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Navigating risks: insights on unrelated overseas renal transplantations from two Saudi centers

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Abstract

Background Due to a shortage of cadaveric organs for transplantation, some Saudi patients seek to purchase kidneys in other countries. However, kidney transplantation (KT) abroad is often associated with negative outcomes. This study shared the experiences of two Saudi transplantation centers regarding unrelated KT overseas.

Methods This retrospective comparative cohort study included patients who underwent commercial KT abroad (Group I) and local patients who received living unrelated KT between September 2017 and July 2024, with available follow-up for at least one year. The primary outcome was to compare the perioperative outcomes. The secondary outcome was to compare the cumulative graft survival between both groups using cox-regression analysis.

Results Group I included 96 patients and group II included 108 patients. Group I had a statistically significant longer 30-day hospital stay (9.4 ± 1.6 vs. 7.9 ± 1 days, $P < 0.001$). Primary functioning graft was significantly lower in Group I (83.3% vs. 93.5%; $p = 0.01$). Group I was associated with statistically significant higher incidence of surgical site infection (SSI) ($P = 0.03$), lymphocele ($P = 0.007$) and UTI ($P = 0.002$). The 1-, 2-, 3-, and 5-year cumulative graft survivals were 80%, 79%, 74%, and 54%, respectively in group I compared to 98%, 97%, 90%, and 60%, respectively in group II. [HR = 2, 95% CI = 1.1–3.8, $P = 0.02$]

Conclusion Commercial transplantation graft survival rates are lower, and overall outcomes are worse than those of traditional unrelated transplantation in the midterm. Educating patients about the risks associated with overseas KT and promoting public registration for deceased organ donation could help mitigate this practice.

Clinical trial number Not applicable.

Keywords Overseas kidney transplantation, Commercial kidney transplantation, Unrelated living donor transplant, Graft survival

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Introduction

The global burden of kidney failure is increasing. Kidney transplantation (KT) remains the preferred treatment for end-stage renal disease (ESRD) [1]. However, waiting times for KT continue to increase despite ongoing efforts to enhance the supply of deceased and living donor organs. Consequently, many patients, despite ethical concerns, are turning to the option of commercial living KT [2–5]. Most countries currently allowing commercial KT are in the developing world, including Brazil, China, Egypt, India, Iraq, Pakistan, the Philippines, Romania, Russia, South Africa, Turkey, and Venezuela [6]. Concerns have been raised about the medical safety of KT abroad, highlighting issues such as lower graft survival rates, increased infection rates, and inadequate communication between transplant centers and follow-up facilities [3].

Conflicting data concerning the outcomes and complications associated with living-unrelated KT has been published [3–7]. Data from the Far East showed no significant differences in graft survival and perioperative complications between commercial and non-commercial KT. Meanwhile, Western countries' data showed statistically significantly lower patient and graft survival rates and higher infection and complication rates among the commercial KT groups [3]. Recent data, including Saudi patients with overseas commercial KT, showed a significantly higher rejection rate in patients transplanted overseas (OR = 5.4, $p < 0.001$) [5].

In the current study, we aimed at exploring the outcomes of commercial KT and compare it to the local unrelated KT at two Saudi transplantation centers.

Methods

This retrospective cohort study was conducted at two Saudi transplantation centers (AFHSR and KSAFH). The study included all patients who underwent live unrelated KT abroad, attended for follow-up at both centers between September 2017 and July 2023 and were followed up for at least one year. Patients with no data regarding the transplantation process (countries, date of surgery, type of donor, immunosuppression medications) or with no available follow-up data were excluded from the study. The study was approved by the local ethical committee of both centers (AFHSR: AFHSRMREC/SURGERY, SECTION OF TRANSPLANTATION/746; KSAFH: KSAFH-RET:2024 – 595), informed consent to participate was obtained from all the participants.

