against the law in nearly every country, thousands of patients from the Canada, United States, Japan, Italy, Israel and the Persian Gulf states travel to other, often developing countries, looking for commercial transplantation. Most countries that currently permit commercial renal transplantation are from the developing world (i.e., Brazil, China, Egypt, India, Iraq, Pakistan, Philippines, Romania, Russia, South Africa, Turkey and Venezuela).[7] Furthermore, to perform the procedure rapidly, standards for transplantation are often compromised.[8] The concerns regarding the medical safety of kidney transplantation abroad have been noted, including worse graft survival, higher infection rates and poor communication between transplant sites and the follow-up centre.[8-13] Besides these medical issues, the ethical aspects surrounding markets in human kidneys are equally controversial.

Non-biologically related, non-emotionally related commercial renal transplantation is proscribed in Canada. Further, the transplantation community in Canada disagrees with it. However increasingly, akin to other developed countries, patients are leaving their country of residence to receive kidney transplants abroad, and then are returning home for continued care.[8-17] The concerns over the ethical impact of commercial renal transplantations have been discussed extensively.[18-21] The ethical debates are often even more contentious than the clinical implications. The foremost issues include the exploitation of the donor and the poor, the increased risk to the donor, the advantage of wealthy recipients, the fear of decreasing cadaveric donations, and concerns that commercial renal transplantations could have a negative impact on the availability of organs not suitable for living donations, such as heart and lung.[22,23]

Much of the literature regarding the medical outcomes of kidney transplantation abroad comes from transplant centres outside of North America. To date, only one series in Canada and one American transplant centre has reported the medical outcomes of kidney transplantation surreptitiously performed overseas. We retrospectively describe the medical outcomes of patients at a single Canadian institution who went overseas for kidney transplantation and returned to Canada for continued medical care.

Methods

A retrospective study of kidney transplant patients was conducted from a single transplant centre (St. Joseph's Healthcare, Hamilton, Ontario, Canada). This centre is a tertiary care centre in an urban setting that performs about 100 living related and deceased donor transplants annually. Consistent with other transplant centres across Canada, live and deceased donor transplants are performed in patients who are Canadian citizens or landed immigrants. Between September 2001 and July 2007, patients were identified who had travelled overseas for commercial kidney transplantation. The occurrence of commercial renal transplantation performed overseas was verified for each patient. This particular subset of patients all received pre-transplant chronic disease management at this centre and were all awaiting deceased donor transplantation in Canada. Commercial renal transplant was performed in these patients overseas and they subsequently returned to this centre for post-transplantation medical and surgical management. Patients who received their transplants before immigrating to Canada, as well as those who received their transplantation through waiting lists in other countries, were excluded from this study.

Pre-transplant medical, surgical and dialysis history were recorded when available through retrospective chart review for all identified patients. Donor, recipient, transplantation and postoperative information from the overseas transplant centre provided by the patients was recorded when available. When contact information from the overseas centre was available, attempts were made to contact them directly. The transplant information included date, location and type of transplant, induction therapy, and immunosuppression. We recorded the post-transplantation course at our centre, including post-transplant creatinine, nadir creatinine, creatinine at last follow-up, episodes of rejection, as well as other medical and surgical complications. Post-transplantation complications were limited to medical and surgical problems related directly to the procedure itself. Follow-up information was collected until April 2008.

Results

Between September 2001 and July 2007, we identified 10 patients (7 males, 3 females) who travelled abroad for commercial renal transplantation and who returned to our institution for post-transplant care. All of the patients received their first renal transplantation and no patients were lost to follow-up. The mean age was 49.5 years ± 15.4 (range: 24 to 69). Ethnicity included 2 patients of Chinese descent, 2 patients of East Indian descent, and the remainder Caucasian. Eight patients had comorbidities that included hypertension; however, based on the chart review, the most common cause of ESRD was IgA nephropathy in 4 patients

and hypertension in 3 patients. All patients were on dialysis prior to their commercial renal transplantation with a mean of 24.2 ± 18.3 months. Six patients were on hemodialysis, while 4 patients were on peritoneal dialysis. Of the latter, 3 patients were subsequently placed on hemodialysis prior to transplantation (Table 1).

