

# Paid Living-Unrelated Renal Transplantation Abroad: Too Much Unknown

## *Yurtdışında Akraba Olmayan Canlıdan Yapılan Böbrek Nakli: Birçok Bilinmeyen Var*

### ABSTRACT

**OBJECTIVE:** Despite the unethical characteristic and unfavorable consequences, paid living-unrelated renal transplantation is still considered as an option for end-stage renal disease patients. This study aimed to compare the medical and surgical complications along with allograft functions of PLURT patients with age and gender matched transplant recipients who received a living or deceased donor kidney at our center.

**MATERIAL and METHODS:** End-stage renal disease patients received PLURT (group 1) in a foreign country and age, and gender matched renal transplant recipients that received renal transplantation from living-related donors (LRT patients; group 2) and deceased donors (DDRT patients; group 3) followed between 2003-2010 at our transplantation center were included in the study.

**RESULTS:** There were no significant differences between groups (Group 1&2 and group 1&3) regarding age, sex, urea, creatinine, creatinine clearance, and proteinuria. Data about patients that received renal transplantation from living-related and deceased-donors at our center were sufficient when compared with PLURT patients. PLURT has a negative impact on patients' survival because of surgical and medical problems.

**CONCLUSION:** In the present study, PLURT, LRT and DDRT patients had early and late complications of renal transplantation which were similarly seen in recent studies. The main problem for unfavorable results of PLURT is the commercial aspect of renal transplantation without considering the risks for ESRD patients.

**KEY WORDS:** Transplant tourism, Renal transplantation, ESRD

### ÖZ

**AMAÇ:** Son dönem böbrek yetmezliği bulunan hastalar etik olmamasına ve olumsuz sonuçlara karşın yabancı ülkelerde akraba dışı canlı vericilerden nakil olmaktadır. Çalışmamızın amacı, dış ülkelerde canlıdan böbrek nakli yapılan ve sonrasında merkezimizde izlenen hastalarla merkezimizde canlıdan ve kadavradan yapılan nakil yapılan hastaların böbrek işlevlerini, mortalite ve morbiditeleri karşılaştırmaktır.

**GEREÇ ve YÖNTEMLER:** Yaş, cinsiyet ve diyaliz süreleri uyumlu olan SDBY hastalar, dış merkezlerde canlıdan nakil yapılan hastalar (Grup 1), merkezimizde canlıdan nakil yapılan hastalar (Grup 2) ve yine merkezimizde kadavradan nakil yapılan hastalar (Grup 3) çalışmaya alındı.

**BULGULAR:** Her 3 grup arasında yaş, cinsiyet, kreatinin, kreatinin klirensi ve proteiniüri açısından anlamlı fark yoktu. Grup 2 ve 3'te bulunan hastaların nakil öncesi ve sonrası verileri yeterli iken, grup 1'deki hastalarda birçok bilinmeyen vardı. Grup 3'teki hastaların cerrahi ve medikal komplikasyonlar nedeniyle yaşam süresi kısalmıştı.

**SONUÇ:** Çalışmamızda, her 3 grupta böbrek naklinin erken ve geç komplikasyonları açısından anlamlı fark yoktu. Grup 1'deki hastalarda medikal ve cerrahi komplikasyonlar çok fazla saptandı. Bu durum yurt dışında olguların yeterince değerlendirilmeden nakil yapılmasına bağlıdır.

**ANAHTAR SÖZCÜKLER:** Transplant turizmi, Böbrek nakli, Son dönem böbrek yetersizliği

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## INTRODUCTION

Because of improvements in survival and quality of life compared to dialysis, renal transplantation became the preferred renal replacement therapy in end-stage renal disease (ESRD) patients in both developed and developing countries. Since supplying kidney from deceased and living donors is one of the major problems because of financial, ethical, and social reasons; ESRD patients whose living donors are not suitable for organ donation are forced to search alternative opportunities like paid living-unrelated renal transplantation (PLURT or commercial) especially in third-world countries (1). The ethical aspect of PLURT has been debated by authors for many years (2). Beside the ethical aspect, the complications of PLURT that cause morbidity and mortality have been reported by recent studies (3-4). The declaration about organ trafficking and transplant tourism which was announced by the Steering Committee of the Istanbul Summit suggested that ‘travel for transplantation is the movement of organs, donors, recipients or transplant professionals across jurisdictional borders for transplantation purposes’(5). We aimed to compare the medical and surgical complications along with allograft functions of PLURT patients followed at our center with age and gender matched transplant recipients who received a living (LRT) or deceased donor (DDRT) kidney at our center.