Intervention

Recipients in this cohort sought overseas transplants at their own risk without the consent or endorsement of their treating nephrologists. Although our centers do not support transplant tourism, we do not deny access to care for those in need. Most patients arrived within the first week after KT. All patients were evaluated by the transplant team regarding date and place of transplantation, date of catheter and drain removal, their general condition, kidney function, wound status and medications. For all patients, graft Doppler ultrasonography (US) and plain X-ray (KUB) were performed to assess graft perfusion, the presence of any collection, and the presence of JJ stent. Patients were admitted on arrival. Patients were managed based on the availability of medical reports and kidney function. We administered immunosuppression (IS) with ATG or Basiliximab therapy according to the local hospital protocol for patients with impaired graft function and no available report. No induction therapy was given for patients with no report and good kidney function on arrival. Patients were followed until stabilization of their condition and discharged on triple IS maintenance protocol (tacrolimus, mycophenolate mofetil (MMF), and prednisolone) plus cytomegalovirus (CMV) prophylaxis for 3–6 months and Pneumocystis Jirovecii (PCJ) prophylaxis for 6 months.

Data acquisition

A review of records was performed on all transplanted patients from other countries who attended either center for their post-transplant care. We collected the baseline characteristics of the study group **(Group I)**, including age, sex, pre-KT comorbidities, causes of end-stage renal disease (ESRD), hemodialysis duration, and hepatitis status. Transplant data included the donor source, country visited, length of hospital stay, date and location of the transplant, transplant-related variables (such as induction therapy and immunosuppressive agents used, delayed graft function, and kidney function at discharge), and post-KT complications (including post-KT diabetes, rejection episodes, and other medical and surgical complications related to the procedure). A control group **(Group II)** of local unrelated live donors KT, in the same period who underwent surgeries at the same centers, was reviewed for similar data collection.

Measured outcomes

The primary outcome was to compare perioperative outcomes, including graft function, 30-day hospital stay, and 90-day postoperative complications. Graft function included primary functioning graft (PFG), slow graft function (SGF), and delayed graft function (DGF). DGF was defined if the patient reported dialysis in the early postoperative period or required dialysis on arrival at the local hospital. SGF was defined if the patient arrived at the local hospital within the first 5 days post-transplant with serum creatinine (Cr) ≥ 266 mmol (3.0 mg/dL). 30-day hospital stay included initial hospitalization in the local transplant center post-KT and any admission in

the first 30 days. Post-operative complications included rejection episodes, new-onset diabetes, surgical complications, and infections. UTI was considered in the presence of a positive urine culture. CMV infection was diagnosed with suspected clinical manifestations and virus detection by PCR or in the tissue biopsy of the affected organ. BK nephropathy was diagnosed only for patients with deterioration of kidney function with either PCR or graft. The secondary outcome was to compare the graft survival between both groups. Graft survival included those who died with functioning grafts.

Statistical analysis

Continuous data were expressed as mean ± SD or median (IQR) according to the pattern of distribution. Categorical variables were expressed as numbers and percentages. Comparisons between both groups were performed using Chi-square and independent sample T-tests. The survival data was obtained by life tables and comparison was done using cox-regression analysis test. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) Version 29 (IBM, New York, USA).

Table 1 Comparison of demographic criteria of overseas commercial transplanted (Group I) and locally transplanted (Group II) groups

	Group I No = 96	Group II No = 108	*p*-value
Age. *Mean ± SD. Yrs.**	54.3 ± S16.6	48.7 ± 16.2	0.01
Gender**	64 (66.6%)	67 (62%)	0.4
Male	32 (33.3%)	41 (38%)	
Female			
BMI. *Mean ± SD.Kg/m²**	29 ± 3.8	27 ± 4.4	0.001
Cause of renal failure**	21 (21.8%)	26 (24%)	0.4
Diabetes	52 (54.2%)	58 (54%)	
Hypertension	17 (17.8%)	18 (16.5%)	
Both	1 (1%)	4(3.7%)	
Polycystic kidney disease	5 (5.2%)	2(1.8%)	
Others			
Type of Dialysis**	94 (98%)	106 (98%)	0.9
HD	2 (2%)	2 (2%)	
PD			
Duration of dialysis #	3 (2–4)	2 (1–4)	0.9
Median (IQR). Yrs			
Transplantation number**	96(100%)	104(96.3%)	0.1
First transplantation	0	4(3.7%)	
Second transplantation			
Induction Immunosuppression**	60(62.5%)	103 (95.3%)	0.01
Basiliximab	25 (26%)	5 (4.7%)	
ATG	11(11.5%)	0	
Unknown			
30-days hospital stay. *Mean ± SD. Days**	9.4 ± 1.6	7.9 ± 1	< 0.001
Graft Function**	80(83.3%)	101 (93.5%)	0.01
Primary functioning graft (PFG)	6(6.3%)	6(5.6%)	
Slow Graft Function (SGF)	10(10.4%)	1(0.9%)	
Delayed Graft Function (DGF)			
Follow-up duration #	38(14–51)	40 (29–52)	0.8
Median (IQR). Mo			

