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Long term graft and recipient outcome of deceased donor renal transplantation at the National Kidney and Transplant Institute

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Abstract

Background: The number of patients with end-stage renal disease (ESRD) is increasing and the gap between the demand for kidney transplantation (KT) and available donors is widening. Thus, deceased donation is very important to the donor pool for ESRD.

Objectives: This study aims to determine the long-term graft and recipient outcome of deceased donor renal transplantation at the NKTI from 2002-2007 and to determine the donor and recipient factors that affect graft and recipient survival.

Materials and methods: This is a retrospective cohort of deceased donor KT from January 2002 to December 2007. Data were reviewed and collected from NKTI medical records and the Philippine Renal Disease Registry (PRDR). Recipient and donor demographic profile were expressed as frequency counts, percentages and means with standard deviation. Kaplan Meier was used to determine graft and patient survival and logistic regression to establish correlation between certain factors and survival

Results: Among 1,598 KT, 1488 were from living donors and 110 from deceased donors. 91 patients were included in this study. The mean recipient age was 40.40 ± 11.8 years and 65.9% were males. The primary renal diseases were chronic glomerulonephritis (63.7%), diabetic nephropathy (18.7%) and hypertensive nephrosclerosis (6.6%). Around 39.6% had 3 HLA mismatches and 61.5% had at least 1 DR match. Majority received induction therapy (90.1%) and 64.8% had tacrolimus-based immunosuppressive regimen. The patient survival rate at 1, 3, 5 and 7 years was 91, 89, 86 and 86 percent while graft survival was 89, 79, 73 and 68 percent respectively. Infection was the leading cause of death. Cold Ischemia Time was significantly associated with patient survival (P = 0.033) while patients with male donors had significantly better graft survival (P= 0.001)

Conclusion: There was an acceptable outcome of KT from deceased donors up to 7 years post KT.

Introduction

Kidney transplantation (KT) is the preferred treatment for end stage renal disease (ESRD). A successful transplant triples the life expectancy of a renal failure patient. The projected life expectancy with a transplant was 17.19 years compared with only 5.84 years on dialysis [1]. Hence, despite an initial higher risk of death, long-term survival for patients who underwent transplantation is significantly better compared with patients who remain on dialysis.

In addition, KT is more cost effective and improves quality of life. A study showed that the costs of patient therapy by hemodialysis is far greater than transplantation and its maintenance three and a half times costlier [2]. The difference in quality of life between dialysis and transplant patients is statistically significant with 18.12% greater in transplant patients. Another study showed that KT provides greater survival benefits to patients with end-stage renal disease, at less cost [3].

There is an increasing prevalence of ESRD and the demand for KT is increasing. Majority comprise living donation and unfortunately decease donation has not increased at an equivalent rate to meet the demand for KT [4]. In the Philippines, there are 10,000-12,000 new cases of ESRD annually [5]. 50- 60% will need KT but only 10% is done. Of those being transplanted, 90% from living donors and only 10% from deceased organ donation.

Various studies has been done in the Philippines regarding outcomes of deceased donor KT as shown in Table 1 [6-9]. These studies showed a remarkable improvement in the outcome of deceased donor KT.

Objectives

General objectives

1. To determine the long-term graft and recipient outcome of deceased donor renal transplantation at the National Kidney and Transplant Institute from 2002-2007

2. To determine the donor and recipient factors that affect graft and recipient survival

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Key words: *Cadaveric donor kidney transplantation, graft survival, patient survival*

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Table 1. Studies on deceased donor kidney transplant in the Philippines.