## MATERIAL and METHODS

This is a case control study which was conducted in Selcuk University, Meram School of Medicine (SUMSM). End-stage renal disease patients that received PLURT (group 1) in a foreign country and age, and gender matched renal transplant recipients that received renal transplantation from living-related donors

(group 2) and deceased donors (group 3) followed between 2003-2010 at our transplantation center were included in the study. Paid living-unrelated renal transplant recipients were the citizens of Turkey who resided in Turkey and underwent transplantation in a different country and then returned to Turkey for follow-up care in our transplantation center. Living related and deceased donor renal transplant patients were also the residents of Turkey who underwent transplantation in (SUMSM) Transplantation Center. All of the patients had been living and being dialyzed prior to renal transplantation in Konya, Turkey. Demographic data of recipients, and donors (when available) and details of peri-transplantation period (when available) were obtained from medical discharge reports given to the PLURT patients and charts of LRT and DDRT patients using SUMSM database. Demographic and laboratory data collected from recipient and donor of other groups were used for the study. Based on the patients’ statements, it was recognized that donors were matched according to HLA and ABO blood groups. The local ethics committee approved the study protocol and all patients were included in the study after signing written informed consent forms.

## STATISTICAL ANALYSIS

The statistical analysis was carried out by the Statistical Package for Social Sciences for Windows ver. 15.0 (SPSS Inc., Chicago, IL, USA). Data are expressed as the mean  $\pm$  SD, with a significance level of  $P < 0.05$ . For dichotomous variables, the frequency of positive occurrences were given along with their corresponding percentages. Statistical comparisons of individual groups were based on Student’s t-test for continuous variables whereas the correlations between groups were evaluated by Spearman test.

**Table I:** Demographic and laboratory data of each group.

PARAMETER	Group 1 (n:14)	Group 2 (n:11)	Group 3 (n:10)	Group1 & Group2 P value	Group1 & Group3 P value
Age (year)	50 $\pm$ 12	50 $\pm$ 8	50 $\pm$ 8.5	NS	NS
Gender (M/F)	10/1	10/1	9/1	NS	NS
Urea (mg/dl)	36.9 $\pm$ 5.2	50.2 $\pm$ 10.3	46.2 $\pm$ 14.3	NS	NS
Creatinine (mg/dl)	1.2 $\pm$ 0.5	1.6 $\pm$ 0.85	1.4 $\pm$ 0.8	NS	NS
Sodium (mEq/l)	138 $\pm$ 2.7	138 $\pm$ 2.8	135 $\pm$ 5.7	NS	NS
Potassium (mEq/l)	4.1 $\pm$ 0.7	4.2 $\pm$ 0.6	4.2 $\pm$ 0.4	NS	NS
Calcium (mg/dl)	9.4 $\pm$ 0.7	9.3 $\pm$ 0.7	9.4 $\pm$ 0.9	NS	NS
Phosphorus (mg/dl)	3.2 $\pm$ 0.6	3.0 $\pm$ 0.7	3.0 $\pm$ 0.6	NS	NS
iPTH (pg/ml)	187 $\pm$ 113	203 $\pm$ 78	250 $\pm$ 63	NS	0.014*
Creatinine Clearance (ml/min)	78 $\pm$ 12	69 $\pm$ 12	73 $\pm$ 5	NS	NS
Proteinuria (mg/day)	851 $\pm$ 534	953 $\pm$ 644	522 $\pm$ 247	NS	NS
Hemoglobin (g/dL)	13.3 $\pm$ 1.9	13.8 $\pm$ 2.1	13.7 $\pm$ 2.6	NS	NS

NS: not significant, iPTH: intact PTH

## RESULTS

Demographic and laboratory data of each group are shown in Table I. There were no significant differences between groups (Group 1&2 and group 1&3) regarding age, sex, urea, creatinine, creatinine clearance, proteinuria and hemoglobin levels. Of the 14 PLURT patients, 5 were transplanted in Egypt, 4 in Iraq, 2 in Pakistan, 2 in Russia, and 1 in India. Two of the PLURT recipients had renal transplantation twice in different countries because of loss of the first allograft due to chronic allograft nephropathy (CAN). One of these patients had his first transplantation in Germany in 1984. After 8 years he lost his allograft and underwent re-transplantation in Russia in 1992. He had been followed at our transplantation center for 5 years without rejection. The second patient who had renal transplantation twice had his first transplantation from his own father in England in 1978. After 16 years he also lost his first allograft and underwent re-transplantation in India in 1994. He had been followed in another hospital for 16 years and was admitted to our center in 2010.

