

Graft survival rate in pediatric renal transplantation: A single center experience

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ABSTRACT

Objective: Renal transplantation is the best option for treatment of the end-stage renal diseases and has more advantages than dialysis. The objective of this study was to determine the ten-year graft survival rate of renal transplantation and its contributing factors among a group of Iranian patients aged 18 years or younger.

Methodology: In a retrospective cohort we aimed to study the ten-year graft survival rate of renal transplantation and its contributing factors among pediatric patients who have been transplanted from March 1999 to March 2009 in Shiraz Namazi Hospital Transplantation Center, southern Iran. Kaplan-Meier method was used to determine the survival rate, log rank test to compare survival curves, and Cox regression model to determine hazard ratios and to model variables affecting survival.

Results: The 1, 3, 5, 7 and 10 year-graft survival rates were 96.8, 88.8, 82.8, 78.1, 78.1 percent, respectively. Cox regression model revealed that the duration of hospitalization was one of the important factors in graft survival rate in renal transplantation.

Conclusion: In this study, the 10 year-graft survival rate for pediatric renal transplantation was 78.1%. Graft survival was significantly related to hospital stay after the operation. Donor source, cold ischemia time, immunosuppressive drugs regimen, time to diuresis, and cause of ESRD did not influence the survival rate.

KEYWORDS: Survival rate, Pediatric renal transplantation, Cox regression model, Kaplan-Meier.

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INTRODUCTION

Renal replacement therapy (dialysis & transplantation) for patients with end-stage renal disease (ESRD) is on the rise globally and the same epidemiologic trend is also being observed in Iran.^{1,2} Three methods used for treatment of patients with ESRD are hemodialysis, peritoneal dialysis and renal transplantation.³⁻⁶ Renal transplantation is the best option for treatment of the end-stage renal diseases⁷⁻¹¹, and has more advantages than dialysis.¹²⁻¹⁵ By renal drafting, patients with ESRD experience more survival rate and better quality of life in all ages.^{7,10,13,14} In the previous studies of our center, survival rate in deceased donor¹⁶, living donor¹⁷ and diabetics patients¹⁸ were reported and

the objective of this study was to determine the ten-year survival rate of renal transplantation and its contributing factors in patients aged 18 years and younger who were transplanted from March 1999 to March 2009 in Shiraz Namazi Hospital Transplantation Center, southern Iran.

METHODOLOGY

This study is a retrospective cohort which aimed to investigate the ten-year graft survival rate of renal transplantation and its contributing factors in patients (164 cases) aged 18 years and younger (which made up 12% of all patients) who were transplanted from March 1999 to March 2009 in Shiraz Namazi Hospital Transplantation Center, southern Iran.

In this study the precise time of transplantation was considered as "initial event" and the time of irreversible rejection of transplantation in which patient needs dialysis was considered as the "end point event". To determine the survival rate, Kaplan-Meier method and to compare survival curves, log rank test and for determining Hazard Ratio and also modeling of survival affecting variables, Cox Regression Models were used. The variables investigated in this study are the age of the donor, gender of the donor and recipient, blood type and Rh of the donor and recipient, the marital status of the donor, donor source, immunosuppressive drugs regimen, cause of ESRD, time to diuresis, vascular complications, cold ischemic time, the duration of dialysis before the operation and the duration of hospitalization after the operation.

The Required data was collected from patients' files at Namazi Hospital. To determine the graft survival status, available files at the nephrologists' offices, the Center for Special Diseases, and the Association for Supporting of Renal Patients and in some cases, available telephone numbers in patients' files were used. SPSS software version 11.5 was utilized to analyze the data and a *p-value* of less than 0.05 was considered significant.

RESULTS

From 164 patients with transplantation, 160 patients were followed successfully and among these patients, there were 25 cases (15.6 percent) with transplantation rejection. The numbers and percentages shown in the tables are based on the total number of transplanted patients (164 cases) and calculated survival rates are based on followed cases (160 cases). As seen in Table-I, 55.5% of recipients were men, and they comprised 62.8% of

donors. The mean age of recipients and donors were 14.00 ± 3.16 years and 25.78 ± 13.08 , respectively. The mean values for duration of hospitalization after the operation and cold ischemia time were 12.76 ± 5.32 and 54.36 ± 63.15 , respectively. "O" was the most frequent blood type among recipients and donors with 45.7 and 54 percent of cases, respectively.