BMI: body mass index, ATG - anti-thymocyte globulin, HD: hemodialysis, PD: peritoneal dialysis, # Mann-Whitney U test, * Independent sample T-test, ** Chi-square test

Results

The study group (Group I) included 96 patients (64 males) with a mean ± SD age of (54.3 ± 16.6 years). Their first KT took place in Egypt (34), Pakistan (30), China (8), India (10), Jordan (8), and the Philippines (6). Group II included 108 patients (67 males) with ± SD age of 48.7 ± 16.2 years ($p = 0.001$). Demographic criteria of both groups were illustrated in Table 1.

Group I had a statistically significant longer 30-day hospital stay (9.4 ± 1.6 vs. 7.9 ± 1 days) ($P < 0.001$). In Group I, 80(83.3%), 6 (6.3%), and 10 (10.4%) patients had primary functioning graft (PFG), slow graft function (SGF), and delayed graft function (DGF), respectively. Whereas 101 (93.5%), six (5.5%), and one (1%) had PGF, SGF, and DGF, respectively in group II ($P = 0.01$). Seven patients (7.3%) in Group I and two patients (1.8%) in Group II experienced acute rejection episodes ($P = 0.05$). All patients with T-cell mediated rejection (TCMR) received pulse steroids and anti-thymocyte globulin (ATG) at doses of 4–7 mg/kg. Two patients in group I developed combined TCMR and acute antibody-mediated rejection (ABMR) and were managed by ATG at 6–7 mg/kg, pulse steroids, five sessions of plasma exchange, intravenous immunoglobulin at 100 mg/kg after each exchange, and rituximab at 375 mg/m² once weekly for four doses.

In addition, Group I was associated with statistically significant higher incidence of surgical site infection (SSI) ($P = 0.03$), lymphocele ($P = 0.007$) and UTI ($P = 0.002$). In group I, 80.9% of early recurrent UTIs was because of Escherichia coli. Extended-spectrum beta-lactamases (ESBL) and multidrug-resistant organisms (resistant to three or more drugs) were present in 82.4% of the isolates. One patient in group I had urinary leakage who required re-exploration and redo- ureteroneocystostomy (Table 2).

One-year patient survival was significantly lower in Group I (94.8%) than in Group II (100%) ($P = 0.01$). In Group I, nine patients died in the first year, with five deaths due to myocardial infarction, two due to stroke, and two due to viral pneumonia. Four of these patients had a functioning graft at the time of death. The mean ± SD serum creatinine was significantly higher in group I at 1- year [112.6 ± 34.5 vs. 91.7 ± 29.8 mmol/L, $P < 0.001$] and 5-years [142.3 ± 34.5 vs. 111 ± 22.5, $P < 0.001$] of follow up. At the last follow-up, 68 (71%) and 92 (85%) had functioning grafts in groups I and II, respectively. In group I, the 1-, 2-, 3-, and 5-year cumulative graft survivals were 80%, 79%, 74%, and 54%, respectively. In Group II, the 1-, 2-, 3-, and 5-year cumulative

Table 2 90-days postoperative complications in both groups

	Group I	Group II	*P* value
Acute rejection*	7 (7.3%)	2 (1.8%)	0.05
T cell mediated rejection (TCMR)	5	2	
Banff grade IB	3	2	
Banff grade II A	2	0	
Both TCMR and ABMR	2	0	
Infection*	12 (12.5%)	2 (1.8%)	0.002
UTI	3(3.12%)	0	0.1
CMV	2 (2.0%)	1 (0.9%)	0.4
BKV	3(3.12%)	0	0.1
HBV	1(1.04%)	1(0.9%)	0.9
HCV			
New onset diabetes **	13(13.5%)	9 (8.3%)	0.2
Surgical site infection (SSI) *	8 (8.33%)	2 (1.85%)	0.03
Hematoma **	11 (11.45%)	8 (7.4%)	0.3
Lymphocele **	18 (18.75%)	7 (6.48%)	0.007
Incisional Hernia *	3 (3.12%)	1 (0.92%)	0.2
Postoperative urine leak *	1(1%)	0	0.2

*Fischer exact test, ** Chi Square test

graft survival rates were 98%, 97%, 90%, and 60%, respectively. [HR = 2, 95% CI = 1.1–3.8, *P* = 0.02] (Fig. 1).

