석 사 학 위 논 문

Long-term Clinical Outcomes in Deceased Donor Kidney Transplantation: A Single-center Experience

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이 논문을 석사학위 논문으로 제출함

2019년 8월

계 명 대 학 교 대 학 원

의학과 내과학 전공

권 진 경

권진경의 석사학위 논문을 인준함

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Table of Contents

List of Tables

List of Figures

1. Introduction

The incidence and prevalence of end-stage renal disease (ESRD) have continued to increase rapidly worldwide (1). Kidney transplantation (KT) remains the treatment of choice in ESRD patients because of excellent quality of life and higher survival rate (2,3). Nevertheless, the rising prevalence of ESRD overwhelms the pool of available organs for donation, leading to a disparity between organ supply and demand (4). Deceased donor kidney transplantation (DDKT) can be a good option to solve the organ shortage (5). Nevertheless, long-term allograft survival in DDKT remains lower than that of living donor KT because of the greater chances of allograft loss or premature death, as well as other various co-morbidities (6,7). Therefore, to improve the long-term clinical outcomes of allograft survival in DDKT, it is very important to understand various factors related to allograft survival in DDKT. The purpose of our study was to clarify the clinical features that affect allograft survival and long-term clinical outcomes and to evaluate predictors for long-term allograft survival.

2. Materials and Methods

2.1. Study Design:

We retrospectively analyzed the medical records of 422 patients who received KT from deceased donors at Keimyung University Dongsan Medical Center between October 1997 and October 2017. We divided KT recipients into 2 groups: non-graft failure and graft failure.

We evaluated allograft function at 1 year after KT, rates of biopsy-proven rejection, rates of delayed recovery of graft function (DGF), rates of medical complications after KT, rates and causes of graft failure and patient death, and risk factors for graft failure.

The Institutional Review Board of Keimyung University Dongsan Medical Center approved this study (DSMC 2019-05-040).

2.2. Immunosuppression Protocols:

We used basiliximab (20 mg on days 0 and 4, respectively; Simulect, Novartis, Basel, Switzerland) or antithymocyte globulin (ATG) (1.5 mg/kg at day 0 and 1.0 mg/kg between day 1 and day 3, respectively; Thymoglobulin, Genzyme, Cambridge, Mass., USA) as the immunosuppressant for induction treatment in kidney transplant recipients (KTRs) depending on the immunologic risks. We used tacrolimus (Prograf, Astellas Pharma Inc., Toyama, Japan) and checked trough levels. Prednisolone (30 mg, once a day), and mycophenolate mofetil (MMF) (500 mg, twice a day; Cellcept, Hoffmann-La Roche Inc., Nutley, USA) were the immunosuppressant used for maintenance

treatment.

2.3. Demographic and Clinical Data:

Baseline patient characteristics included age, gender, body mass index (BMI), numbers received KT, dialysis type before KT, cause of ESRD, co-morbidities such as diabetes mellitus (DM), hypertension (HTN), dyslipidemia, hepatitis B/hepatitis C virus (HBV/HCV) infection, malignancy, donor age and gender, human leukocyte antigen (HLA) mismatches, panel reactive antibody (PRA) class I/II, induction immunosuppressant, and maintenance immunosuppressant. The clinical outcomes included allograft function at 1 year after KT, rejection, DGF, and medical complications after KT, including HTN, DM, and various infections.

2.4. Statistical Analyses:

Student's *t*-test was used for continuous variables with a normal distribution and the variables were expressed as means ± standard deviations. The chi-square or Fisher's exact test was used for categorical variables and the variables were expressed as numbers and percentages. Death-censored graft survival rates according to the tacrolimus trough levels (TTLs) were obtained using Kaplan-Meier analysis with the log-rank test. Risk factors for graft failure were analyzed using Cox regression analysis. *P* values less than 0.05 were considered statistically significant. Statistical analysis was performed using the SPSS statistical software package (version 18.0, SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Baseline and Clinical Characteristics in Deceased Donor Kidney Transplantation:

Follow-up duration was 93.1 ± 70.8 months. The mean age of the KTRs was 46 ± 12 years and that of donors was 42 ± 15 years. The proportion of males among KTRs was 55.5%. The rate of first KT was 83%, and the rate of hemodialysis was 83.6%. The most common cause of ESRD was glomerulonephritis, followed by DM, HTN, and autosomal dominant polycystic kidney disease (62.5%, 10.2%, 7.1%, and 2.4%, respectively). The most common co-morbidity was HTN, followed by DM, dyslipidemia, HBV infection, and malignancy (61.6%, 16.1%, 10.2%, 6.2%, and 5.5%, respectively). The mean number of HLA mismatches was 3.2 ± 1.7, and the proportions of basiliximab and tacrolimus as induction, maintenance immunosuppressant were greater than those of thymoglobulin and cyclosporine (70.5%/86.8% vs. 11.6%/12.7%, respectively). The proportion of PRA class I ≥ 50% and PRA class II ≥ 50% were 49.8%, and 50.5%, respectively (Table 1). The mean eGFR at 1 year after KT was 65.4 ± 24.8 mL/min/1.73 m^2. The rate of acute/chronic rejection was 17.1%/7.1%. The proportion of DGF was 16.1%, and the most common infections after KT were viral, followed by bacterial (32.5% and 23.7%, respectively; Table 2).

