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Impact of type of donor on graft and patient survival rate in kidney transplanted patients in Iran

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ABSTRACT

Introduction: End-stage renal disease (ESRD) is an increasing problem in the world. Kidney transplant is considered as preferred therapeutic method for ESRD. Options for organ transplantation include living related donor (LRD), living unrelated donor (LURD) and cadaveric donor.

Objectives: This study was aimed to evaluate the effect of type of donor on graft and survival rate of patients.

Patients and Methods: This study was cross-sectional, which used Meier method to calculate the patient survival rate. Additionally log-rank test was applied to compare the survival curves; analysis of variance (ANOVA) was applied to compare continuous variables and χ^2 test was used to compare the data. Data were analyzed using SPSS version 19 and P values less than 0.05 was considered significant.

Results: The mean duration of follow-up in LRD, LURD and cadaveric recipients were 60.37±34.2, 79.17±33 and 61.17±34 months respectively. Five-year survival, in LRD was 100 months, in LURD recipients was 87±0.01 months, and in cadaveric recipients was 91±0.03 months. The mean survival of graft in LRD, LURD and cadaveric recipients were 115.5±3.1, 103.27±1.2 and 102.15±4.5 months, respectively. Log-rank test showed a significant difference between graft survival in recipients ($P=0.038$).

Conclusion: The results showed that LRD is one of the factors affecting graft survival. Hence, graft survival rate showed high length among patients who their graft was from LRD compared to LURD and cadaveric.

Implication for health policy/practice/research/medical education:

Given that the survival rate of the transplanted kidney in patients from relatives is more than others (not relatives), it is recommended that in priority choose alive relatives as a kidney donor in transplant centers.

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Introduction

End-stage renal disease (ESRD) is an increasing problem in the world (1). Kidney transplant is considered as a preferred therapeutic method for patients with ESRD and it is offered importantly for better quality of life, cardiovascular stability and improved survival (2-4). Options of organ transplant include living related donor

(LRD), living unrelated donor (LURD) and cadaveric donor while the cadaveric is an important option, but graft survival rate from an alive donor is more than the cadaver (5). Therefore, regarding survival rate of one-year in the 1960s from alive donor, kidney transplant survival was 75% to 90% and in cadaver was 50% to 60%. While during 1970 to 1980s, one-year survival rate had increased

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rapidly in cadaveric kidney transplant. Nowadays, one-year survival rate of cadaveric kidney transplant is 89% and from alive donors is 95%. During this period the long-term survival rate also improved and now the average lifespan of a transplant from alive donors and cadaveric kidney transplant is around 20 years and close to 14 years, respectively (6). High survival with alive donor compared to cadaver donor has been widely reported (7). Therefore, a shift towards alive donor transplants is increasing worldwide (8). A similar trend has been observed in our unit over the last decade (9).

Objectives

The purpose of this study was to evaluate the effect of type of donor on graft and survival rate of patients in the Imam Khomeini hospital in transplantation center of Urmia city, Iran.

Patient and Methods

Study population

This study was a cross-sectional study and the sample of study consisted of all patients who had received kidney transplant from the beginning of 2001 until the end of 2011.

The data of patients were collected using a checklist through available records in the kidney transplantation center and the clinic of sector in Imam Khomeini hospital. To determine the status of the patients or graft survival, phone number of patients were used to follow-up and complete the data. To comply with ethical aspects, all stages of collecting, maintaining appropriate data and the results of data were reported anonymously. Transplantation recipients were identified regarding urinary tract infection after transplantation and studied variables in this study were included the age and gender of the kidney donor and recipient, type of dialysis, causes of death, immunosuppression, cold ischemia, warm ischemia and time on dialysis before transplant. In this study, transplantation date is considered as the first event (initial event) and date of death or last follow-up is considered as the final event (end-point event).

Ethical issues

1) The research followed the tenets of the declaration of Helsinki. 2) Informed consent was obtained 3). This study was approved by the Ethics Committee of Urmia University of Medical Sciences.