Six transplants were from living unrelated donors, while 4 patients received deceased donor kidneys. Partial documentation from the transplanting centres was only available for 2 patients. For the remaining patients, there was no information available or the information was limited to the date of transplantation. Details with respect to the induction therapy were available in all 10 patients. The mean post-transplant creatinine on last follow-up was 142.2 ± 54.7 μmol/L (normal 60-110 μmol/L) or 1.6 ± 0.6 mg/dL (normal 0.6-1.2 mg/dL). Five patients were on cyclosporine, mycophenolate mofetil (MMF) and prednisone for induction immunosuppression, while 2 patients were on tacrolimus, MMF and prednisone. The remaining 3 patients were on either methylprednisolone, methylprednisolone and basiliximab, or cyclosporine, rapamycin, prednisone and anti-thymocyte globulin. The countries to which the patients travelled to receive their renal transplants are listed in Table 2.

Complications after transplantation were predominantly infectious, although surgical complications were also frequently noted (Table 3). Three patients had extended spectrum beta-lactamase (ESBL) organisms; one of which had recurrent urinary tract infections, while another developed an ESBL *Klebsiella septicemia* in addition to cytomegalovirus colitis. Two other patients also presented with Klebsiella infections; patient 4 had a Klebsiella peritonitis and patient 10 had a Klebsiella urinary tract infection and pneumonia.

Table 1. Descriptive statistics

Mean age	**49.5 ± 15.4 years**
Etiology of renal failure	
IgA nephropathy	4
Hypertension	3
Henoch-Schönlein purpura	2
Focal segmental glomerulosclerosis	1
Dialysis	
Hemodialysis	6
Peritoneal dialysis	4 (3 patients subsequently went on hemodialysis
Mean time on dialysis	24.2 ± 18.3 months
Type of renal transplant	
Deceased donor	4
Living unrelated	6
Mean length of follow-up	29.8 ± 26.8 months
Mean post-transplant creatinine	142.2 ± 54.7 μmol/L
Most common immunosuppression regimen	Cyclosporine, mycophenolate mofetil, prednisone

Patient 2 had a postoperative urine leak and required a percutaneous drain while in Pakistan. The patient subsequently underwent a ureteral re-implantation secondary to ureteral necrosis. When the patient arrived at our centre, he had a percutaneous drain and a large urinoma infected with Candida. The infection progressed to a pyelonephritis and septicemia. Despite a transplant nephrectomy, the patient died secondary to Candidal sepsis.

Hepatitis C infection was contracted by patient 8 who was known to be seronegative prior to transplantation. Surgical complications included a urinoma in one patient and a perinephric hematoma in another. One patient also had hydronephrosis secondary to a retained ureteral stent. Interestingly, 3 patients had delayed graft function and 2 of these patients received their allografts from live donors. Acute rejection was documented in 2 patients. Two grafts failed and one was the result of a recurrence of IgA nephropathy. Only one patient had an uncomplicated postoperative course.

Overall patient survival in this small series was 90% and the graft survival at 1 year and beyond 2 years is 90% and 80%, respectively. Based on data from the Canadian Organ Replacement Register (CORR) from 2001 to 2007 for our centre, graft survival and patient survival rates were 98% and 100%, respectively. Documentation of the transplantation procedure, donor information, patient progress and medication doses, when available, were highly variable. In most instances, no information was provided by the transplant centre. When contact information was available, attempts were made to contact the transplant centre directly. This was successful only in one case.

Discussion

In the present series, despite small numbers, when we compared all transplants performed at our centre over the same period to the ones performed overseas, both graft and patient survival rates were lower, although statistical analysis was not performed due to small numbers. Both surgical and infectious complications were substantial; however, there was a significantly higher incidence overseas compared to transplants performed at our centre.

Transplantation is the best treatment of choice for most people with ESRD. The longer a patient is on dialysis prior to transplantation, the poorer the outcome after transplantation. For a healthy person, the risk of donating a kidney is

Table 2. Countries where renal transplants were performed

China	4
Pakistan	3
India	1
Mexico	1
Phillipines	1

Table 3. Postoperative course

Patient	Postoperative course
1	ESBL urinary tract infection
2	DGF; urinoma with Candidal urinary tract infection; transplant nephrectomy, died of candidal septicemia
3	DGF; CMV colitis; ESBL Klebsiella septicemia
4	DGF; recurrence of IgA nephropathy; perinephric hematoma; Klebsiella peritonitis; transplant failed within 1 year
5	Hydronephrosis from retained ureteral stent, acute rejection
6	Acute rejection
7	Recurrent ESBL urinary tract infection
8	Hepatitis C infection
9	No significant complications
10	Klebsiella UTI and pneumonia

ESBL: extended spectrum beta-lactamase DGF: delayed graft function; UTI: urinary tract infection.

very low and kidneys from living donors provide excellent outcomes for recipients.[2,3,24-27] The major obstacle in achieving this goal is the shortage of cadaveric organs compared to the increasing number of patients awaiting renal transplantation. The types of donors include cadaveric, living-related and living-unrelated donors. The practice of living-unrelated renal transplantation has always been overshadowed by the medical and ethical concerns.