3.2. Graft and Patient Survivals in Deceased Donor Kidney Transplantation:

The 1-, 3-, 5, 10-year, and 20-year death-censored graft survival rates in DDKT were 98.8%, 95.5%, 90.4%, 72.7%, and 45.3% respectively (Figure 1). The leading cause of death-censored graft failure was rejection (67%), followed by patient death with a functional graft (18%), recurrent glomerulonephritis (5.2%), and infection (5.2%) (Table 3). The 1-, 3-, 5, 10-year, and 20-year patient survival rates in DDKT were 98.1%, 96.1%, 94.7%, 90.6%, and 83.7% respectively (Figure 2). The leading cause of patient death was infection (61%), followed by cardiovascular disease (11%), cerebrovascular disease (5.6%), and malignancy (2.8%) (Table 3).

3.3. Comparison of Baseline and Clinical Characteristics according to Graft Failure in Deceased Donor Kidney Transplantation:

The comparison of demographic characteristics according to graft failure in DDKT is described in Table 4. Among the 422 patients who received DDKT, 97 (23%) were included in the graft failure group and 325 (77%) were included in the non-graft failure group. Compared with the non-graft failure group, the graft failure group showed significantly lower recipient age ($P < 0.001$), higher proportion of glomerulonephritis as a cause of ESRD ($P = 0.008$), higher incidence of dyslipidemia ($P = 0.038$), more HLA mismatches ($P = 0.001$), higher proportion of PRA class I/II >50% ($P < 0.001$) and lower proportions of basiliximab,

thymoglobulin, and tacrolimus ($P < 0.001$, $P = 0.029$, $P < 0.001$, respectively). There were no significant differences between the groups with respect to donor age, recipient gender, body mass index, dialysis type, or other co-morbidities such as HTN, DM, HBV/HCV infection, or malignancy, except for dyslipidemia ($P = 0.038$). The comparison of clinical characteristics according to graft failure in DDKT is presented in Table 5. Allograft function (represented by eGFR) at 1 year after DDKT in the non-graft failure and graft failure groups were 68.8 ± 21.7, and 33.0 ± 28.8 mL/min/1.73m^2, respectively ($P < 0.001$). The incidence of acute/chronic rejection in the graft failure group was significantly higher than that of the non-graft failure group (48.5%/21.8%, and 7.2%/2.5%, respectively; $P < 0.001$). There was no significant difference in the incidence of DGF between the groups. The incidence of HTN was significantly higher in the graft failure group than in the non-graft failure group ($P = 0.016$). The incidences of viral and bacterial infections were significantly higher in the graft failure group than in the non-graft failure group ($P < 0.001$ and $P = 0.044$, respectively). The incidences of tubercular infections, fungal infections, cardiovascular disease, cerebrovascular disease, and malignancy were not significantly different between the groups. Finally, surgical complications after KT (urine leakage, lymphocele, allograft bleeding, wound infection) were not significantly different between the groups.

3.4. Risk Factors associated with Graft Survival in Deceased Donor Kidney Transplantation:

We investigated the risk factors associated with graft failure in DDKT (Table 6). In univariate Cox regression analysis, recipient age,

acute rejection, chronic rejection, HLA mismatches, PRA class I > 50%, PRA class II > 50%, serum creatinine level at 12 months after KT, and viral infection showed significant association with graft survival. In multivariate Cox regression analysis, acute rejection (hazard ratio [HR], 11.385; 95% confidence interval [CI], 5.991-21.637; $P < 0.001$), chronic rejection (HR, 10.399; 95% CI, 4.947-21.858; $P < 0.001$), HLA mismatches (HR, 1.521; 95% CI, 1.227-1.885; $P < 0.001$), serum creatinine level at 12 months after KT (HR, 1.210; 95% CI, 1.093-1.340; $P < 0.001$), and viral infection (HR, 1.859; 95% CI, 1.111-3.109; $P = 0.018$) were independent risk factors for graft failure in DDKT. Recipient age and gender, donor age and gender, thymoglobulin induction, DGF, and PRA class I/II were not significantly different between the groups.

3.5. Subgroup Analysis of Death-censored Graft Survival Rate according to the Number of HLA Mismatches and Immunosuppressant in Deceased Donor Kidney Transplantation:

We calculated graft survival rates according to the number of HLA mismatches, induction immunosuppressant (thymoglobulin/basiliximab), maintenance immunosuppressant (tacrolimus/cyclosporine), and antimetabolites (mycophenolate mofitil/azathioprine) in DDKT. As the HLA mismatch number increased, the death-censored graft survival rate decreased significantly ($P = 0.002$) (Figure 3). However, there were no significant differences according to the types of induction immunosuppressant, maintenance immunosuppressant, or antimetabolites ($P = 0.945$, $P = 0.060$, or $P = 0.330$, respectively; at Figure 4, 5, and 6.)

Table 1A. Baseline Demographic Characteristics in Deceased Donor Kidney Transplantation

Variables	
Recipient	
Age at KT, years	46 ± 12
Male gender, n (%)	234 (55.5)
Body mass index	22.2 ± 3.1
KT number, n (%)	
First	350 (83)
Second	68 (16)
Third	4 (1.0)
Dialysis type before KT, n (%)	
Hemodialysis	353 (83.6)
Peritoneal dialysis	64 (15.2)
Mixed	5 (1.2)
Cause of end-stage renal disease, n (%)	
Glomerulonephritis	264 (62.5)
Diabetes mellitus	43 (10.2)
Hypertension	30 (7.1)
ADPKD	10 (2.4)
Others	75 (17.8)
Co-morbidity, n (%)	
Hypertension	260 (61.6)
Diabetes mellitus	68 (16.1)
Dyslipidemia	43 (10.2)
Hepatitis B virus infection	26 (6.2)
Hepatitis C virus infection	6 (1.4)
Malignancy	23 (5.5)

Values are expressed as means ± SDs, n (%).