Statistical analysis

To calculate the graft survival rate, the transplant date was considered as the first event (initial event) and kidney transplant failure date that led to dialysis and in some cases led to death was considered as the event end (end-point event). Kaplan-Meier method was used to calculate the patient survival rate and as well as log-rank test was used to compare the survival curves. Cox regression

model was applied for modeling the factors affecting survival rate. Mann-Whitney U test was used to compare the continuous variables and χ^2 test was used to compare classified data. Also all relations were presented by odds ratios (ORs) and 95% confidence intervals (CIs). The data were analyzed using SPSS version 19. The level of significance considered less than 0.05.

Results

The total population of transplanted patients were 1268 cases during 10 years which 991 cases (78.15%) were followed up successfully including 531 LRD, 845 LURD and 85 cadaveric donor. In total, 149 cases experienced rejection of kidney transplant that 2 cases (1.3%), 134 cases (89.9%) and 13 cases (8.7%) cases had been reported in LRD, LURD and cadaveric donor, respectively. As shown in Table 1, there were 32 male and 21 female patients. The mean age, time of dialysis, cold and warm ischemia at transplant time were 29.3 years, 13.8 months, 24.6 and 4.8 minutes, respectively. The initial immunosuppression was a cyclosporine-based (7 cases), azathioprine-based (8 cases), steroids-based (3 cases) and mycophenolate mofetil (35 cases). Also for recipients of LURD, there were 526 male and 327 female. The mean age, time of dialysis, cold and warm ischemia at transplant time were 39.9 years, 17.2 months, 23.2 and 4.8 minutes respectively. The initial immunosuppression was a cyclosporine-based (101 cases), azathioprine-based (205 cases), steroids-based (150 cases) and mycophenolate mofetil (389 cases). For recipients of cadaver, there were 39 male and 46 female cases. The mean age, time of dialysis, cold and warm ischemia at transplant time were 32.9 years, 22.7 months, 29.7 and 9.11 minutes, respectively. The initial immunosuppression was a cyclosporine-based (10 cases), azathioprine-based (20 cases), steroids-based (15 cases) and mycophenolate mofetil (40 cases). A total of 120 deaths occurred in all transplanted cases that 111 cases occurred in LURD recipients. The leading cause of deaths included infections ($n=28$), cardiovascular disease ($n=60$), neoplasia ($n=17$) and sudden death ($n=6$). One patient died in the LRD recipients because of cardiovascular disease and in the cadaver recipients were due to infection ($n=4$), cardiovascular disease ($n=4$). The mean duration of follow-up in LRD, LURD and cadaver recipients after transplant were 60.37 ± 34.2 , 79.17 ± 33 and 61.17 ± 34 months, respectively. The 1, 3, 5, 7 and 10-year survival rate of patients based on the type of donor, in LRD were 100, 100, 100, 96 ± 0.04 and $96 \pm 0.04\%$, respectively. In LURD recipients, 10-year survival rate of patients were 94 ± 0.01 , 90 ± 0.01 , 87 ± 0.01 , 86 ± 0.01 and $79 \pm 0.03\%$, respectively. Accordingly, in cadaver recipients 10-year survival rate of patients were 95.29 ± 0.02 , 91 ± 0.03 , 91 ± 0.03 , 91 ± 0.03 and $91 \pm 0.03\%$, respectively (Figure 1). The mean survival rate of patients in LRD, LURD and cadaver recipients were 118.61 ± 1.3 , 106.53 ± 1.2 and 109.36 ± 3.5 months, respectively. Log-