In 85.6% of cases, donor and recipient had the same blood group, while the rest had compatible blood groups. Considering marital status, 55.1% of donors were married. The highest number of transplants belonged to deceased donors (51.2%) and the rest belonged to living-related (34.1%) and living-unrelated (14.6%) donors. The protocol for immunosuppressive therapy in patients encompassed three groups of drugs (Table-II). In the first group, cyclosporine, Imuran, IV methyl Prednisolone and oral Prednisolone were prescribed. The second group drugs were similar to the first group with Cellcept replacing Imuran. The third group included all the first group drugs plus Cellcept. The most frequently consumed drugs belonged to the first group with 80 cases (51%). Duration of hospitalization after operation was between 7 to 14 days in the 63.5% of cases. The 1, 3, 5, 7, and 10-year graft survival rates for renal transplantation were 96.8, 88.8, 82.8, 78.1, 78.1 percents, respectively (Fig.1).

The 1, 3, 5, 7, and 10-year graft survival rates based on different variables, calculated with Kaplan-Meier method, are shown in Tables I and II. To investigate the existence of significant differences in survival rates among different classes of these variables, log-

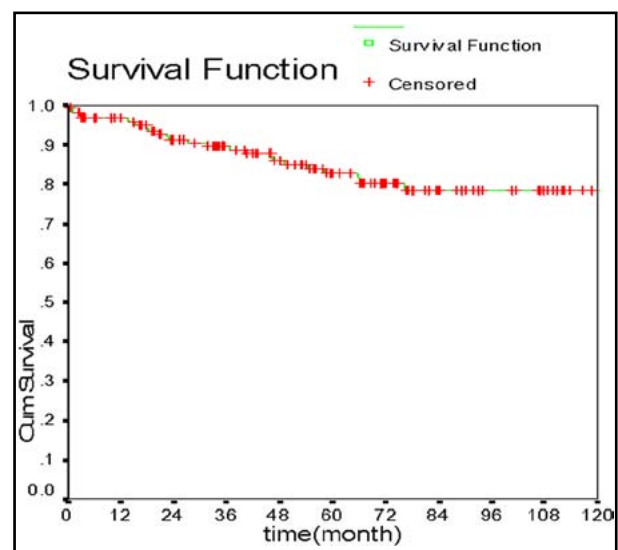


Fig.1: Ten-year graft survival rate in pediatric renal transplantation.

Table-I: 1, 3, 5, 7 and 10-year graft survival rates in pediatric renal transplantation based on different variables.

Variables		N (%)	Survival Rates (%)					P value (log-rank test)
			1yr	3yr	5yr	7yr	10yr	
Total patients		159	96.8	88.8	82.8	78.1	78.1	-
Recipient sex	Male	91(55.5)	97.7	89.8	81.5	72.9	72.9	0.47
	Female	73(44.5)	95.8	87.5	85	85	85	
Donor sex	Male	103(62.8)	94.9	85.7	77.6	75.1	-	0.067
	Female	61(37.2)	98.1	96.1	91.2	84.4	84.4	
Donor age	< 20yr	64(39)	95.21	88.13	83.06	79.87	-	0.964
	20-40yr	76(46.3)	98.63	92.37	83.88	76.62	76.62	
	40-60yr	24(14.6)	95.65	85.58	79	79	-	
Donor blood group	A	38(23.6)	94.7	83.1	71	71	71	0.247
	B	32(19.9)	96.3	96.3	91.2	91.2	-	
	AB	4(2.5)	-	-	-	-	-	
	O	87(54)	96.3	89.3	83.6	75.8	75.8	
Recipient blood group	A	42(25.6)	95.2	84.1	67.8	67.8	67.8	0.072
	B	38(23.2)	96.9	96.9	92.5	92.5	67.8	
	AB	9(5.5)	100	100	100	100	100	
	O	75(45.7)	95.8	87.8	83.7	74.4	74.4	
Donor Rh	Positive	149(92.5)	96.5	88.5	81.8	76.7	76.7	0.415
	Negative	12(7.5)	100	100	90.9	90.9	90.9	
Recipient Rh	Positive	156(95.1)	96.7	89.1	82	77.2	-	0.269
	Negative	8(4.9)	100	100	100	100	100	
Blood group	Same	137(85.6)	96.2	87.8	81.9	76	76	0.314
	Compatible	23(14.4)	100	100	86.9	86.9	86.9	
Donor marital status	Single	70(44.9)	95.56	88.83	83.92	-	-	0.971
	Married	86(55.1)	97.59	92.17	83.31	77.7	77.7	
Donor source	Related	56(34.1)	100	90.74	87.81	83.9	83.19	0.16
	Unrelated	24(14.6)	100	95.45	95.45	83.25	-	
Cause of ESRD	Cadaver	84(51.2)	93.85	84.07	76.72	74.17	-	0.967
	Obstructive	6 (3.8)	100	75	-	-	-	
	Glomerol	22 (14.1)	95	84.4	84.4	84.4	-	
	HTN	9 (5.9)	85.7	85.7	85.7	64.3	64.3	
	ADPKD	2 (1.3)	100	100	100	100	100	
	Others	24 (15.4)	90.6	85	85	85	85	
	Unknown	93(59.6)	98.9	93	82.3	77.2	-	