Author	n	KT Period	Immunosuppression	Induction Therapy	Patient Survival (%)	Graft Survival (%)
Liquete [6]	50	1983 - 1988	CyA+pred CyA+aza+pred	None	1 year – 96 3 year – 81	1 year – 72 5 year – 50
Magcalas [7]	228	1984- 1996	CyA+pred CyA+aza+pred	none	1 year – 81 5 year – 60 10 year - 48	1 year – 70 5 year – 42 10 year – 22
Ninalga [8]	71	1995 - 2001	CyA+aza+pred (46.5%) CyA+MMF+pred (46.5%) Tacro+aza+pred (2.8%) Tacro+MMF+pred (4.2%)	None (84.5%) IL-2 blocker (15.5%)	1 year – 80 3 year – 69	1 year – 65 3 year – 48
Overio [9]	156	2007 - 2010	Tacrolimus based (96.8%) CyA based (3.2%)	IL- 2 blocker (62.2%) Polyclonal antibody (37.8%)	1 year – 94 3 year – 90	1 year – 97 3 year – 96

CyA: cyclosporine; pred: prednisone; aza: azathioprine; tacro: tacrolimus; MMF: mycophenolate mofetil

Specific objectives

1. To describe the recipients' demographic profile
2. To determine the incidence of graft and patient survival rate among recipients of deceased donor KT at 7 years post-KT
3. To describe the recipients' cause of mortality
4. To identify donor and recipient factors that significantly influences graft and patient survival at 7 years post KT

Methodology

Research design

Retrospective cohort study

Study population

All patients ≥18 years of age who underwent primary deceased donor KT from January 2002 to December 2007 at the National Kidney and Transplant Institute were included in this study. Excluded were pediatric patients, foreigners and those who were lost to follow up for at least 12 months post KT.

Materials and methods

The following data were reviewed and collected from medical records and PRDR: a) recipients' demographic characteristics such as age, gender, cause of kidney disease, presence of diabetes mellitus, immunosuppressive regimen, induction therapy and immunologic status (Panel reactive antibody (PRA), number of HLA-ABDR mismatches and HLA-DR mismatches); b) donor factors such as age, gender and cold ischemia time (CIT)

Patients were followed up to 7 years post-KT to determine graft and patient survival.

Definition of terms

- Patient survival is the survival from the date of transplant until the date of death.
- Graft survival is the presence of renal function adequate to prevent the patient from resuming maintenance dialysis.
- Graft loss is patient's permanent return to dialysis.

Statistical analysis

The demographic profile of recipients and donors were expressed as frequency count, percentage and mean with standard deviation. Kaplan meier was used to determine graft and patient's survival rate. To establish correlation between certain factors and survival, logistic regression analysis was utilized.

Ethical consideration

Confidentiality of the subjects were maintained. Anonymity were ensured and each patient was assigned a case number.

Results

From January 2002 to December 2007, a total of 1,598 KT were performed at the NKTI, 1488 (93.1%) were from living donors and 110 (6.9%) were from deceased donors. Among the 110 recipients of deceased grafts, 91 (82.7%) patients were included in this study and 19 (17.3%) patients were excluded due to the following reasons: 3 subjects were foreigners; 10 pediatric patients and 6 subjects had incomplete data.

Demographic characteristics

The mean recipient age was 40.40 ± 11.8 years and 65.9% were males. The primary renal diseases were chronic glomerulonephritis (63.7%), diabetic nephropathy (18.7%) and hypertensive nephrosclerosis (6.6%). Around 39.6% had 3 HLA mismatches and 61.5% with at least 1 DR match. Majority received induction therapy (90.1%) and 64.8% had tacrolimus-based immunosuppressive regimen (Table 2).

Graft and patient outcome

The survival rate at 1, 3, 5 and 7 years for patients was 91, 89, 86 and 86 percent while graft survival was 89, 79, 73 and 68 percent respectively (Figure 1 and Figure 2). The leading cause of death was infection (76%) followed by cardiovascular disease (14%). Most of the death occurred less than 5 years post-KT (Table 3).

Factors associated with graft and patient survival at 7 years post-kidney transplant

There were no recipient factors that was significantly associated with graft and patient survival at 7 years post-KT (Table 4 and Table 5).

Cold ischemia time was significantly associated with patient survival rate among the donor factors while the gender of the donor was significantly associated with graft survival rate.

