Comparison of Health Status and Quality of Life of Related Versus Paid Unrelated Living Kidney Donors

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The aim of this cross-sectional study was to assess the health status and quality of life (QOL) of paid unrelated versus related living kidney donors postdonation at Shiraz Transplant Center in Iran. We invited all donors (n = 580, 347 paid unrelated, 233 related) who underwent donor nephrectomy at our center from 2004 to 2010 to participate in a health survey and physical examination. Of 580 donors, 144 consented to participate; participation of paid unrelated donors was significantly lower than related (52/347 vs. 92/233; p < 0.001). Participants underwent a complete physical examination, QOL assessment (using a 36-item short form health survey [SF-36] questionnaire) and laboratory work-up. The paid unrelated donors compared with related donors were younger (34.2 ± 7.2 vs. 40.7 ± 9.7 years, p < 0.001), had shorter time since donation (2.9 ± 1.6 vs. 3.8 ± 2 years, p = 0.004), had higher estimated GFR (72.6 ± 22 vs. 63.8 ± 15.3 mL/min/1.73 m², p = 0.006) and had a higher percentage of patients with microalbuminuria (35% vs. 0%, p < 0.001). Additionally, general health and social functioning scores among paid unrelated donors were significantly lower (p < 0.001 and p = 0.02, respectively) than related donors. Other SF-36 scores, although lower in paid unrelated donors, did not reach statistical significance. Iranian paid unrelated donors have lower QOL and higher incidence of microalbuminuria compared with related donors.

Keywords: Glomerular filtration rate, quality of life, renal insufficiency, tissue donors, proteinuria

Abbreviations: CKD, chronic kidney disease; e-GFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; HROQL, health related quality of life; IPKF, Iranian Patients’ Kidney Foundation; LKDs, living kidney donors; LRKDs, living related kidney donors; PUKD, paid unrelated kidney donors; QOL, quality of life; SF-36, 36-item short form health survey

Received 27 March 2013, revised 16 July 2013 and accepted for publication 21 July 2013

Introduction

Paid unrelated living kidney donation is increasingly becoming a widely debated topic in the transplant community as the gap between the demand and supply of transplantable kidneys widens globally. Although paid donation is practiced in other countries, Iran is the only country in the world that has implemented a regulated paid unrelated living kidney donation program, generally called the Iranian model (1–4). This model has gained worldwide attention because it is a highly controversial solution to the shortage of transplantable kidneys (1–3,5).

The history of kidney transplantation in Iran dates back to 1967 when the first living donor kidney transplantation was performed at Shiraz University (1–4). However, deceased donor kidney transplants were not performed in Iran until year 2000 when legislation of the “Organ Transplantation and Brain Death Act” was passed (1,2). Prior to this, a government regulated and funded unrelated living kidney donation program was established in Iran in 1988 to increase kidney transplantation to compensate for the increasing demand (1,2). The significant increase in the number of kidney transplants and transplant centers that followed the implementation of this program led to an annual paid unrelated kidney transplantation rate of 20.1 per million population in 2000. Considering an annual end-stage renal disease (ESRD) incidence of 49.9 per million population in 2000, implementation of this model resulted in significant reduction of the waiting list in Iran (2). By the end of 2010, 26,982 living donor kidney transplantations (22,662 paid unrelated, 4,320 related) had been performed in Iran (1,2).