rank test p-values are inserted in these tables. Only, duration of hospitalization showed a significant relationship with graft survival. The survival rate of patients who were hospitalized for 7 to 14 days after the operation was higher than others. There were no significant differences between survival rates for other investigated variables.

Although the graft survival rate in patients who had been transplanted from deceased-donor was less than the other two groups, but the difference was not significant ($P = 0.16$), and even after integrating the living-related and living-unrelated donor groups and comparing that with the deceased-donor group, there was no significant difference between their graft survival rates ($P =$

0.059). Those variables with a P value of less than 0.2 in univariate log-rank test were inserted into Cox model, but as shown in Table-III, only duration of hospitalization after operation had a relationship with survival rate. Hazard ratio in patients who had a history of being hospitalized between 7 to 14 days was 0.212 (CI = 0.053-0.854, $P = 0.029$).

DISCUSSION

Our study showed that 1, 3, 5, 7, and 10-year survival rates for renal transplantation were 96.8, 88.8, 82.8, 78.1, 78.1 percent respectively. Similarly, Sumboonnanonda et al reported a graft survival of 98% and 84% at 1 and 5 years.¹⁹ In another study from 1986 to 1998, however, 1, 3, and 5 year graft survival

Table-II: 1, 3, 5, 7 and 10-year graft survival rates in pediatric renal transplantation based on operative and post-operative variables.

Variables		N (%)	Survival Rates (%)					P value (log-rank test)
			1yr	3yr	5yr	7yr	10yr	
Immunosuppressive regimen *	G1	80(51)	97.44	92.1	84.72	78.65	78.65	0.8
	G2	76(48.4)	97.2	86.8	79.43	49.43	-	
	G3	1(0.6)	100	100	-	-	-	
Time to diuresis	Immediate	120(91.5)	97.6	91.2	83.9	78.3	78.3	0.106
	Delayed	12(8.5)	90.9	72.7	63.6	63.6	-	
Artery	Simple	19(83.8)	96.5	90.6	83	78.7	78.7	0.597
	Double	20(14.1)	100	88.5	80.5	70.4	-	
	Triple	3(2.1)	100	66.7	-	-	-	
Arterial anastomosis	Int.iliac	125(88)	96.7	90	81.6	75.7	75.7	0.584
	Ext.iliac	-	-	-	-	-	-	
	Both	17(12)	100	87.1	87.1	87.1	87.1	
Cold ischemic time	<2 hr	23(92)	100	94.1	82.4	82.4	-	0.54
	≥2hr	4(8)	100	-	-	-	-	
Admission time	<1week	22(13.8)	95	-	-	-	-	0.005
	1-2 weeks	101(63.5)	100	89.2	89.2	83.72	83.72	
	2-3 weeks	25(15.7)	92	79.45	79.45	73.78	73.78	
	>3 week	11(6.9)	90	65.63	65.63	65.63	65.63	

*G1: (Cyclosporine, Imuran, IV methyl Prednisolone and oral Prednisolone).

G2: (Cyclosporine, Cellcept, IV methyl Prednisolone and oral Prednisolone).

G3: (Cyclosporine, Imuran, Cellcept, IV-methyl Prednisolone and oral Prednisolone).

rates were 93%, 75% and 63%, respectively.²⁰ The rates in our study are higher compared to these which might be due to improvement of techniques and immunosuppressive therapy.