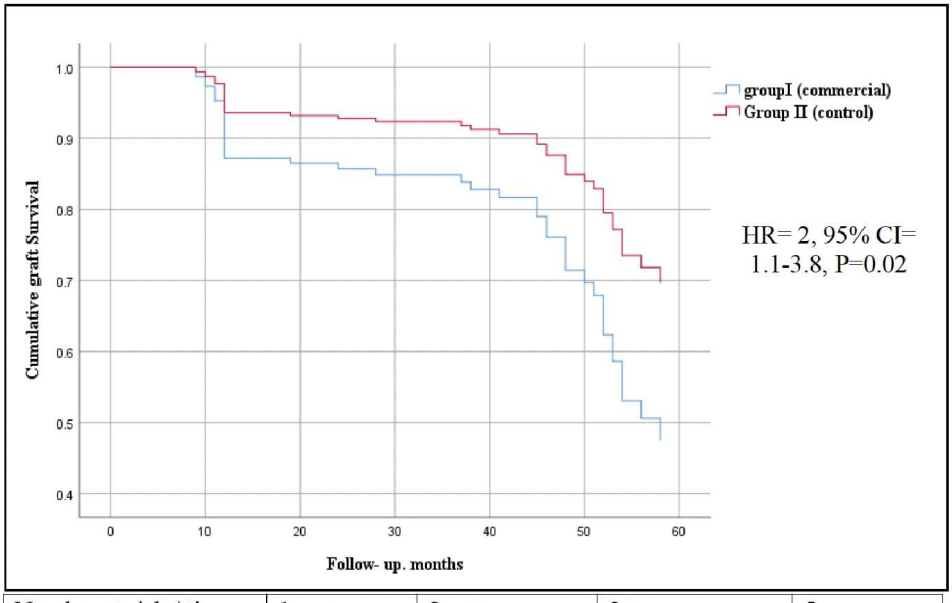
Discussion

The overseas KT is a significant international concern [8]. The primary reason for seeking KT abroad was the lack of available donors. In our study, we observed unfavorable outcomes in the commercial KT group, in the form of higher incidence of surgical complications (SSI and lymphocele) as well recurrent UTI. Moreover, this Group had a higher rate of acute rejection episodes. This could be explained by the inappropriate induction immunotherapy protocol in the form of improper selection according to the patients' immunological risk [5], or the inadequate dose as most of these patients were discharged from the transplant center within 3 days.

Consequently, the 1-year patient survival was significantly lower in commercial KT group compared to the control group and to the reported 1-year survival rate of 98.4% of living KT in Saudi Arabia [9].

There are conflicting reports regarding the outcomes of patients receiving commercial KT, with both unfavorable and favorable results documented [10]. Several international studies have reported favorable outcomes, including one of the most extensive analyses comparing graft and patient survival rates. In 2000, Morad et al. examined Malaysian patients ($n = 515$) who underwent commercial KT from either live of deceased donor and compared them to 258 local live-donor KT. He reported comparable patient and graft outcomes at 1, 3, and 5 [11]. In our study, graft survival and patient outcomes were significantly better in the local transplant group. However, overseas KT may carry additional risks and complications, but it still offers better long-term survival and quality of life than remaining on dialysis.

Recent studies show that commercial KTs often have worse outcomes. For example, sever et al. followed 115 patients who received commercial KTs (mostly from unrelated donors) in countries like India, Iran, and Iraq



Number at risk / time	1-year	2-years	3-years	5-years
Group I (commercial)	84	60	43	9
Group II (control)	101	85	57	6

Difference was calculated using cox-regression analysis.

Fig. 1 Life-table of the cumulative graft survival in both groups

[12]. Alarmingly, 15 patients got unusual infections (malaria, fungal infections), and long-term results were poor: a 7-year graft survival (53% vs. 73% for living-related KTs at their center) and 7-year patient survival (74% vs. 80% for living-related KTs) [12].