All Iranian patients with ESRD irrespective of their age, gender, race, religion or socioeconomic status are classified as “patients with special diseases” and are provided free health insurance by the government. This insurance covers all the costs of hemodialysis, peritoneal dialysis and transplantation surgery. The immunosuppressive drugs are also subsidized by the government and are covered by
the government provided insurance. However, the recipients are responsible for payment to the donors in the case of paid donation (1–4). When a chronic kidney disease (CKD) patient needs renal replacement therapy, a physician describes to the patient all treatment options including transplantation with the emphasis on better results from related donation. However, if the patient does not have a living related kidney donor (LRKД) or does not choose to be on the deceased donor waiting list, a referral is made to the Iranian Patients’ Kidney Foundation (IPKF), a nonprofit organization which coordinates the matching of potential kidney transplant recipients with paid unrelated kidney donors (PUKДs). The organization is run by volunteer CKD patients with branches all over the country (1–4). Recipients and PUKДs are registered free of charge. After informed consent, a potential recipient is introduced to his or her prospective PUKД. Thereafter, both donor and recipient are referred to a transplant nephrologist for complete work-up and final approval for transplant (1–4). All PUKДs and LRKДs are reimbursed by the government, an amount equal to 10,000,000 Iranian Rials (approximately 400 US Dollars), conversion rate by Central Bank of Iran [www.cbi.ir] on July 13, 2013: 24,787 Iranian Rials for 1 US Dollar, with 1 year of government provided free medical insurance. PUKДs, in addition, also receive an extra reimbursement directly from the recipient. The amount of this extra reimbursement is not regulated and fluctuates with inflation; currently, the typical amount is around 100,000,000 Iranian Rials (approximately 4000 US Dollars). This typical amount is usually enough for low-income or unemployed donors to start a small business. In the Iranian model, PUKДs and potential recipients negotiate face to face at an IPKF provided space without involvement of any broker (1–4). If a potential donor demands an unusually higher amount of extra reimbursement compared with the typical amount, the recipient will be introduced to another potential donor by IPKF. Likewise, if a recipient offers an unusually lower amount, the potential donor will be introduced to another recipient by IPKF. However, there are nongovernmental charitable organizations that help the recipients to afford the typical extra reimbursement amount. Therefore, most of the time, the potential donor and recipient reach an agreement on an amount close to the typical range. Thereafter, with approval of a transplant nephrologist, transplantation takes place at one of the designated academic transplant centers (1–4).

Despite significant reduction of the waiting list, there are major ethical concerns about the Iranian model, particularly the effects of donation on the health status and quality of life (QOL) of PUKДs and lack of long-term follow-up for these donors (1–4, 6, 7). Previous studies have shown that a majority of Iranian PUKДs are poor, low-income or unemployed young married men who have experienced major stressful life events in the months preceding donation and financial gain is one of their main motivations for donation (6–8). These donors have also been reported to have lower than normal QOL scores (6, 7). Social stigma associated with selling parts of their body for money is believed to be one of the reasons for the observed poor QOL of PUKДs (6). Moreover, a large proportion of Iranian PUKДs have been shown to be unaware of the possible short- and long-term complications of nephrectomy and the need for regular long-term follow-up after donation (9). Consequently, Iranian PUKДs have been demonstrated to have poor postdonation follow-up (2, 6). On the other hand, LRKДs usually have altruistic motivations for donation and have been reported to enjoy a better QOL after donation (10–13). Moreover, LRKДs have better economic status compared with PUKДs in general and most have their own insurance coverage after the expiration of the government provided, 1-year free medical insurance, while this is not true in most cases of PUKДs. Although there are previous reports from Iran that have evaluated the health status and QOL of Iranian PUKДs compared with the general population (6, 7), to our knowledge, no comparative study between Iranian PUKДs and LRKДs has been performed so far. In this cross-sectional study we aimed to assess the health status and QOL of PUKДs and LRKДs postdonation at Shiraz Transplant Center, a major referral transplant center in the south of Iran.

Materials and Methods

This cross-sectional study was approved by institutional review board of Shiraz University of Medical Sciences and was performed in accordance with the Declaration of Helsinki and Good Clinical Practice Guidelines. At the recruitment phase of the study (September 2011), all living kidney donors (LKДs) who underwent donor nephrectomy at Shiraz Transplant Center from 2004 to 2010 were invited by telephone to participate in a health survey and routine physical examination. The contact information of LKДs who had nephrectomy before 2004 was not available.

After giving written informed consent for participation in the study, each participant provided a medical history and underwent a complete physical examination. Health related QOL (HRQOL) was assessed using a 36-item short form health survey (SF-36), a well-known generic tool for assessing HRQOL that is validated in the Iranian population (14). Laboratory work-up, including complete blood count, renal function panel and evaluation of 24-h urine albumin excretion were also done for all participants. The estimated glomerular filtration rate (eGFR) was calculated using 4-variable modification of diet in renal disease study equation. Microalbuminuria was defined as urinary albumin excretion of 30–300 mg/24 h. As per our center’s protocol, before donation all donors at our center are screened negative for proteinuria defined as urinary protein excretion > 150 mg/24 h.

Statistical analysis was performed using the SPSS 15 (SPSS, Inc., Chicago, IL) statistical software package. Independent sample t-test was used to compare the continuous data between 2 groups; chi-square or Fisher exact tests were used to compare the categorical data. p < 0.05 was considered statistically significant.