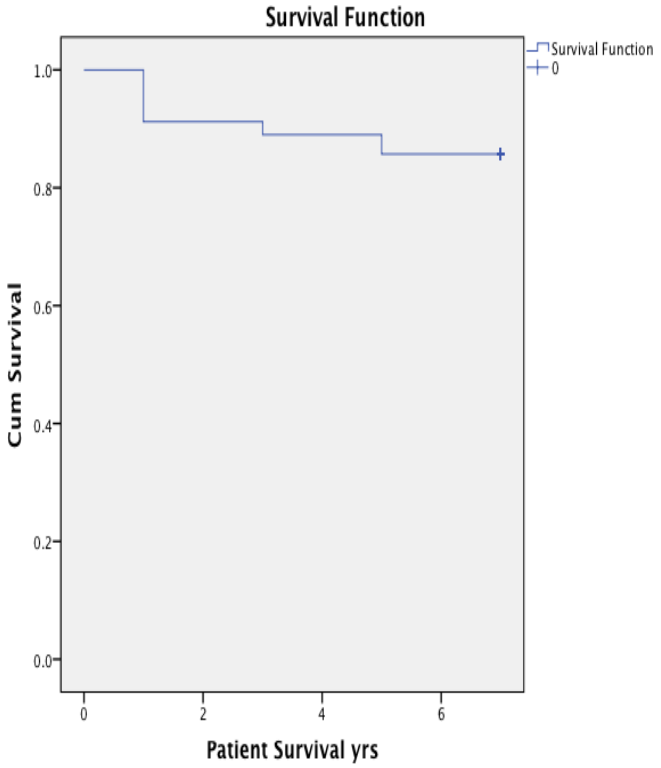

Figure 1. Kaplan Meier Patient survival rate.

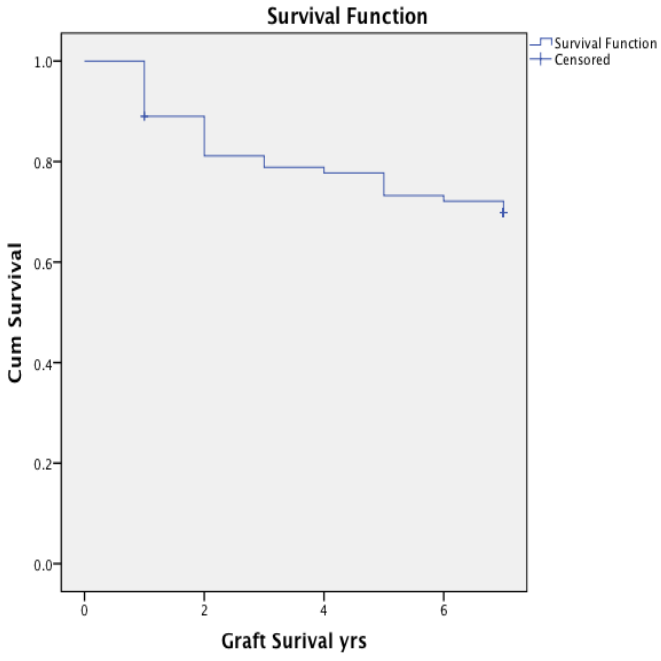

Figure 2. Kaplan Meier Graft survival rate.

The patient survival rate among patients was significantly different when grouped according to cold ischemia time. (Log Rank = 6.81, p=0.033). The cold ischemia time (CIT) with less than 12 had highest estimated mean survival rate (6.83 years), followed by 12-24 CIT (6.46 years). Patients with CIT greater than 24 had the lowest estimated survival rate (5.52 years) (Table 6). Graft survival of patients was significantly different when grouped according to donor's gender (Log Rank = 11.055, p=0.001). Patients who had male donors had significantly higher estimated survival rate (6.06 years) than patients with female donors (3.69 years) (Table 7).

Discussion

There has been continuous improvement in graft and patient survival from 1983 to 2010 [6-9] (Table 8).