Of the 14 PLURT patients, two died; due to donor-originated multiple myeloma (6) in one, and congestive heart failure in one. Medical and surgical complications occurred during the post-transplantation period are shown in Table II.

All of the LRT and DDRT patients had adequate information about induction therapy, had discharge notes and knew their donors. None of the LRT and DDRT patients died after transplantation. Medical and surgical complications of LRT and DDRT patients during follow-up period are shown in Table III.

## DISCUSSION

The main result of the present study was that there were no significant differences between the groups (Group 1&2 and group 1&3) regarding allograft functions including serum creatinine, creatinine clearance and proteinuria. However, two deaths occurred in PLURT group while there were no deaths in LRT and DDRT groups. On the other hand, the finding that hospitalization rates for a myriad of causes were higher in DDRT patients compared to PLURT and LRT was notable.

Unfavorable results about long term graft and patient outcomes of transplant tourism have been addressed in recent studies. They showed that living-unrelated renal transplantation graft and patient survival rates were better than deceased-donor transplantations and also were comparable with those of living-related donor transplantations (7-10). Despite the beneficial results of these studies regarding patient survival and allograft functions, PLURT has a negative impact on patient survival because of surgical and medical problems (4, 11-13). Sever et al. (14) analyzed complications, survival and renal outcomes of 106 commercially transplanted patients. In this study, graft survival rates of PLURT patients at two, five and seven years were found 84, 66, and 52%, respectively, while it was 86, 78,

and 73% for LRT patients performed by their transplantation center (p:0.036). However, survival rates of PLURT patients for the same periods were found to be 90, 80, and 74% while it was 90, 85, 80% for LRT patients, respectively. Another study by Gill et al. (15) reported a comparison of 33 patients with renal transplantation abroad and appropriate matched cohort of patients who underwent transplantation and were followed by University of California Los Angeles. The data of one-year allograft survival was 89% for patients who had transplantation abroad and 98% for the matched UCLA cohort. As a result of this study graft and patient survival did not seem to be significantly worse among PLURT patients, however, transplantation abroad was associated with high rate of acute rejection and increased severity of complications after transplantation (15).

When one looks at the data of our PLURT patients, it is quite apparent that few patients had information about their donors and discharge notes summarizing medical and surgical aspects of pre- and immediate post-transplantation periods. Of 14 PLURT patients, none had information about induction therapy, only 3 of them had a discharge note, and only 5 of them met their donors. A closer look to the discharge notes revealed that none included data about donors, type of induction therapy instituted and details of surgical technique. The data regarding clinical details about donors, induction regimens utilized and surgical technique was of paramount importance to recognize and treat medical and surgical complications, particularly infections, during the peri-transplant period and thereafter. Cytomegalovirus, EBV, and hepatitis serology and cancer screening results of the donors of PLURT patients are important to know given these donors come from the underprivileged and the poor who have high rates of hepatitis carrier state most of the time. Hence, limited access to this essential information may put the newly transplanted patients at risk both in the immediate postoperative period and during the long term. Recent studies concerning transplantation abroad also supported our findings that there was a scant data about donor information regarding general health, age and viral status and pre and post-transplantation period of patients that underwent a transplantation abroad (15-17).

In the present study PLURT, LRT and DDRT patients had early and late complications of renal transplantation which were similar to findings in recent studies (14, 18-19). Compared with 4 PLURT patients, 2 of both DDRT and LRT patients had chronic allograft nephropathy, suggesting that allograft survival would be inferior in the follow-up period in transplant tourism. Nonetheless, there are conflicting results about graft and patient survival in the literature. Canales et al. (16) reported a single graft loss and patient death in their series of PLURT patients. Meanwhile, Prasad et al. (17) also reported decreased graft and patient survival in PLURT patients when compared with living-unrelated donor transplants performed in Toronto. Hospitalization period after renal transplantation of DDRT patients was significantly longer than both LRT