Table 1. Characteristics of the patients according to type of donor

Variable, n (%)		LRD (n=53)	LURD (n=853)	Cadaveric (n=85)	P
Recipient gender	Male	32 (60.4)	526 (61.7)	39 (45.9)	0.018
	Female	21 (39.6)	327 (38.3)	46 (54.1)	
Donor gender	Male	38 (71.7)	520 (96.1)	68 (80)	0.001
	Female	15 (28.3)	33 (3.9)	17 (20)	
Type of dialysis before RT	HD	50 (94.3)	765 (89.7)	82 (96.5)	0.17
	PD	1 (1.9)	46 (5.4)	3 (3.5)	
	None	2 (3.8)	42 (4.9)	0 (0)	
Causes of death	Infection	0 (0)	28 (25.2)	4 (50)	0.14
	Cardiovascular disease	1 (100)	60 (54.1)	4 (50)	
	Cancer	0 (0)	17 (14.1)	0 (0)	
	Sudden death	0 (0)	6 (5.4)	0 (0)	
Immunosuppression	Cyclosporine	7 (13.2)	101 (12)	10 (11.7)	0.48
	Azathioprine	8 (15)	205 (24.1)	20 (23.5)	
	Steroids	3 (5.7)	150 (17.7)	15 (17.6)	
	Mycophenolate mofetil	35 (66)	389 (46)	40 (47)	
Age Recipient		29.36± 12.2	39.98± 14.5	32.9± 13.3	0.034
Age Donor		30.7± 10.8	27.8± 4.8	29.7± 13.9	0.001
Time on dialysis before RT (month)		13.8±14	17.2±17.2	22.7± 12.8	0.002
Cold ischemia time (min)		24.6± 8.7	23.27± 13.7	29.7± 12.8	0.07
Warm ischemia time (min)		4.8± 2.3	4.8± 2.27	9.11± 15.8	0.001
Serum Creatinine discharge time		1.7± 1.9	1.4± 1.3	1.7± 1.4	0.001

RT, renal transplantation; HD, hemodialysis; PD, peritoneal dialysis; LDR, living related donor; LURD, unrelated living donor; BMI, body mass index.

rank test showed a significant difference between patients' survival rate regarding the type of donor ($P=0.043$). Additionally, the 1, 3, 5, 7 and 10-years graft survival rate based on the type of donor in LRD were 96.15 ± 0.03 , 96.15 ± 0.03 , 96.15 ± 0.03 , 96.15 ± 0.03 and $96.15 \pm 0.03\%$, respectively. Moreover, 10-years graft survival in LURD recipients were 94 ± 0.01 , 87 ± 0.01 , 83 ± 0.01 , and 80 ± 0.01 and also $73 \pm 0.03\%$, respectively. Furthermore, 10-years graft survival in cadaver recipients were 93 ± 0.03 , 86 ± 0.04 , 82 ± 0.05 , 79 ± 0.06 and $79 \pm 0.06\%$, respectively (Figure 2). The mean survival rate of graft in LRD, LURD and cadaver recipients were 115.5 ± 3.1 , 103.27 ± 1.2 and 102.15 ± 4.5 months, respectively. Log-rank test showed a significant difference between survival rate of graft in the recipients regarding the type of donor ($P=0.038$).

Discussion

Kidney transplant among alive donors is becoming popular because of better organs and excellent outcomes (9). In this study, the results showed that LRD is one of the factors affecting graft survival, so that graft survival rate showed high length among patients who their graft was from LRD compared to LURD and cadaveric, which the results are consistent with study by Bakr and Ghoneim (10), and others (11-14). However, several studies did not find a significant relationship between type of donor and graft survival rate (5,15-18). In our study, risk of graft rejection in LRD and cadaver recipients was less than that of reference group and were 0.252 and 0.945, respectively (hazard ratio and regression coefficient; Table 2). Despite no significant relationship was detected between the type

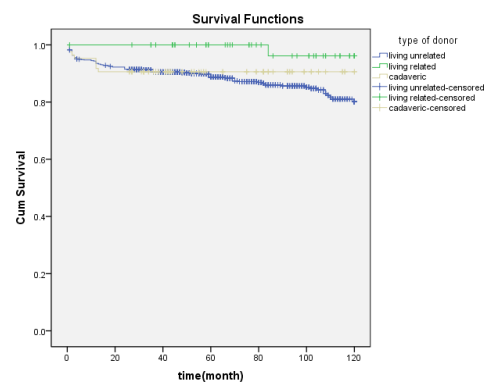


Figure 1. Comparison patient survival rate according to type of donor after transplantation in transplanted patients.

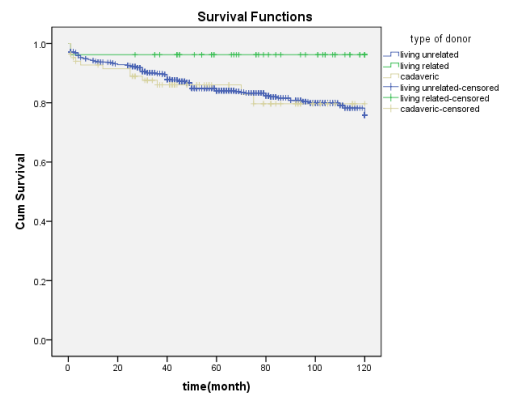


Figure 2. Comparison graft survival rate according to type of donor after transplantation in transplanted patients.