ADPKD: autosomal dominant polycystic kidney disease; HLA: human leukocyte antigen; KT: kidney transplantation

Table 1B. Baseline Demographic Characterestics in Deceased Donor Kidney Transplantation (continued).

Variable	
Donor	
Age at KT, years	42 ± 15
Male gender, n (%)	296 (69.8)
HLA mismatches	3.2 ± 1.7
HLA-AB mismatches	2.4 ± 1.2
HLA-DR mismatches	1.2 ± 0.7
Panel reactive antibody class I ≥ 50%, n (%)	211 (49.8)
Panel reactive antibody class II ≥ 50%, n (%)	214 (50.5)
Induction immunosuppressant, n (%)	
Basiliximab	299 (70.5)
Thymoglobulin	49 (11.6)
Maintenance immunosuppressant, n (%)	
Tacrolimus	368 (86.8)
Cyclosporine	54 (12.7)

Values are expressed as means ± SDs, n (%).

ADPKD: autosomal dominant polycystic kidney disease; HLA: human leukocyte antigen; KT: kidney transplantation

Table 2. Clinical Outcomes in Deceased Donor Kidney Transplantation

Variables	
Allograft function at 1 year after KT	
Serum creatinine (mg/dL)	1.6 ± 1.5
eGFR (mL/min/1.73m^2)	65.4 ± 24.8
Rejection, n (%)	
Acute rejection	72 (17.1)
Chronic rejection	30 (7.1)
Delayed recovery of graft function, n (%)	68 (16.1)
Medical complications after KT	
DM, n (%)	53 (12.6)
HTN, n (%)	7 (1.7)
Infection, n (%)	
Viral infection	137 (32.5)
Bacterial infection	100 (23.7)
Tuberculosis	10 (2.4)
Fungal infection	9 (2.1)
Follow-up duration, months	93.1 ± 70.8

Values are expressed as means ± SDs, n (%).

DM: diabetes mellitus; eGFR: estimated glomerular filtration rate; HTN: hypertension; KT: kidney transplantation

Table 3. Causes of Graft Failure and Patient Death in Deceased Donor Kidney Transplantation

Variables	
Graft failure, n (%)	97 (23.0)
Cause of graft failure, n (%)	
Acute rejection	24 (24.7)
Chronic rejection	41 (42.2)
Recurrent glomerulonephritis	5 (5.2)
Infection	5 (5.2)
Patient death with a functioning graft	17 (17.5)
Others	5 (5.2)
Patient death, n (%)	36 (8.5)
Cause of patient death, n (%)	
Cardiovascular disease	4 (11)
Cerebrovascular accident	2 (5.6)
Infection	22 (61)
Malignancy	1 (2.8)
Others	7 (19.6)

Values are expressed as means ± SDs, n (%).

Table 4A. Comparison of Baseline Characteristics according to Graft Failure in Deceased Donor Kidney Transplantation

Variables	Non-graft failure (n=325)	Graft failure (n=97)	*P*-value
Recipient			
Age at KT, years	47.7 ± 11.4	40.1 ± 12.5	< 0.001
Male gender, n (%)	184 (55.6)	50 (51.5)	0.416
Body mass index (kg/m^2)	22.3 ± 2.9	21.8 ± 3.5	0.201
KT number, n (%)			0.597
First	267 (82.2)	83 (85.6)	
Second	54 (16.6)	14 (14.4)	
Third	4 (1.2)	0	
Dialysis type before KT, n (%)			0.056
Hemodialysis	279 (85.8)	74 (76.3)	
Peritoneal dialysis	43 (13.2)	21 (21.6)	
Mixed	3 (0.9)	2 (2.1)	
Cause of ESRD, n (%)			
Glomerulonephritis	192 (59.1)	72 (74.2)	0.008
Diabetes mellitus	38 (11.7)	5 (5.2)	0.083
Hypertension	20 (6.2)	10 (10.3)	0.178
ADPKD	10 (3.1)	0	0.126
Others	65 (20.0)	10 (10.3)	0.033

Values are expressed as means ± SDs, n (%).

ADPKD: autosomal dominant polycystic kidney disease; ESRD: end-stage renal disease; HLA: human leukocyte antigen; KT: kidney transplantation; PRA: panel reactive antibody

Table 4B. Comparison of Baseline Characteristics according to Graft Failure in Deceased Donor Kidney Transplantation (continued).

Variables	Non-graft failure (n=325)	Graft failure (n=97)	*P*-value
Co-morbidity, n (%)			
Diabetes mellitus	56 (16.4)	12 (14.8)	0.867
Hypertension	207 (60.7)	53 (65.4)	0.449
Dyslipidemia	27 (8.4)	16 (15.8)	0.038
Hepatitis B virus infection	17 (5.3)	9 (8.9)	0.080
Hepatitis C virus infection	6 (1.9)	0	0.343
Malignancy	16 (5.0)	7 (6.9)	0.410
Donor			
Age at KT, years	42.1 ± 14.8	40.1 ± 15.8	0.224
Male gender, n (%)	227(71.6)	69 (68.3)	0.532
Number of HLA mismatches	3.5 ± 1.7	4.1 ± 1.5	0.001
HLA-AB mismatches	2.3 ± 1.2	2.7 ± 1.1	0.018
HLA-DR mismatches	1.1 ± 0.8	1.4 ± 0.6	<0.001
PRA class I > 50%, n (%)	142 (43.7)	69 (71.1)	< 0.001
PRA class II > 50%, n (%)	145 (44.6)	69 (71.1)	< 0.001
Induction immunosuppressant, n (%)			
Basiliximab	251 (77.2)	48 (49.5)	< 0.001
Thymoglobulin	44 (13.5)	5 (5.2)	0.029
Maintenance immunosuppressant, n (%)			
Tacrolimus	300 (92.3)	68 (70.1)	< 0.001
Cyclosporine	25 (7.7)	29 (29.9)	< 0.001

Values are expressed as means ± SDs, n (%).

