Commercial kidney transplantation is an important risk factor in long-term kidney allograft survival

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Transplant tourism, a form of transplant commercialization, has resulted in serious short-term adverse outcomes that explain reduced short-term kidney allograft survival. However, the nature of longer-term outcomes in commercial kidney transplant recipients is less clear. To study this further, we identified 69 Canadian commercial transplant recipients of 72 kidney allografts transplanted during 1998 to 2013 who reported to our transplant center for follow-up care. Their outcomes to 8 years post-transplant were compared with 702 domestic living donor and 827 deceased donor transplant recipients during this period using Kaplan-Meier survival plots and multivariate Cox regression analysis. Among many complications, notable specific events included hepatitis B or C seroconversion (7 patients), active hepatitis and/or fulminant hepatic failure (4 patients), pulmonary tuberculosis (2 patients), and a type A dissecting aortic aneurysm. Commercial transplantation was independently associated with significantly reduced death-censored kidney allograft survival (hazard ratio 3.69, 95% confidence interval 1.88–7.25) along with significantly delayed graft function and eGFR 30 ml/min/1.73 m^2 or less at 3 months post-transplant. Thus, commercial transplantation represents an important risk factor for long-term kidney allograft loss. Concerted arguments and efforts using adverse recipient outcomes among the main premises are still required in order to eradicate transplant commercialization.

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Transplant tourism and organ trafficking are widely condemned.[1–3] One reason for this condemnation is that these have resulted in serious adverse outcomes for kidney recipients, as compiled in many reports.[4,5] The most common adverse outcomes reported from North America, for example, include short-term recipient complications such as urine leaks, a variety of infections, hospitalization, and typically reduced short- to medium-term kidney allograft survival compared with that of domestic allografts.[6–8] Early complications and allograft function are conceptually linked: reduced allograft survival in this instance is attributed mainly to these early post-transplant events. Continuing to report commercial transplant occurrences in the medical and ethics literature will remain important. However, as the literature on transplant tourism evolves and transplant centers gather more experience in the post-transplant care of commercial transplant recipients, using data derived from older reports of poor recipient outcomes as the main recipient-oriented premise for dissuading potential transplant tourists worldwide from obtaining commercial organs can be subject to challenge.[9] Furthermore, the nature of longer-term recipient outcomes, the relationship of these outcomes to kidney allograft survival, and the underlying reasons for any outcome disparities between commercial and domestic transplant recipients might be distinct from those of shorter-term outcomes. Such outcomes have not been critically assessed and may even have implications for future discussions about aspects of transplant commercialization apart from tourism.

RESULTS

A total of 69 commercial transplant recipients received 72 allografts between 1 January 1998 and 31 December 2013 from various countries in Asia, Africa, Europe, and South America, with 3 patients each receiving a second allograft, corresponding to an average rate of 4 to 5 transplants/year. Among these 69 patients were 20 who received 22 allografts received before 28 February 2005 (3 transplants/year) and whose survival to 3 years post-transplant has been reported previously.[6] After this period, there were 49 recipients who received 50 allografts between 1 March 2005 and 31 December 2013, corresponding to a rate of 5 to 6 transplants/year. During the overall 1998 to 2013 study period, there were correspondingly 827 deceased donor and 702 living donor kidney transplants performed at our center and for which data were available. Thirty-four of 69 commercial transplant

recipients (50%) presented for pretransplant assessment in Canada; panel reactive antibody titers, which are typically obtained just prior to placement on the Canadian waiting list, were available for only 5 (panel reactive antibody range 8%–100%), in contrast to availability for all domestic recipients (panel reactive antibody range 0%–100%). Pretransplant wait time was 48.6 ± 37 months (range 0.9–166) for domestic recipients and 28.4 ± 34 months (range 3–192) for commercial transplant recipients. There were no explicitly stated reasons (e.g., wait time, sensitization, or rare blood group) for decisions to obtain a commercial allograft. Only 1 commercial transplant recipient before 2005 and none afterward were Canadian-born. Most patients presented with prescriptions for tacrolimus, mycophenolate mofetil or enteric-coated mycophenolate sodium, and prednisone that were provided by their transplant center. Table 1 provides summary demographic information as well as clinical information at 3 months post-transplant for the 1998 to 2013 population. Donor and cross-match information was sparse and considered unreliable. Recipients were mostly unable to describe the donor selection process.