**Table II:** Demographic data and medical and surgical complications of PLURT patients.

Patients	Age	Sex	Country of Transplant	Comorbid Conditions	Induction Therapy	Initial IS	Complications	Presence of discharge Note	Cost of Tx (US Dollars)	Duration of Hospitalization Abroad	Meeting with the Donor
Patient 1	47	M	Egypt	DM	Unknown	Tac+MMF+Cs	Deceased secondary to Donor originated-Multiple Myeloma	No	Unknown	Unknown	No
Patient 2	61	M	Iraq	None	Unknown	Tac+MMF+Cs	None	No	Unknown	Unknown	No
Patient 3	54	M	Pakistan	DM	Unknown	Eve+MMF+Cs	CAN	No	30000	11 days	Yes
Patient 4	33	F	Egypt	HT	Unknown	Cyc+MMF+Cs	Ectopic pregnancy	Yes	Unknown	10 days	No
Patient 5	37	M	Iraq	HT	Unknown	Cyc +MMF+Cs	None	No	Unknown	15 days	No
Patient 6	39	M	Iraq	HT	Unknown	Cyc +MMF+Cs	Bladder carcinoma	Yes	15000	15 days	No
Patient 7	70	M	First Germany Second Russia	Chr Hep B	Unknown	Cyc +MMF+Cs+Aza	CAN Deceased secondary to CVD	No	Unknown	30 days	No
Patient 8	50	M	Egypt	None	Unknown	Siro+MMF+Cs	CAN	Yes	Unknown	4 days	No
Patient 9	50	M	Pakistan	HT	Unknown	Tac+MMF+Cs	None	No	24000	10 day	Yes
Patient 10	51	M	First England Second India	HT Ch Hep B	Unknown	Tac+MMF+Cs	CAN	No	18000	15 days	Yes
Patient 11	31	M	Egypt	HT	Unknown	Tac+MMF+Cs	Acute cellular rejection	No	25000	6 days	No
Patient 12	67	M	Egypt	HT COPD	Unknown	Tac+MMF+Cs	ARF secondary to diarrhea	No	50000	8 days	Yes
Patient 13	56	M	Russia	HT Hep C	Unknown	Tac+MMF+Cs	None	No	20000	28 days	No
Patient 14	49	M	Iraq	DM HT	Unknown	Tac+MMF+Cs	CAN	No	27000	Unknown	Yes

**ARF;** Acute Renal Failure, **Cs:** Corticosteroid, **CAN;** Chronic Allograft Nephropathy, **COPD;** Chronic Obstructive Pulmonary Disease, **CVD;** Cardiovascular Disease, **IS;** Immunosuppression, **Tac;** Tacrolimus, **MMF;** Mycophenolate Mofetil

**Table III:** Demographic data and medical and surgical complications of LRT and DDRT patients.

Patients	Age	Sex	Country of Transplant	Comorbid Conditions	Induction Therapy	Initial IS	Complications	Presence of discharge Note	Cost of Tx	Duration of Hospitalization Abroad	Donor
Patient 1	60	M	Turkey	DM COPD	Basilix+Cs	Tac+Eve +Cs	Pneumonia CHF secondary to MR HVARAF CAN	Yes	None	10 days	LRT
Patient 2	42	M	Turkey	None	Basilix+Cs	Tac+MMF+Cs	Lymphocele	Yes	None	27 days	LRT
Patient 3	43	M	Turkey	None	Basilix+Cs	Tac+MMF+Cs	Aseptic femur necrosis Pulmonary Embolism	Yes	None	7 days	LRT
Patient 4	44	M	Turkey	COPD HT CAD	Basilix+Cs	Siro+MMF+Cs	Cataract Toxic erythema CAN	Yes	None	10 days	LRT
Patient 5	56	M	Turkey	None	Basilix+Cs	Siro+MMF+Cs	Inguinal Hernia Pneumonia	Yes	None	10days	LRT
Patient 6	52	M	Turkey	HT NODAT	Basilix+Cs	Tac+MMF+ Cs	Pneumonia	Yes	None	12days	LRT
Patient 7	57	M	Turkey	DM	ATG+Cs	Cic+MMF+ Cs	Diabetic wound infection and retinopathy Glaucoma Sinusitis Erectile Dysfunction Acute Gastroenteritis Urinary tract infection CAN	Yes	None	15	Deceased Donor
Patient 8	60	F	Turkey	HT	ATG+Cs	Tac+MMF+ Cs	Lymphocele	Yes	None	28	Deceased Donor
Patient 9	46	F	Turkey	HT	ATG+Cs	Tac+MMF+ Cs	Acute cellular rejection ARF secondary to diarrhea Avascular femur necrosis Pyelonephritis Pneumonia CAN	Yes	None	14	Deceased Donor
Patient 9	45	M	Turkey	None	ATG+Cs	Tac+MMF+ Cs	None	Yes	None	5	Deceased Donor
Patient 10	41	M	Turkey	HT	ATG+Cs	Tac+MMF+ Cs	Pneumonia	Yes	None	6	Deceased Donor
Patient 11	54	M	Turkey	HT BPH COPD	ATG+Cs	Tac+MMF+ Cs	Pulmonary aspergilloma Pneumothorax	Yes	None	77	Deceased Donor
Patient 12	46	M	Turkey	HT	ATG+Cs	Tac+MMF+ Cs	Pneumothorax Inguinal Hernia UTI	Yes	None	7	Deceased Donor