ADPKD: autosomal dominant polycystic kidney disease; ESRD: end-stage renal disease; HLA: human leukocyte antigen; KT: kidney transplantation; PRA: panel reactive antibody

Table 5. Comparison of Clinical Characteristics according to Graft Failure in Deceased Donor Kidney Transplantation

Variables	Non-graft failure (n=325)	Graft failure (n=97)	*P*-value
Allograft function at 1 year after KT			
Serum creatinine (mg/dL)	1.3 ± 1.0	2.5 ± 2.2	< 0.001
eGFR (mL/min/1.73m^2)	68.8 ± 21.7	33.0 ± 28.8	< 0.001
Rejection, n (%)			< 0.001
Acute rejection	23 (7.2)	49 (48.5)	
Chronic rejection	8 (2.5)	22 (21.8)	
Delayed graft function, n (%)	47 (14.6)	21 (20.8)	0.162
Medical complications after KT			
DM, n (%)	37 (11.5)	16 (15.8)	0.447
HTN, n (%)	2 (0.6)	5 (5.0)	0.016
Infection, n (%)			
Viral infection	87 (27.1)	50 (49.5)	< 0.001
Bacterial infection	68 (21.2)	32 (31.7)	0.044
Tubercular infection	5 (1.6)	5 (5.0)	0.064
Fungal infection	6 (1.9)	3 (3.0)	0.452
Cardiovascular disease, n (%)	50 (15.6)	12 (11.9)	0.422
Cerebrovascular accident, n (%)	31 (9.7)	9 (8.9)	0.832
Malignancy, n (%)	12 (3.7)	6 (5.9)	0.410
Surgical complications after KT			0.895
Urine leakage, n (%)	2 (0.6)	0	
Lymphocele, n (%)	4 (1.2)	1 (1.0)	
Allograft bleeding, n (%)	5 (1.6)	3 (3.0)	
Wound infection, n (%)	1 (0.3)	0	

Values are expressed as means ± SDs, n (%).

DM: diabetes mellitus; eGFR: estimated glomerular filtration rate; GN: glomerulonephritis; HTN: hypertension; KT: kidney transplantation

Table 6. Risk Factors associated with Graft Failure in Deceased Donor Kidney Transplantation

Variables	Univariate			Multivariate		
	HR	95% C.I.	*P*-value	HR	95% C.I.	*P*-value
Recipient age	0.965	0.947-0.982	<0.001	0.990	0.968-1.012	0.357
Recipient male gender	1.134	0.730-1.760	0.576			
Donor age	1.010	0.994-1.025	0.213			
Donor male gender	1.006	0.627-1.613	0.982			
Thymoglobulin induction	0.328	0.043-2.516	0.283			
Delayed recovery of graft function	1.355	0.773-2.376	0.289			
Acute rejection	14.379	8.023-25.771	<0.001	11.385	5.991-21.637	< 0.001
Chronic rejection	12.951	6.616-25.353	<0.001	10.399	4.947-21.858	< 0.001
HLA mismatches	1.326	1.127-1.559	0.001	1.521	1.227-1.885	< 0.001
PRA class I > 50%	1.643	1.018-2.653	0.042	1.197	0.637-2.249	0.577
PRA class II > 50%	1.668	1.027-2.709	0.039	1.619	0.961-2.725	0.070
Serum creatinine at 12 months after KT	1.272	1.178-1.373	<0.001	1.210	1.093-1.340	< 0.001
Viral infection	2.006	1.292-3.115	0.002	1.859	1.111-3.109	0.018

C.I.: confidence interval; HR: hazard ratio; HLA: human leukocyte antigen; PRA: panel reactive antibody