Table 2. Risk factors for graft survival

Factor		Regression coefficient	Hazard ratio (95% CI)	P
Type of Donor	ULDR	-	1	
	LDR	-1.38	0.252(0.03- 0.5)	0.04
	Cadaveric	-0.05	0.945(0.5- 1.5)	0.87
Type of dialysis	None	-	1	
	PD	-0.304	0.738(0.1-0.9)	0.512
	HD	0.873	2.4(1-3.5)	0.008
Warm ischemia time (min)		0.729	2.5(1-3.6)	0.001
Age of recipient		0.87	2.4(1.2-4.2)	0.001
Serum Creatinine discharge time		1.75	2.5(1.5-3.8)	0.001

HD; hemodialysis, PD; peritoneal dialysis.

Table 3. Risk factors for patient survival

Factor		Regression coefficient	Hazard ratio (95% CI)	P
Type of Donor	ULDR	-	1	
	LDR	-1.88	0.152 (0.04- 1.01)	0.063
	Cadaveric	-0.387	0.679 (0.32- 1.5)	0.4
Age of recipient		1.03	1.2 (0.8-1.6)	0.001
Serum Creatinine discharge time		1.07	0.92 (0.5-1.1)	0.001

of donor and patient survival rates (Table 3), survival rate was high among LRD recipients compared to LURD and cadaver recipients. However, in a study by Fuggle et al, a significant relationship was detected between type of donor and survival rate of patients (19). In this study, one possible reason for the lower survival rate of graft and patients among LURD recipients and cadaver recipients compared to LRD recipients may be related to high occurrence of acute rejection in patients who have received organ from LURD and cadaver organ.

Likewise, survival rate in LRD recipients for 1 and 5 years were 100% and 100%. We also found, graft survival rates were 96% and 96% for 1 and 5 years, respectively. In the study of Patel et al, the survival rates of patients in LRD recipients for 1 and 5 years were 93.8% and 83.1%, and graft survival rates were 96.1% and 89% for 1 and 5 years, respectively (20). Additionally patient survival rates in LURD recipients for 1 and 3 years were 94% and 90%, while graft survival rates were 94% and 87% for 1 and 3 years, respectively. In the study by Ahmed et al, the survival rates of patients in LURD recipients for 1 and 3 years were 97.7% and 95%, while graft survival rates were 98.7% and 93.7% for 1 and 5 years, respectively (9). Log-rank test showed a statistical significant difference between graft survival rate ($P=0.038$) and patients' survival rate ($P=0.043$), for the recipients regarding the type of donor, while in the study of Markus et al, no significant difference was reported between graft survival rate ($P=0.91$) and patients' survival rate ($P=0.686$) (21).

Numerous studies have reported the chronic glomerulonephritis as main cause of ESRD in patients (9, 21). There was no significant difference between recipients regarding the type of donor. Similar to the results of numerous studies, differences were observed between

recipients' age ($P=0.34$) and donors' age ($P=0.001$) (1,21,22). In the study of Tekin et al, no significant difference was observed in recipients' age ($P=0.582$) (4). Additionally, differences were observed in recipients' gender ($P=0.018$), donors' gender ($P=0.001$), time of dialysis ($P=0.002$), warm ischemia time ($P=0.001$), serum creatinine at discharge ($P=0.01$) and also on other variables like type of immunosuppression ($P=0.48$) and cold ischemia time ($P=0.07$).

Conclusion

The results of this study showed that LRD is one of the factors affecting graft survival. Hence, graft survival rate showed high length among patients who their graft was from LRD compared to LURD and cadaveric.

Limitations of the study

It was a single-center non-randomized study. All patients did not respond to our call.

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Authors' contribution

SS; study design and manuscript drafting. MGG; study design, data collection and statistical analysis. KM; study design and manuscript reviewing. HRK; statistical analysis. ATA and MMF contributed to the development of the study.

Conflicts of interest

The authors declare no conflict of interest.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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