Our study showed an improvement in graft survival when compared to studies done from 1983 to 2001 probably due to the improved immunosuppressive regimen, use of induction therapy and shorter CIT. When compared with the United States Renal Data System (USRDS) of 2013, our study was comparable in which their 1, 3 and 5 year patient survival rate were 94%, 86.6% and 75.5% while graft survival rates were 91.8%, 82.6% and 70.5% respectively [10].

Table 2. Demographic profile of recipients.

Characteristics		Frequency	Percentage
Age (years)	Less than50 years old	71	78.0
	50 years old and above	20	22.0
Gender	Male	60	65.9
	Female	31	34.1
Presence of Diabetes Mellitus	Yes	14	15.4
	No	77	84.6
Primary Renal Disease	Chronic glomerulonephritis	58	63.7
	Diabetic nephropathy	17	18.7
	Hypertensive nephrosclerosis	6	6.6
	Chronic pyelonephritis	3	3.3
	Autosomal dominant polycystic kidney disease	5	5.5
	Others	2	2.2
Number of HLA-ABDR Mismatch	0	1	1.1
	1	6	6.6
	2	21	23.1
	3	36	39.6
	4	18	19.8
	5	9	9.9
Number of DR Matches	0	24	26.4
	1	56	61.5
	2	11	12.1
Panel Reactive Antibody (PRA)	Class 1 >20%	2	3.6
	<20%	54	96.4
	Class 2 >20%	0	0
	<20%	56	100
	No data	35	
Immunosuppressive Agents	Tacrolimus-based	59	64.8
	CyA-based	27	29.7
	Sirolimus- based	5	5.5
Induction Therapy	None	9	9.9
	Basiliximab	53	58.2
	Daclizumab	5	5.5
	Alemtuzumab	24	26.4

Table 3. Causes of Death.

Cause of Death	Frequency (n = 13)	Percentage	Period of Death Post-KT (years)	
			< 5	≥ 5
Infection Pneumonia (10)	10	76.9	9	1
Cardiovascular	2	15.4	1	1
Pulmonary Embolism	1	7.7	1	0

Table 4. Recipient Factors influencing 7-year patient survival.

Patient Survival					
Factors	No. of Events	Censored	Estimated Mean Survival (in years)	Log-rank Statistic Value	P-Value
Recipient Age					
Less than 50 y/o (n=71)	9	62	6.465	0.784	0.376
50 y/o and above (n=20)	4	16	5.8		
Recipient Gender					
Female (n=31)	4	27	6.29	0.058	0.809
Male (n=60)	9	51	6.333		
Primary Renal Disease					
Glomerulonephritis (n=58)	9	49	No estimates were computed because most cases were censored.	1.833	0.872
Diabetic Nephropathy (n=17)	3	14			
HPN (n=6)	1	5			
CPN (n=3)	0	3			
APKD (n=5)	0	5			
others (n=2)	0	2			
DM					
yes (n=14)	2	12	6.143	0.001	0.977
no(n=77)	11	66	6.351		
Induction					
none(n=9)	0	9	No estimates were computed because most cases were censored.	1.582	0.208
with induction(n=82)	13	69			
Immunosupression(ISA)					
CYA base(n=27)	6	21	No estimates were computed because most cases were censored.	2.468	0.291
Tacrolimus base(n=59)	7	52			
Sirolimus base(n=5)	0	5			
PRA I					
<20%(n=54)	7	47	No estimates were computed because most cases were censored.	0.283	0.595
>20%(n=2)	0	2			
PRA II					
<20%(n=56) >20% (n=0)	7	49	6.393	No comparison analysis was performed because the factor variable had only one value for every stratum.	
DR Match					
0 (n=24)	4	20	6.25	0.417	0.812
1 (n=56)	7	49	6.429		
2 (n=11)	2	9	5.909		
AB MM					
0 (n=1)	0	1	No estimates were computed because most cases were censored.	4.328	0.503
1 (n=6)	1	5			
2 (n=21)	4	17			
3 (n=36)	7	29			
4 (n=18)	0	18			
5 (n=9)	1	8			

Table 5. Recipient Factors influencing 7-year graft survival.