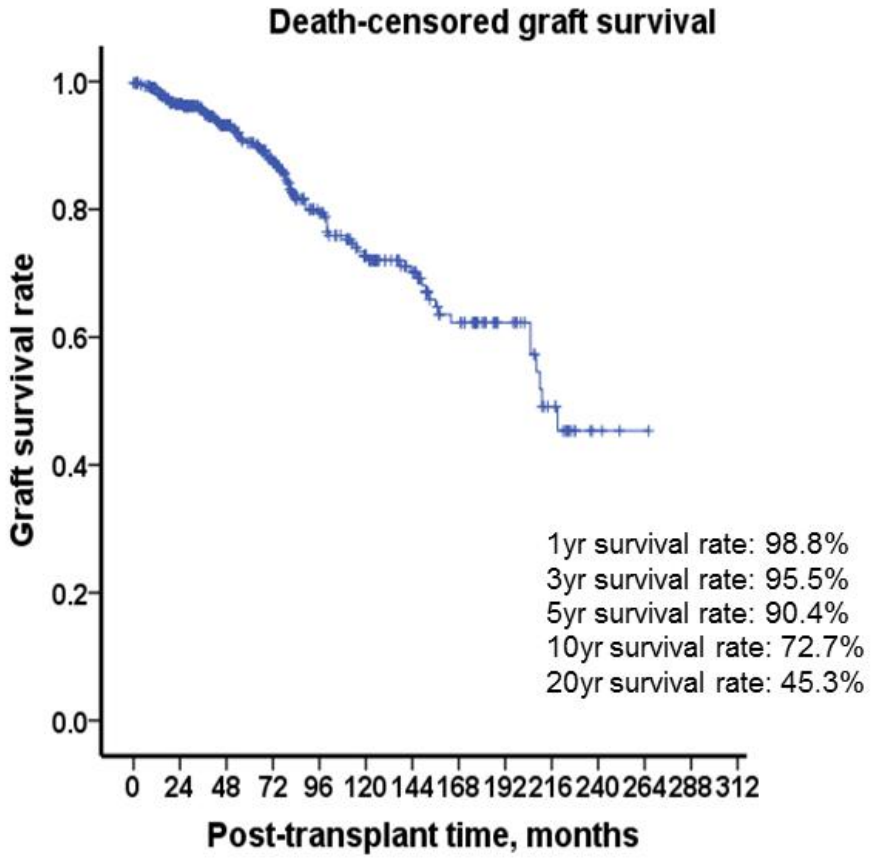

Figure 1. Death-censored graft survival rate in deceased donor kidney transplantation.

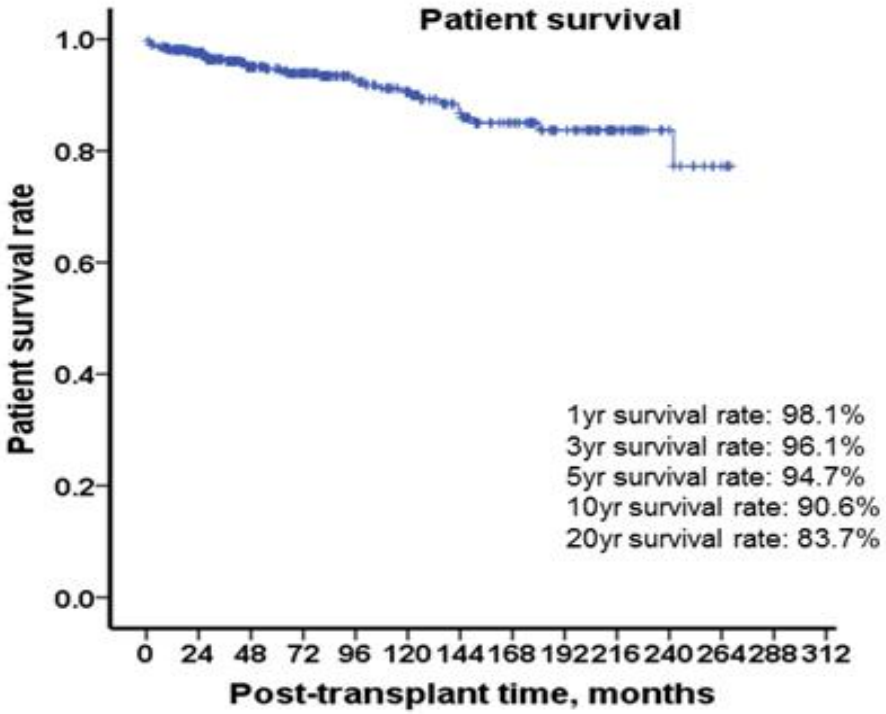

Figure 2. Patient survival rate in deceased donor kidney transplantation.

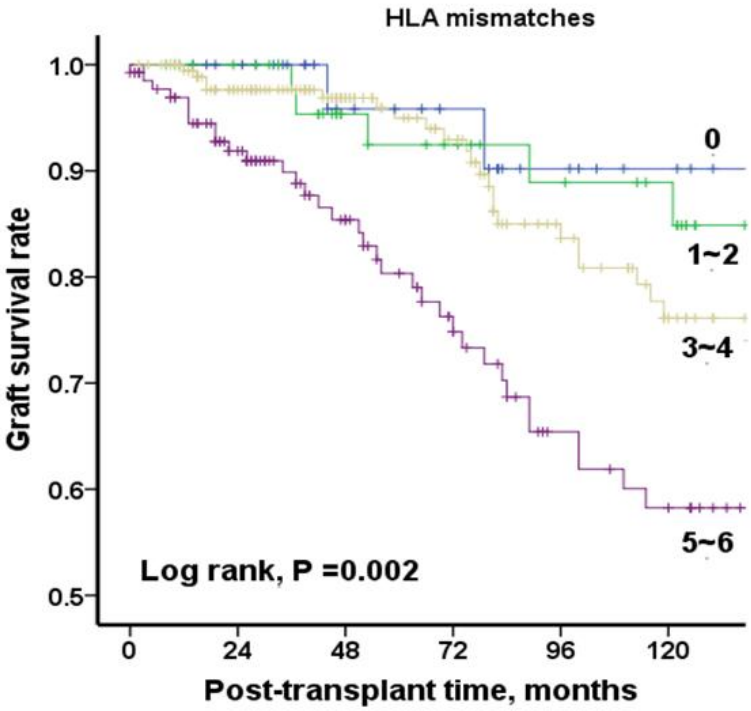

Figure 3. Allograft survival rate according to the number of HLA mismatches in deceased donor kidney transplantation.