**ATG;** Anti-Thymocyte globulin, **Basilix;** Basiliximab, **BPH;** Benign prostate hyperplasia, **CHF;** Chronic Heart Failure, **Cs;** Corticosteroid, **Eve;** Everolimus, **LRT;** Living-related Transplantation, **IS;** Immunosuppression, **Tac;** Tacrolimus, **MMF;** Mycophenolate Mofetil **UTI;** Urinary Tract Infection

and PLURT patients. This may be attributed to surgical and infectious complications secondary to intense induction immunosuppressant with ATG in patients with DDRT. In our study, despite these unfavorable complications there was no difference in terms of graft survival among the groups (group 1 versus group 2 and 3) and patient survival was better in LRT and DDRT patients when compared with PLURT patients. The main complications faced after PLURT probably resulted from unhealthy donors and/or poor hygienic conditions (14, 19-21).

In addition to unfavorable medical and surgical results, PLURT also poses some ethical problems. The Istanbul declaration suggested that 'treatment of patients from outside the country or jurisdiction is only acceptable if it does not undermine a country's ability to provide transplant services for its own population' (5). Given the PLURT is most of the time carried out in developing countries in which waiting times in transplantation are longer than industrialized countries, it seems that fulfilling the stipulation supposed by Istanbul Declaration is very unlikely. Poverty in the PLURT country and organ shortage through legal means in the home country works hand-in-hand here to drive the system. To our opinion, governments of both types of countries should take measures simultaneously to hamper the illegal loop. Crooks et al. (22) discussed patients' experiences about transplantation abroad. They mentioned about the factors that struggle patients to commercial transplantation. One of them was the high cost of the transplantation in the patient's own country. This is not true for our country because the Turkish Social Security system covers all expenses of a transplantation even for the patients who did not have a regular coverage. The second most frequently noted factor was that of waiting times, with the promise of more timely care in other countries potentially drawing them abroad (23-24). At our institution, we do not encourage our patients on the waiting list to go abroad to get a PLURT. However, mainly due to long, especially unknown, waiting times many patients desperately look for ways to get a transplant. And these patients sometimes use the pre-transplant preparation data of our center in a foreign country to get a PLURT against our advice.

According to registry reports of Turkish Society of Nephrology, number of all kind of renal transplants performed in 2008 (total 1209) is still far behind of the developed countries due to low rate of deceased donation in Turkey (25). In order to increase the number of renal transplantation, which is the most convenient renal replacement therapy method with regard to the cost-effectiveness, the collaboration between academia, Ministry of Health of Turkey and the Society of Nephrology should be improved, and an efficient organization such as United Network of Organ Sharing (UNOS) should be built. One additional factor for low transplantation figures is the status of transplantation from living unrelated donors in Turkey. This type of donation has been prohibited until recently due to a series of events took place in a village where many residents sold their

kidneys. Currently, living unrelated donation, including altruistic donation, is subject to the decision of a centrally formed ethical committee approval. The bureaucratic hierarchy may also push the patients to seek organs in illegal or unethical ways.

Despite these unfavorable results, our patients paid too much money (US \$15000-50000) for renal transplantation. Rizvi et al. reported 2500 patients with renal transplantation from Pakistan in 2007. More than half of these recipients were foreigners who paid US\$20.000-30.000. According to data from this review, evaluation of donors was limited to blood group renal function and screening for hepatitis B and C and HIV without any tissue matching, immunosuppressive drug monitoring, renal biopsy and imaging (26). Sever et al. (3) also gave information about donors' financial status after surgery. They reported that donors could never solve any financial problems because of transplant brokers who received most of the money.

The results of our study are limited to small size of each group patients. Furthermore much of the data about PLURT patients were obtained from interviews with patients and relatives. Therefore the findings and results of our study may not be generalized to other transplantation centers in Turkey.

## CONCLUSION

In conclusion; with the help of communication tools like internet, PLURT is a current alternative for ESRD patients which consist of 5-10% of all organ transplantation all over the world (27-28). The main consequence of commercial transplantation is too much unknown about donors and medical and surgical aspects of transplantation that can affect morbidity and mortality of the recipients. Effective measures should be taken by collaboration of the transplant community and government officials to discourage patients undertaking substantial health risks abroad.

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