There have been a handful of papers reviewing the outcome of more than 100 cases of commercial transplantation (Table 4). Surgical complications following commercial transplantations have been described as the major cause of morbidity and mortality in both the early and late post-transplant periods.[8-14,15,17,20,28-30] Consistent with those reports, our current series shows that the rate of surgical complications was quite high. Chugh and Jha reported that it is likely that some of these living-unrelated donor transplantations are performed by questionably qualified physicians in mushrooming private back-street clinics with minimal sanitary facilities.[20,29,30]

It has been reported that commercial living-unrelated transplantations in the Third World have higher rates of serious post-transplantation complications, morbidity and mortality.[1,8-17,28,30] Over half of all renal transplant recipients in tropical countries develop serious infection at some point in the post-transplant period and 20% to 40% of them succumb to these infections.[1,30,31] A multitude of factors (i.e., unhygienic condition, hot and humid climate, scanty diagnostic techniques) contribute to the dismal outcome.

In other series, despite patients travelling to large transplant centres where transplants are performed daily, the medical and surgical complications were excessive; this has yet to be clarified.[32] Beyond the possibility of poor hygiene, other factors may play a contributory role, such as poor donor health, poor immunosuppression monitoring, poor post-transplant hygiene and delayed recognition.

There are contradictory reports regarding the final outcome of the patients with commercial transplantations with unfavourable and favourable results.[1] Favorable outcomes have been reported in several international series, including the largest series that compared graft and patient survival with controls transplanted at home. In 2000, Morad and colleagues reported on Malaysian patients (n = 515) transplanted in India and China, and found a >90% graft and patient survival. Comparing the 258 patients who received their kidneys from living donors, the infectious complications, patient and graft survival were similar between the two groups.[16] It is important to note that the study analysis only included patients who returned from their commercial renal transplantations and not all the patients who left.

Another report from 1997 of Saudi Arabian patients (n = 540) who travelled to India for commercial renal transplantation between 1978 and 1993 showed a graft survival rate of 96% and patient survival rates of 95%, 91%, and 91% at 1-, 3-, and 5-years, respectively; these rates are similar to those achieved in patients transplanted in Saudi Arabia. However, there was a higher HIV and HBV infection rate in the cohort that was transplanted in India.[10]

There are two contemporary, yet smaller series, which have also reported favourable outcomes from commercial renal transplantations. The series by Sun and colleagues from Taiwan reported a cohort of 31 patients who travelled to China to receive commercial cadaveric renal transplants.[6] Their outcomes were compared to 44 patients who received non-commercial cadaveric renal transplants (n = 34) or living-related transplants (n= 10) in Taiwan during the same period. Both graft and patient survival rates were similar between groups at 1-, 3-, 5-, 8- and 10-year follow-ups. Furthermore, infectious complications were also comparable between the groups.[6]

This is in contrast to more recent smaller studies that found poorer graft and patient survival. A study by Sever and colleagues showed the mid-term outcome of 115 patients who received commercial renal transplantations in various countries (mostly in India, but also Iran and Iraq).[8] The mean follow-up period was 65 months; there were 121 major complications that required hospitalization. Among the medical complications, remarkably, unconventional infections were observed in 15 recipients (10 malaria, 3 aspergillosis, 2 mucomycosis). Graft and patient survival rates at 7 years were found to be 53 and 74%, respectively, for the commercial transplantations, while corresponding figures were 73 and 80% for the living related transplantations performed at their centre. They concluded that although mid-term graft survival is worse, patient survival was comparable with that of conventional living-related transplantation. It is important to note that in the commercial transplantation group, the perioperative morbidity and mortality were unknown, a large number of patients were lost to follow-up (who prob-

ably either lost their grafts or died) and long-term results might not be as favourable because potentially fatal diseases, such as chronic hepatitis B and C.