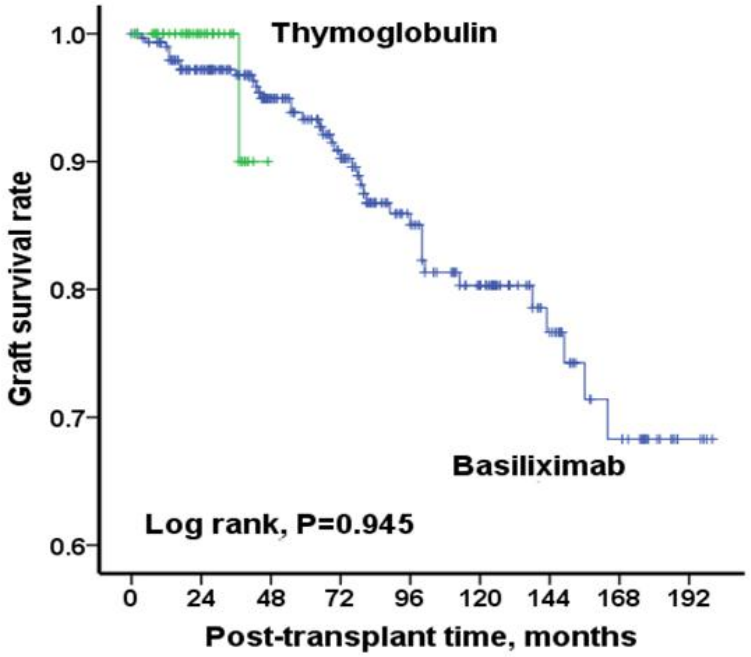

Figure 4. Allograft survival rate according to the induction immunosuppressant in deceased donor kidney transplantation.

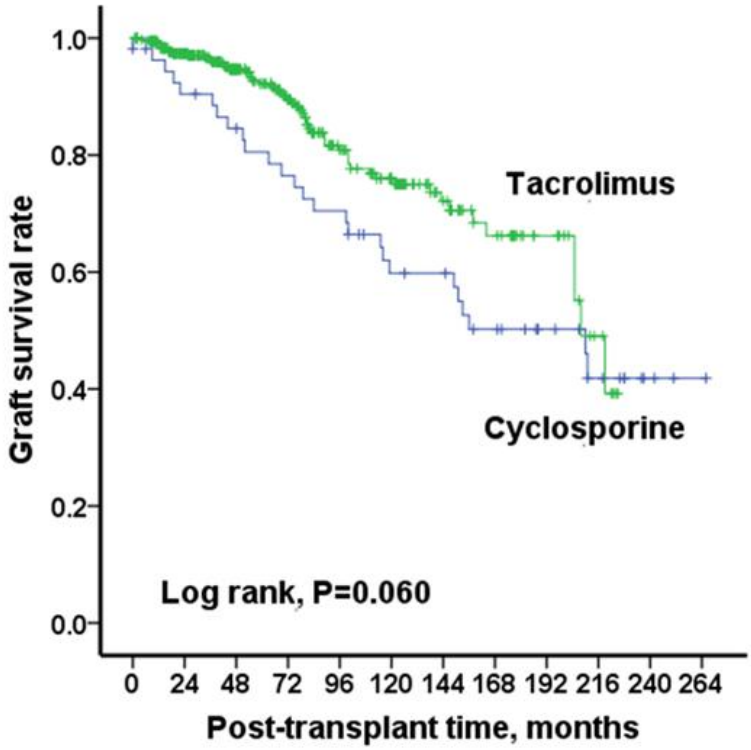

Figure 5. Allograft survival rate according to the maintenance immunosuppressant in deceased donor kidney transplantation.

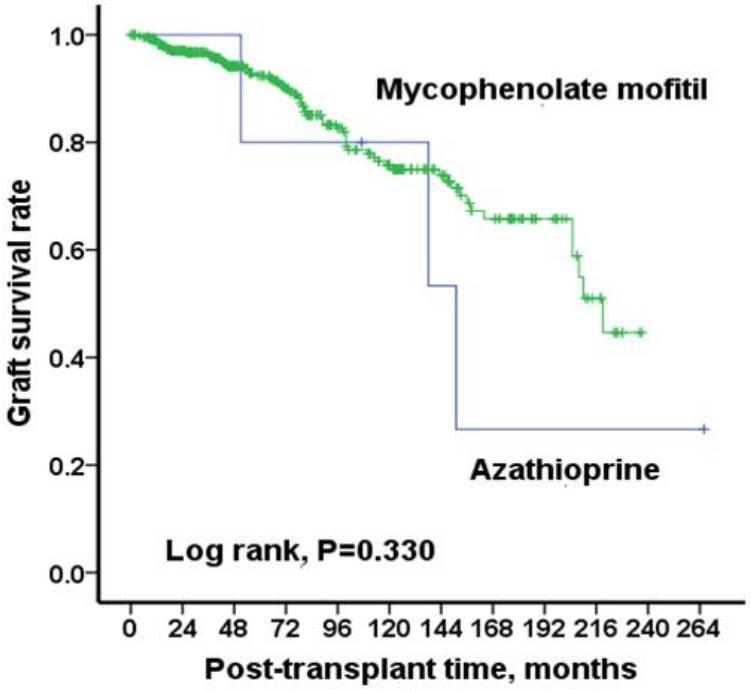

Figure 6. Allograft survival rate according to antimetabolites in deceased donor kidney transplantation.