Results

The flow diagram of the study is demonstrated in Figure 1. As shown, out of 580 LKДs with available contact information who were invited to participate in this study,
participation of PUKDs was significantly lower than LRKDs (52/347 [15%] vs. 92/233 [39%]; p < 0.001). Among the LKDs who responded to the invitation (n=259), participation of PUKDs was again significantly lower than LRKDs (52/128 [41%] vs. 92/131 [70%]; p < 0.001).

The relationship of 92 LRKDs to the recipients was as follows: 32 (35%) siblings, 22 (24%) parents, 20 (22%) partners, 11 (12%) children and 7 (8%) aunts or uncles. PUKDs had no relationship with the recipients.

As demonstrated in Table 1, at the time of follow-up, the PUKDs as compared with the LRKDs were younger (34.2 ± 7.2 vs. 40.7 ± 9.7 years, p < 0.001), had a higher percentage of males (81% vs. 35%, p < 0.001), had a shorter follow-up time since donation (2.9 ± 1.6 vs. 3.8 ± 2 years, p = 0.004), had higher e-GFR (72.6 ± 22 vs. 63.8 ± 15.3 mL/min/1.73 m², p = 0.006), had lower serum albumin levels (4.25 ± 0.66 vs. 4.53 ± 0.38 g/dL, p = 0.007) and had a higher percentage of patients with microalbuminuria (35% vs. 0%, p < 0.001). Additionally, general
the need for regular follow-up postdonation have been suggested as the major reasons for lack of long-term follow-up among PUKDs (2,6,9). Educating the LKDs, providing an extended long-term government sponsored medical insurance program beyond 1 year, and probably even payment for clinic visits could enhance their adherence with postdonation follow-up.

The goal of health care today is not only to cure the physical illnesses but also to improve the patients’ QOL (13). Items evaluated by QOL assessment tools are indicators of patients’ well-being and have been demonstrated to correlate with clinical endpoints like survival (15,16). Therefore, QOL scores have been suggested to be considered as surrogate clinical endpoints themselves (15,16). Previous studies from developed countries have shown that altruistic LKDs have normal or even better than normal QOL scores after donation (10–13). In contrast, PUKDs in Iran have been reported to have lower QOL scores compared with the general population (6,7). A direct comparison of PUKDs with LKDs in our study confirms the lower HRQOL scores of the former compared with the latter, postdonation. The above results warrant careful mental and psychological assessment of PUKDs predonation. Unfortunately, none of the previous studies including ours have assessed the QOL scores of LKDs predonation.

Future studies are needed to assess the full impact of donation on the QOL scores of PUKDs as well as to evaluate the correlation of QOL scores with clinical outcomes like survival in this population.

In our study, on follow-up, PUKDs had significantly higher e-GFR compared with LKDs, a finding likely explained by the younger age of the PUKDs. However, 35% of PUKDs were observed to have microalbuminuria, whereas none of the LKDs had microalbuminuria despite a longer follow-up. In a previous report from Iran, the prevalence of microalbuminuria was 10.4% in a group of LKDs consisting mostly of PUKDs at a shorter follow-up of a mean 17.2 ± 5 months postdonation (17). On the contrary, the prevalence of microalbuminuria in altruistic LKDs from the United States was reported to be 12.7% at a mean 12.2 ± 9.2 years postdonation in a study by Ibrahim et al (12). In a meta-analysis by Garg et al (18), the pooled incidence of proteinuria in 4793 LKDs at an average of 7 years (range 2–25 years) postdonation was 12% (95% confidence interval: 8–16%). Whether the observed higher prevalence of microalbuminuria within a shorter time period postdonation puts Iranian PUKDs at a higher risk of developing CKD should be evaluated in future studies with long-term follow-ups. Based on our observations, it is advisable to follow the Iranian PUKDs at regular follow-up visits for development of proteinuria postdonation.

Our study has several limitations including a cross-sectional design and short follow-up of donors. Despite our best efforts, we were able to enroll only a small proportion of total LKDs in our study. The baseline demographic and health and social functioning scores among PUKDs were significantly lower compared with LKDs (44.8 ± 7.1 vs. 49.5 ± 6.5, p < 0.001 and 43.2 ± 10.2 vs. 47.2 ± 9.8, p = 0.02, respectively). Other SF-36 scores, although lower in PUKDs, did not reach statistical significance.