Graft Survival					
Factors	No. of Events	Censored	Estimated Mean Survival (in years)	Log-rank Statistic Value	P-Value
Recipient Age					
Less than 50 y/o (n=71)	24	47	5.592	1.906	0.167
50 y/o and above (n=20)	3	17	6.231		
Recipient Gender					
Female (n=31)	8	23	5.903	0.374	0.541
Male (n=60)	19	41	5.621		
PRD- Renal Disease					
Glomerulonephritis(n=58)	17	41	5.817	1.222	0.943
Diabetic Nephropathy(n=17)	6	11	5.223		
HPN (n=6)	1	5	6		
CPN(n=3)	1	2	5.333		
APKD (n=5)	1	4	5.8		
Others(n=2)	1	1	6.5		
DM					
Yes (n=14)	5	9	5.13	0.541	0.462
No(n=77)	22	55	5.823		
Induction					
None(n=9)	1	8	6.444	1.558	0.212
With induction(n=82)	26	56	5.641		
Immunosupression(ISA)					
CYA base(n=27)	9	18	5.453	0.488	0.783
Tacrolimus base(n=59)	16	43	5.768		
Sirolimus base(n=5)	2	3	6.6		
PRA I					
<20%(n=54)	18	36	5.613	0.05	0.824
>20%(n=2)	1	1	7		
PRA II					
<20%(n=56) >20% (n=0)	19	37	5.663	No comparison analysis is performed because the factor variable has only one value for every stratum.	
DR Match					
0 (n=24)	6	18	6.009	0.553	0.758
1 (n=56)	17	39	5.665		
2 (n=11)	4	7	5.364		
AB MM					
0 (n=1)	0	1	No estimates are computed because most cases are censored.	5.806	0.326
1 (n=6)	0	6			
2 (n=21)	7	14			
3 (n=36)	14	22			
4 (n=18)	5	13			
5 (n=9)	1	8			

Table 6. Donor factors Influencing 7-year patient survival.

Patient Survival					
Factors	No. of Events	Censored	Estimated Mean Survival (in years)	Log-rank Statistic Value	P-Value
Donor Age					
≤ 20 y.o (n=21)	1	20	6.714	4.605	0.1
21-40 y/o (n=61)	9	52	6.377		
≥ 41y.o (n=9)	3	6	5		
Donor Gender					
Female (n=13)	3	10	5.615	1.086	0.297
Male (n=78)	10	68	6.436		
Cold Ischemia Time					
<12 (n=24)	2	22	6.833	6.81	0.033
12- 24 (n=44)	4	40	6.455		
>24 (n=23)	7	16	5.522		

Table 7. Donor factors influencing 7-year graft outcome.

Graft Survival					
Factors	No. of Events	Censored	Estimated Mean Survival (in years)	Log-rank Statistic Value	P-Value
Donor Age					
≤ 20 y.o (n=21)	4	17	5.952	3.142	0.208
21-40 y/o (n=61)	19	42	5.841		
≥ 41y.o (n=9)	4	5	4.333		
Donor Gender					
Female (n=13)	8	5	3.692	11.055	0.001
Male (n=78)	19	59	6.06		
Cold Ischemia Time					
<12 (n=24)	6	18	6.417	0.674	0.714
12- 24 (n=44)	14	30	5.523		
>24 (n=23)	7	16	5.348		

Table 8. Studies on graft and patient survival from 1983 to 2010.