4. Discussion

The 1-, 3-, 5, 10-year, and 20-year death-censored graft survival rates in DDKT were 98.8%, 95.5%, 90.4%, 72.7%, and 45.3% respectively. In the 2018 United State Renal Data System (USRDS) annual report, the graft survival rates of 1-, 5-, and 10-year graft survival rates in DDKT were 86.8%-93.1%, 66.1%-75.3%, 43.7-48.3%, respectively (8). In the European Renal Association - European Dialysis and Transplant Association (ERA-EDTA) Registry annual report 2015, the 1-, 2,- and 5-year graft survival rates were 90.9%, 88.1%, and 78.9%, respectively (9). The graft survival of our study was not inferior to those of Western countries. In terms of causes of death-censored graft failure, we found that some causes such as rejection and viral infection corresponded to rates reported in previous studies (10-12). In our study, acute and chronic rejections were the most common causes of graft failure, consistent with findings of previous studies. In the early periods after the beginning of DDKT in our center, we used immunosuppressant intensively, maintaining tacrolimus trough levels of 5-10ng/mL for the first 3 months after DDKT because of the high risk of rejection at the early period of KT. However, we reduced the immunosuppressant dose, maintaining tacrolimus trough level 5-10ng/mL for only 1 month and 3-8ng/mL recently. Because of this change of immunosuppressive protocol, the proportion of acute and chronic rejection may have increased. Therefore, appropriate use of immunosuppressant in the early period of DDKT is critical to long-term graft outcome.

The risk factors that influenced graft failure in our study were serum creatinine level at 1 year after KT, acute rejection, chronic rejection,

HLA mismatches, and viral infection. First year serum creatinine level could be a predictor of long-term graft survival (13), as shown in the present study. Rejection is a major impediment to long-term graft survival according to a previous study (14), and several studies performed in United States indicated that HLA mismatches play a substantial role in graft survival (15-16). We showed that these factors were statistically significant. For viral infections, López-Oliva et al. (17) suggested that CMV infection after renal transplantation was a risk factor for long-term graft failure. Heo et al. (18) suggested that HCV infection was associated with decreased long-term graft survival. Despite the fact that we did not classify each viral pathogen separately, viral infection emerged as a significant risk factor for graft failure. Therefore, preventing viral infection and checking donor/recipient immunologic factors may be very important to prevent rejection and improve long term graft outcome.

The 1-, 3-, 5, 10-year, and 20-year patient survival rates in DDKT were 98.1%, 96.1%, 94.7%, 90.6%, and 83.7% respectively. In the 2018 USRDS annual report, the overall patient survival rate of 1-, 5-, and 10-year graft survival rate in DDKT were 93.6%-96.6%, 80.3%-84.7%, 61.1%-64.0%, respectively (8). In the ERA-EDTA Registry annual report 2015, the overall patient survival rate of 1-, 2,- and 5-year graft survival rate were 96.1%, 94.3%, and 88.0%, respectively (9). The outcome of patient survival rate was good as the studies of western countries. A cohort study performed from Brazil found that infection and cardiovascular death were the most prevalent causes of patient death (19), which is consistent with our study results. Because infections caused by use of high doses of immunosuppressant were the most common causes of patient death in our study, using an adequate dose of immunosuppressant is very important.

In contrast with our study, Si Nga et al. and Wong et al. suggested that donor age was a significant factor for long term graft survival (20-21). The disparity might have occurred because our study data showed that both the graft failure and the non-graft failure group had nearly identical age ranges (42.1 ± 14.8 and 40.1 ± 15.8 years, respectively) possibly affect our results. In our study, recipient age was younger in the graft failure group. This may explain why follow-up duration of young recipients was longer than that of older recipients, possibly resulting in a higher proportion of graft failure in young recipients. For PRA, a study performed in China suggested that the patient group with peak PRA > 50% showed poorer graft outcome than did the group with peak PRA < 50% (22). In the present study, the graft failure group showed higher numbers of HLA mismatches and higher PRA, consistent with results of previous studies. Use of immunosuppressant is essential to maintenance of graft function and provision of better long-term graft outcome (23). Comparing basiliximab and thymoglobulin as induction immunosuppressant, there was no significant differences between the two regimens in the present study. The proportion of patients who used thymoglobulin and basiliximab was high, which could explain why thymoglobulin and basiliximab showed better clinical outcomes. However, in Kaplan-Meier curves, there were no significant differences in terms of death-censored graft survival rates between the thymoglobulin and basiliximab groups; furthermore, on multivariate analysis, the induction immunosuppressant was not a significant risk factor for graft failure. The disparity might have occurred because the follow-up duration was different between for groups using thymoglobulin as an induction immunosuppressant after 2013. This is consistent with results of another study reporting that basiliximab and thymoglobulin did not influence long-term clinical

outcomes in DDKT (24).

5. Summary

The factors independently associated with low allograft survival rate were low allograft function at 1 year after KT, higher rejection rate, more HLA mismatch numbers, and higher incidence of viral infections. To improve allograft survival rates in DDKT, careful monitoring for allograft function during the early period after KT and regular work-up for viral infections are necessary. Furthermore, check-up of the donor/recipient's previous immunologic status, including the number of HLA mismatches and stability of immunologic status between rejection and infection would improve long-term survival of allografts.

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Long-term Clinical Outcomes in Deceased Donor Kidney Transplantation: A Single-center Experience

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(Abstract)

Introduction: Deceased donor kidney transplantation (DDKT) remains important despite the fact that its long-term survival rate is lower than that of living donor KT. Therefore, it is necessary to understand the factors related to allograft survival in DDKT. We aimed to evaluate long-term clinical outcomes and factors related to allograft survival in DDKT.

Materials and Methods: This study included 422 patients who received KT from deceased donors at Keimyung University Dongsan Medical Center between October 1997 and October 2017. We investigated graft and patient survival rates, causes of graft failure and patient death, risk factors associated with graft failure, clinical characteristics

according to HLA mismatch number, immunosuppressive agents, and graft failure.