Specific post-transplant complications seen in the early cohort (1998–2005, $n = 22$) have been reported previously,[6] but they included primary graft nonfunction, fungal sepsis, cerebrospinal abscess, wound infection, malignancy, and urine leaks. There was decreased overall allograft and patient survival to 3 years. Similar to these earlier commercial transplant recipients, the 2005 to 2013 recipients ($n = 49$) who received 50 renal allografts were ignorant of the donor selection process. Of these 50 transplant procedures, 27 were performed in South Asia, 13 in East Asia, 5 in Africa, 4 in West Asia, and 1 in South America. Medical documentation remained often incomplete, and translation was sometimes needed. Notable infectious complications (2005–2013) included hepatitis B seroconversion ($n = 2$), hepatitis C seroconversion ($n = 5$) with active hepatitis ($n = 3$) and fulminant hepatic failure ($n = 1$), pulmonary tuberculosis ($n = 2$), and extended spectrum beta-lactamase *Escherichia coli* urosepsis ($n = 1$). Surgical complications included 2 abdominal wall hernias and a type A dissecting aortic aneurysm occurring 2 months post-transplant. Only 1 patient in the 2005 to 2013 cohort required hospitalization on arrival, compared with 7 in the earlier cohort.[6]

Kidney allograft survival to 8 years for the 3 groups of patients (domestic living donor allograft recipients, domestic deceased donor allograft recipients, and commercial allograft recipients) is shown in Figure 1, whereas the corresponding death-censored allograft survival is shown in Figure 2. In both

Table 1 | Demographic and clinical characteristics of domestic and commercial kidney transplant recipients at St. Michael's Hospital, 1998 to 2013

Parameter	Living donor domestic transplants (1) $n = 702$	Deceased donor domestic transplants (2) $n = 827$	Commercial transplants (3) $n = 72$	*P* value (1 vs. 2)	*P* value (1&2 vs. 3)
Demographics					
Age at transplant (yr)	45.4 ± 13.2 (16–76)	53.2 ± 12.3 (18–78)	48.4 ± 14.4 (16–77)	<0.0001	0.46
Sex (male [%]/female [%])	431 (61)/271 (39)	509 (62)/318 (38)	49 (68)/23 (32)	0.95	0.26
No. of transplants 1/2/3 (*n* [%])	668 (95)/32 (4)/2 (0.2)	775 (93)/51 (6)/1(0.1%)	65 (90)/7 (10)/0 (0)	0.28	0.28
Race/ethnicity (*n* [%])					
Caucasian	497 (71)	384 (46)	13 (18)	<0.0001	<0.0001
Black	38 (5)	113 (14)	7 (10)	<0.0001	0.96
East Asian	68 (10)	158 (19)	20 (27)	<0.0001	<0.01
South Asian	77 (11)	138 (17)	32 (45)	<0.01	<0.0001
Native American	6 (1)	1 (0.1)	0 (0)	0.03	0.72
Other/unknown	16 (2)	33 (4)	0 (0)	0.36	0.20
Cause of end-stage renal disease (*n* [%])					
Diabetes	104 (15)	137 (16)	17 (24)	0.34	0.07
Hypertension	53 (7)	108 (13)	9 (12)	<0.01	0.59
Glomerulonephritis	305 (44)	323 (40)	30 (42)	0.08	0.92
Polycystic kidney disease	104 (15)	81 (9)	6 (8)	<0.01	0.33
Interstitial nephritis	44 (6)	41 (5)	2 (3)	0.26	0.30
Obstructive uropathy	29 (4)	31 (4)	0 (0)	0.70	0.05
Others/unknown	61 (9)	106 (13)	8 (11)	0.06	0.81
Clinical parameters at 3 months					
Body mass index (kg/m^2)	26.6 ± 5 (20–46)	25.0 ± 5 (20–46)	25.1 ± 6 (14–41)	<0.0001	0.16
Serum creatinine (μmol/l)	131 ± 79 (43–1102)	136 ± 85 (40–769)	141 ± 80 (61–395)	0.22	0.80
eGFR (ml/min/1.73 m^2)	59 ± 22 (5–150)	56 ± 23 (6–150)	56 ± 23 (12–100)	0.07	0.34
Delayed graft function (%)	6	14	10	<0.0001	0.82
Acute rejection (%)	10	14	17	<0.01	0.25
Blood pressure (mm Hg)	128 ± 15/79 ± 9 (82–177/60–107)	130 ± 17/78 ± 10 (85–180/52–110)	127 ± 17/79 ± 9 (100–210/60–102)	<0.01	0.21
Total cholesterol (fasting, mmol/l)	4.8 ± 1 (1.9–9.9)	4.7 ± 1 (1.7–9.1)	4.9 ± 1 (2.1–7.4)	0.94	0.10
Blood glucose (fasting, mmol/l)	6.3 ± 2 (2–22)	6.6 ± 3 (3–37)	6.2 ± 2 (3–14)	0.01	0.54
Major adverse cardiac events (*n*, %)	84 (13)	169 (20)	24 (17)	<0.0001	0.11

eGFR, estimated glomerular filtration rate, by the Modification of Diet in Renal Diseases (MDRD)-7 equation. Values are mean ±SD (range) unless otherwise indicated.