While patient survival was similar to other commercial KTs, graft survival was worse [12]. Another study of 16 patients found even higher risks: 1-year survival: 80–96% (much lower than the >95% seen in living-related KTs) and 5-year survival: Just 60% [13]. Moreover, many patients had severe infections (hepatitis B, drug-resistant bacteria, and fungal infections) [13]. Our study, however, did not see these unusual infections in commercial KT patients—possibly due to stricter screening.

Additionally, Sajjad et al. highlighted that some commercial transplant centers may have suboptimal surgical conditions, potentially increasing infection risks. In our study, we observed a significantly higher incidence of surgical site infections ($P=0.03$), lymphocele ($P=0.007$), and urinary tract infections ($P=0.002$) in Group I. While we cannot confirm the specific conditions of the transplant centers where these patients received their organs, the increased infection rate in Group I suggests that factors such as perioperative management, sterility protocols, and post-operative care may have contributed to these outcomes. Meanwhile, donors are mainly from lower socioeconomic groups in developing countries who often need more access to follow-up care. In some instances, these donors may even carry infectious diseases such as tuberculosis, AIDS, and hepatitis [3].

De Souza et al. reported a 1-year infection rate of 42.2%, with UTI being the most common. This finding is consistent with the established view that UTI are the most prevalent infections among patients undergoing KT [14]. Similarly, in our cohort, patients who underwent overseas commercial KT had higher rates of SSI and UTI rates.

The onset of acute rejection significantly reduces long-term graft survival, especially if rejection is not completely reversed [15]. In our study, seven patients who underwent overseas KT experienced graft rejection, whereas only two patients from the local cohort experienced similar issues. Because overseas KT is often commercially motivated, patients at these centers typically experience the shortest postoperative hospital stay and are encouraged to return to their home countries upon discharge which affect the protocol of IS induction [5].

Study limitations

The primary limitations of our study include the small sample size and the fact that it was conducted at two centers. Moreover, the age difference between Group I and Group II patients is a potential confounder of some outcomes, such as infections and length of hospital stay. Furthermore, the observational and retrospective designs with the inherent selection bias, however such studies cannot be performed in a prospective manner. One of the major limitations is the lack of detailed data regarding the induction immunosuppressive (IS) therapy administered to patients in Group I. While we inferred suboptimal induction protocols from the high rejection rates, the absence of precise documentation on IS regimens limits our ability to draw definitive conclusions. Additionally, our study did not quantify the number of patients with very low calcineurin inhibitor (CNI) levels upon arrival. However, our findings suggest that inadequate immunosuppression contributed to poorer outcomes.

Another complicating factor is the multiple locations where the transplants in Group I were performed. The variability in surgical expertise, perioperative management, post-operative care, and local healthcare infrastructure likely influenced the observed outcomes, making direct comparisons between the groups more complex. The unavailability of warm and cold ischemia times for Group I is another limitation, as ischemia time significantly affects transplant outcomes.

Conclusions

Commercial KT is associated with a higher incidence of infections and rejection episodes than locally performed unrelated KT. Further studies are critical for investigating commercial KT's long-term outcomes and identifying the factors that drive this practice.

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Author contributions

H M El Hennawy: protocol development, manuscript writing, manuscript review, and senior author. O Safar: protocol development, manuscript writing, manuscript review. A S Al Faifi: data analysis, manuscript writing. M H El Hennawy: manuscript Review and editing. B Alghamdi: protocol development and data collection. A Ali: protocol development. M Alqahtani: protocol development and manuscript Review. M F Zaitoun: data collection. S A Alasmari: protocol development and data collection. A Serageldeen: data collection and manuscript review. T A. Abouelgreed: data collection and manuscript review. K Fourtounas: data collection and manuscript review. M Ayyad: data collection and manuscript review. A Ali: data collection and manuscript review. M H Zahran: manuscript review, editing, and senior author.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethical approval and consent to participate

The study was approved by the local ethical committees of both centers (AFHSR: AFHSRMREC/SURGERY, SECTION OF TRANSPLANTATION/746; KSAFH: KSAFH-RET:2024 – 595). The committee stated that participation in the questionnaire is considered approval of the participant.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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