We found that survival was significantly related to hospital stay after the operation. Survival rates of patients who were hospitalized for 7 to 14 days after operation were higher than others. In this study, there were no significant differences

between survival rates in transplantations with deceased-donor (cadaveric), living-related donor and living-unrelated donor. Similarly, Abbud-Filho and colleagues found that graft survival did not differ significantly by donor type.²¹

Another study showed that among live donor kidney transplant recipients, donor-recipient relationship (related vs. unrelated) had no significant effect on graft survival.²² We combined

Table-III: Multivariate analysis using Cox regression model.

Variables		β	P-value	HR	95% CI for HR
Time to diuresis	Delayed	Reference group	0.103	1	0.113-1.221
	Immediate	-0.988		0.372	
Donor sex	Female	Reference group	0.526	1	0.466-4.466
	Male	0.366		1.44	
Recipient blood group	O	Reference group	0.406	1	0.465-2.85
	A	0.144		1.151	
	B	-1.226		0.293	
	AB	-14.07		00	
Donor source	Irrelative	Reference group	0.302	1	0.462-18.2
	Relative	1.067		2.9	
	Cadaver	1.262		3.55	
Admission time	<1week	-0.266	0.037	0.766	0.151-3.88
	1-2 week	-1.54		0.212	
	2-3 week	-0.495		0.610	
	>3week	Reference group		1	

the living- related and unrelated donor groups and compared it with the deceased-donor group and found that there was no significant difference between their graft survival rates. This finding is confirmed by the 2001 annual report of North American Pediatric Renal Transplant Cooperative Study which noted that 1-year allograft survival rate did not differ between cadaver-donor and living-donor recipients.²³ On the other hand, allograft survival rate was higher in living-donor recipients compared with deceased-donor recipients at all times after renal transplantation.²⁴

When transplant cases with donor and recipient of the same blood groups were compared to those with compatible blood groups, we found no significant difference between their survival rates. This finding is similar to those of El-Husseini and colleagues who investigated graft survival rate in pediatric living-donor renal transplantations.²² Park and colleagues, however, noted that survival rate was significantly higher in grafts where donors and recipients had identical blood groups.²⁵

Studies have shown that cold ischemia time does not influence graft survival in pediatric renal transplantations^{22,26,27}, a matter which is in line with our findings. However, it should be noted that the number of patients for whom cold ischemia time was documented was small in our study.

This study showed that time to diuresis after the operation did not affect the survival. This is in contrast with El-Husseini et al study where cases with immediate diuresis after transplantation had a significantly higher graft survival rate than those with delayed diuresis. This difference was not observed; however, when multivariate analysis was performed.²² Absence of a significant difference between the two groups in our study might be due to a very limited number of patients with delayed diuresis.

There was no relationship between graft survival and gender, cause of ESRD, and immunosuppressive drugs regimen in our study. Similar results have been also reported in other studies.^{21,22,27}

An important limitation of this study was that the recording of data in patients' files was not always precise. Some factors such as cold ischemia time were only reported for a few patients. Accordingly, we recommend that a larger number of pediatric renal transplantation cases should be investigated in future studies. Also, the effects of other important variables such as HLA, acute rejection, post-transplant creatinine level, and blood pressure on graft survival should be considered.

In Cox model, length of post-transplant hospitalization (LOH) has a significant relationship with graft survival rate. As shown in results, hazard ratio in patients who had a history of being hospitalized between 7 to 14 days was 0.212, much higher than the group with over 3 weeks LOH. This result is similar to *Abiodun Omoloja and et al* study.²⁸

Duration of hospitalization is related to various factors such as creatinine level, urine output, acute rejection, hemoglobin, proteinuria, anemia²⁹ and some other factors. Longer hospital stays in our center usually is due to a problem with the renal grafts such as delayed function from any cause (e.g., acute tubular necrosis or severe humeral rejections that need additional treatment modalities such as plasmapheresis or antithymocyte globulin). Our routine is to discharge the patients when their serum creatinine level is lower than 2 mg/dL and urine output is around 1 mL/ kg/min (7-10 days after the operation). In other words, LOH lower than 1 week or greater than 2 weeks naturally correlate with a problem in the kidney function that might translate into lower long-term graft survival.

CONCLUSION

The 10-year graft survival rate for pediatric renal transplantation was 78.1% in this study. Graft survival was significantly related to hospital stay after the operation. Donor source, blood group, gender, cold ischemia time, immunosuppressive drugs regimen, time to diuresis, and cause of ESRD did not influence graft survival rate.

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AA, AR, JH and HS conceived, designed and did statistical analysis & editing of manuscript.

AA and EK did data collection and manuscript writing.

DM and EK did review and final approval of manuscript.