Author	n	KT Period	Immunosuppression	Induction Therapy	Patient Survival (%)	Graft Survival (%)
Liquete [6]	50	1983 – 1988	CyA+pred CyA+aza+pred	None	1 year – 96 3 year – 81	1 year – 72 5 year – 50
Magcalas [7]	228	1984- 1996	CyA+pred CyA+aza+pred	None	1 year – 81 5 year – 60 10 year – 48	1 year – 70 5 year – 42 10 year – 22
Ninalga [8]	71	1995 – 2001	CyA+aza+pred (46.5%) CyA+MMF+pred (46.5%) Tacro+aza+pred (2.8%) Tacro+MMF+pred (4.2%)	None (84.5%) IL-2 blocker (15.5%)	1 year – 80 3 year – 69	1 year – 65 3 year – 48
Tam	91	2002-2007	Tacrolimus based (64.8%) CyA based (29.7%) Sirolimus based (5.5%)	None (9.9%) IL-2 blocker (58.2%) Monoclonal antibody (31.9%)	1 year – 91 3 year – 89 5 year – 86 7 year - 86	1 year – 89 3 year – 79 5 year – 73 7 year - 68
Overio [9]	156	2007 – 2010	Tacrolimus based (96.8%) CyA based (3.2%)	IL- 2 blocker (62.2%) Polyclonal antibody (37.8%)	1 year – 94 3 year – 90	1 year – 97 3 year – 96
CyA: cyclosporine; pred: prednisone; aza: azathioprine; tacro: tacrolimus; MMF: mycophenolate mofetil						

Infection (76.9%) was the most common cause of death in our study followed by cardiovascular disease (15.4%). Compared to the United States Renal Data System (USRDS) wherein the most common cause of death is cardiovascular disease (31%) followed by infection (19%) and malignancies (10%) [10]. However, in a study in India of 160 deceased donor KT between 2006-2009, the most common cause of death was infection which was comparable to our study [11]. Factors for the high incidence of infections were unhygienic conditions, late presentation and diagnosis, high cost of life-saving antimicrobial agents and lack of sensitive and specific diagnostic tools that were either not available or were too expensive [11,12].

Among the recipient and donor factors studied, the donor's gender was noted to affect the 7-year graft survival in which male donor had better outcome than female (p value = 0.001). This was similar to the study involving 464 renal transplant centers in Europe in which both patient and graft survival were worse with a female donor. Graft survival in female recipients of male donors was 48.4 ± 0.4 year vs. 46.9 ± 0.6 year for female donors (*p value* 0.0020). In male recipients, actuarial survival was 46.5 ± 0.3 year for male donors vs. 42.1 ± 0.5 year for female donors (*p value* < 0.0001). The assumption about the relative benefit of a male donor is that male kidneys have greater nephron number [13].

Patients with CIT of 12 hours had a significant patient survival. This is explained because there was less rejection with shorter CIT hence no need to give solumedrol pulsing hence no infection which is the main cause of patient mortality. The acute rejection with prolonged ischemia time could be reversed with solumedrol pulsing but could cause severe infection which may lead to death. United Network for Organ Sharing (UNOS) data noted a reduction in CIT during the 10-year period (1990-2000) with an overall reduction of 4.8 hour and noted improvement in 3-year graft survival (80% in 1996-2000 vs. 72% in 1990-1995 (p < 0.001) [14] Another study showed that CIT had a significant effect on the 6-year graft survival , a 10-hour increase in CIT was associated with a hazard risk ratio (HRR) of 1.20 for graft failure (p < 0.001) [15]. In our study, CIT <12 hours showed better 7-year graft survival compared to CIT 12-24 hours and >24 hours however it did not achieved statistical significance. In contrast, CIT influence on patient survival achieved statistical significance (P value 0.033). CIT with less than 12 hours had highest estimated mean survival rate (6.83 years), followed by 12-24 hours CIT (6.46 years) and >24 hours CIT had the lowest estimated survival rate (5.52 years).

Conclusion

There was an acceptable outcome of KT from deceased donors up to 7 years post KT. The most common cause of death was infection followed by cardiovascular disease. Among the recipient and donor factors, the donor's gender had effect on the 7-year graft survival in which male deceased donor KT had better graft survival compared to females and CIT was significantly associated with patient survival rate with CIT of less than 12 hours having better survival compared to CIT 12-24 hours and > 24 hours.

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