Salahudeen and colleagues reported the outcomes of 131 patients from the United Arab Emirates and Oman who received their commercial renal transplantations in India.[14] In their cohort, infections were the major cause of death in 56% of patients. Eight patients died in the perioperative period, another 8 died within the first 3 months and 8 more patients died within a year, with a patient survival rate of only 81.5% at 1 year. A total of 5 patients became HIV positive and 1 died within 3 months of transplantation. Other infectious complications causing death in this series included fungemia, pneumonia, sepsis, tuberculosis and viral hepatitis.

In another series from Australia, the authors also highlighted some major concerns about overseas commercial transplantation.[14] They noted in their case series of 16 patients a high early postoperative mortality rate. The 1-year patient survival rate of overseas commercial renal transplants is between 80% and 96%, compared with greater than 95% for Australian living-related transplantations. In their series, although the early survival rate was good, 2 patients died 1 year after their transplant and the 5-year patient survival rate was 60%. This is a marked survival disadvantage compared to the 5-year survival rate of 82% or greater in the Australian deceased donor transplantation group. Notably in this study, there was a high incidence of infectious complications as well. Two patients contracted hepatitis B from which they later died. Further, 3 patients were admitted to hospital with serious cytomegalovirus infections. Another patient returned from Lebanon with an aspergillus infection of the kidney allograft and required a transplant nephrectomy. This patient was also infected with multi-drug resistant *Pseudomonas aeruginosa*.

The series most equivalent is Prasad and colleagues from Toronto, Ontario, Canada.[13] In this series, the authors describe the clinical outcomes of 20 patients who underwent non-biological non-emotional related renal transplants abroad from 1998 to 2005. Comparing this group to recipients of living-related or emotionally-related renal transplants at their centre in the same period, they reported a significantly worse patient and graft survival 3 years post-transplantation in those who received their transplants abroad. Furthermore, 11 patients (52%) had serious post-transplantation infections, all of which were opportunistic. Five patients (23%) were found to have cytomegalovirus viral syndrome or tissue invasive disease. Eight patients (38%) had pyelonephritis and 4 of these from multi-drug resistant *Escherichia coli*. Active tuberculosis was diagnosed in 3 patients (14%) and 4 patients (19%) experienced disseminated aspergillosis. Two patients died from fungal infection related sepsis.

The findings in our cohort have highlighted some important issues; however, there are some limitations to our study. With the small numbers, the lack of control group comparisons and the case series design, it is difficult to draw any robust conclusions. Despite this, the outcome of our cohort is similar to others reported in literature and more importantly to contemporary series from this part of the world. Beyond the ethically founded concerns involved in commercial renal transplantation, the practice itself still cannot be considered safe and without significant risk. As previously highlighted, the risk in morbidity and mortality are considerable in most studies and the high rates of infections, many unconventional and opportunistic, the most alarming. Moreover, in its current form, the problems are often compounded by the paucity of communication and documentation between the transplant centre and the centre performing the post-transplant care. Our experience has been similar to that reported by others.

Educating patients who are considering commercial renal transplantation about the heightened morbidity, mortality, and lower graft survival rates may be beneficial. In the series by Prasad and colleagues, 95% of their cohort who sought commercial renal transplants were not Canadian-born and not Caucasian. In our series, 40% of the patients were not Caucasian.[13] In general, Asian patients tend to wait longer on deceased donor transplant lists because of blood groups and tissue types. Identifying and educating these patients who are at risk for seeking out commercial renal transplantation abroad would be valuable.

One certainly cannot deny the existence of the rapidly expanding market of commercial organ trading. It is estimated that 5% to 10% of kidney transplants performed annually around the globe are currently via organ trade.[32] In Canada, like other Western countries, cadaveric organ donations have reached a plateau that is far from coping with the demand. As such commercial renal transplantation is and will continue to be an ongoing entity; consequently, physicians will be more frequently faced with the challenges of managing the complications.

From a more provocative perspective, one controversial solution to uncontrolled commercial renal transplantation is perhaps through legislative regulations. A controversial editorial in the *British Medical Journal* in 2002 suggested legislation to regulate the purchase of organs for transplantation.[33] This was roundly rejected with abhorrence by the court of public opinion. Nevertheless, controlled regulation of commercial transplantation by the government is a provocative solution to the problems outlined in this paper and, at the very least, warrants further dialogue.

Conclusion

We describe our single institution experience with commercial transplantation and the higher risks associated with these transplants. Patients on the waiting list for deceased

donor transplant considering commercial transplantation abroad should be made aware of the potential pitfalls of this risky venture.

Competing interests: None declared.

This paper has been peer-reviewed.

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