**Discussion**

To our knowledge, this is the first study comparing the health status and HRQOL of Iranian PUKDs with those of LKDs. Our results show that Iranian PUKDs, compared with LKDs, have poor follow-up, lower HRQOL scores and higher incidence of microalbuminuria.

One of the major drawbacks of the Iranian model of living donor kidney transplantation is the lack of long-term follow-up of LKDs (2,3). In our study, the rate of participation of PUKDs was significantly lower than LKDs. Similarly, in a previous report from Iran, only 6 of 500 LKDs who were invited to participate in a health survey responded (2). In another Iranian study, a majority (79%) of PUKDs were reported to have no regular follow-up after donation (6). Inability to pay for follow-up visits, and insufficient knowledge of the complications of the nephrectomy and

| Table 1: Clinical characteristics and SF-36 scores of PUKDs and LKDs on follow-up |
|-----------------|-----------------|-----------------|
| Donors’ characteristic | PUKDs (n = 52) | LKDs (n = 92) | p-Value |
| Age (years) | 34.2 ± 7.2 | 40.7 ± 9.7 | <0.001 |
| Time since donation (years) | 2.9 ± 1.6 | 3.8 ± 2 | 0.004 |
| Gender (male) | 42 (81) | 32 (35) | <0.001 |
| BMI (kg/m²) | 24.9 ± 3.1 | 25.6 ± 3.5 | 0.207 |
| Systolic BP (mmHg) | 115.6 ± 10.9 | 116.4 ± 11.4 | 0.666 |
| Diastolic BP (mmHg) | 69.4 ± 8.8 | 68.6 ± 8.9 | 0.587 |
| Serum Cr (mg/dL) | 1.19 ± 0.25 | 1.19 ± 0.28 | 0.972 |
| e-GFR (mL/min/1.73 m²) | 72.6 ± 22 | 63.8 ± 15.3 | 0.006 |
| Serum albumin (g/dL) | 4.25 ± 0.66 | 4.53 ± 0.38 | 0.007 |
| Serum uric acid (mg/dL) | 5.36 ± 1.36 | 5.14 ± 1.71 | 0.425 |
| Hemoglobin (g/dL) | 14.7 ± 1.9 | 14.5 ± 1.8 | 0.492 |
| Presence of microalbuminuria | 18 (35) | 0 (0) | <0.001 |
| SF-36 scores | | | |
| Physical functioning | 46.3 ± 9.5 | 48.3 ± 8.7 | 0.194 |
| Role-physical | 37.8 ± 15.4 | 38.8 ± 16 | 0.708 |
| Bodily pain | 44 ± 12.5 | 47.9 ± 12 | 0.064 |
| General health | 44.8 ± 7.1 | 49.5 ± 6.5 | <0.001 |
| Vitality | 48.9 ± 12 | 50.4 ± 11.2 | 0.45 |
| Social functioning | 43.2 ± 10.2 | 47.2 ± 9.8 | 0.021 |
| Role-emotional | 33 ± 18.7 | 33.2 ± 21.4 | 0.943 |
| Mental health | 39.5 ± 12.1 | 43.7 ± 12.9 | 0.054 |

Continuous data are expressed as mean ± SD; categorical data are expressed as number (percentage).

BMI, body mass index; BP, blood pressure; Cr, creatinine; e-GFR, estimated glomerular filtration rate; LKDs, living related kidney donors; PUKDs, paid unrelated kidney donors; SF-36, 36-item short form health survey.

**Figure 1: Flowchart of the study selection process.**
clinical data were not routinely collected. Hence, and importantly, we could not compare the postdonation e-GFR and microalbuminuria in PUKDs and LRKDs with their respective values predonation. Finally, as our center does not have a protocol for regular follow-up of donors, we could not collect the information on the changes in e-GFR in the studied groups postdonation.

Despite the above limitations, the results of our study are significant. For the first time, we have shown that PUKDs as compared with LRKDs experience a poor follow-up, lower HRQOL and early onset microalbuminuria postdonation. The clinical significance of the above findings should be further evaluated in future prospective studies with larger sample sizes and longer durations of follow-up.

Acknowledgments

This study was funded by a grant from Shiraz University of Medical Sciences, Shiraz, Iran. We would like to thank Dr. Mitra Mahdavi-Mazdeh for her critical review of the article and Ms. Talicia Tarver for English-language editing of the article.

Disclosure

The authors of this manuscript have no conflicts of interest to disclose as described by the American Journal of Transplantation.

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