Results: Follow-up duration was 93.1 ± 70.8 months. Death-censored graft survival rates of 1-year, 3-years, 5-years, 10-years, and 20-years were 98.8%, 95.5%, 90.4%, and 72.7%, and 45.3%, respectively. The causes of graft failure were rejection (67%), patient death with a functioning graft (18%), recurrent glomerulonephritis (5.2%), and infection (5.2%). Patient survival rates of 1-year, 3-years, 5-years, 10-years, and 20-years were 98.1%, 96.1%, 94.7%, 90.6%, and 83.7% respectively. The causes of patient death were infection (61%), cardiovascular disease (11%), cerebrovascular accident (5.6%), and malignancy (2.8%). On multivariate analysis, serum creatinine levels at 1 year after KT, incidences of acute and chronic rejection, viral infections, and HLA mismatch number were independent risk factors related to allograft failure in DDKT. As the HLA mismatch number increased, the death-censored graft survival rate became significantly lower; however, there were no significant differences with respect to types of induction

and maintenance immunosuppressant. Allograft function at 1 year after KT in the graft failure group was significantly lower than that of the non-graft failure group. The incidences of acute and chronic rejection, viral and bacterial infections were significantly higher in the graft failure group than in the non-graft failure group.

Summary: The independent factors associated with low allograft survival rate were low allograft function at 1 year after KT, high rejection rate, HLA mismatch number, and viral infection. To improve the allograft survival rate in DDKT, careful monitoring for allograft function during the early period after KT and HLA mismatch number, and maintenance of stable balance of immunologic status between rejection and infection are required.

뇌사자 신장이식에서의 장기적인 임상 결과에 대하여: 단일 센터 연구

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(초록)

배경: 뇌사자 신장이식은 이식신의 공급 부족 문제의 핵심적인 대안 중 하나로 여겨지고 있다. 2015년 기준으로 전체 신장이식에서 약 45%를 차지할 정도로 뇌사자 신장이식이 점차 비중이 늘어가고 있으며, 이식신의 공급 부족 문제를 해결하기 위해 뇌사자 신장이식의 장기적인 성적의 향상이 매우 중요한 문제로 여겨지고 있다. 본 연구는 뇌사자 신장이식에서 장기적인 이식신 생존률 및 임상경과에 영향을 줄 수 있는 인자들에 대해 알아보고자 시행하였다.

방법: 본 연구는 1997년~2017년 동안 계명대학교 동산병원에서 시행한 뇌사자 신장이식 환자 422명을 대상으로 시행하였으며 환자는 '이식신 기능 부전'군 및 '이식신 기능'군으로 분류하였다. 본 연구에서 관련 인자로 이식신 생존률, 신이식 환자 생존률, 이식신 기능 부전의 원인, 신이식 환자 사망 원인, 이식신 기능 부전과 관련된 위험 요인들, 그리고 인간 백혈구 항

원 불일치와 면역억제제와 관련된 임상적 특징들에 대해 조사하였다.

결과: 사망을 배제한 이식신의 1년, 5년, 10년, 20년 생존률은 각각 98.8%, 95.5%, 90.4%, 72.7%, 그리고 45.3%이었다. 이식신 기능 부전의 원인으로는 거부반응 (67%), 환자 사망 (18%), 반복되는 사구체신염 (5.2%), 그리고 감염 (5.2%)이었다. 신이식 환자의 1년, 5년, 10년, 20년 생존률은 각각 98.1%, 96.1%, 94.7%, 90.6%, 그리고 83.7%이었다. 신이식 환자의 사망 원인으로는 감염 (61%), 심혈관계 질환 (11%), 뇌혈관계 질환 (5.6%), 그리고 악성 신생물 (2.8%)이었다. 다변량 분석에 의하면 뇌사자 신장이식 12개월 후의 혈청 크레아티닌 수치, 급성/만성 거부 반응의 발생빈도, 바이러스성 감염, 그리고 인간 백혈구 항원 불일치가 뇌사자 신장이식에 있어 이식신 기능부전에 영향을 미치는 독립적인 인자로 나타났다. 인간 백혈구 항원 불일치가 증가할수록 사망을 배제한 이식신의 생존률은 유의하게 감소하였으나, 유도 면역억제제 및 유지 면역억제제의 차이는 유의한 결과를 나타내지 못했다. '이식신 기능 부전', '이식신 기능'의 두 군을 비교하였을 때, '이식신 기능 부전'군의 뇌사자 신장이식 12개월 후의 이식신 기능이 '이식신 기능'군보다 유의하게 낮은 것으로 나타났다. 급성/만성 거부반응의 빈도, 세균성/바이러스성 감염 빈도는 '이식신 기능 부전'군이 '이식신 기능'

군보다 유의하게 높은 것으로 나타났다.

결론: 이식신 생존률에 영향을 미치는 독립적인 인자들은 신이식 12개월 후의 이식신 기능, 이식신 거부 반응 비율, 인간 백혈구 항원 불일치, 그리고 바이러스성 감염으로 나타났다. 뇌사자 신장이식에서 이식신의 생존률을 증대시키기 위해서는 이식 전 인간 백혈구 항원 불일치 정도의 확인 및 이식 후 초기에 주의 깊게 신기능을 추적하고 이식 후 거부반응과 감염 양쪽을 예방할 수 있도록 적절하게 면역학적인 균형을 유지하는 것이 중요할 것으로 생각된다.