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Repeat Kidney Transplantation After Failed First Transplant in Childhood: Past Performance Informs Future Performance

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Abstract

Background and Objectives—Kidney transplant graft survival is almost uniformly superior for initial transplants compared to repeat transplants. We investigate the association between first and second kidney transplant graft survival in patients who underwent initial transplant during their pediatric years and whether age at second transplant is associated with outcome.

Design, Setting, Participants, and Measurements—This is a retrospective analysis of Organ Procurement and Transplantation Network (OPTN)data from October 1987 to May 2009 examining second kidney graft survival in 2281 patients who received their first transplant at <18 years of age using Kaplan-Meier statistics. Factors associated with second graft survival were identified using a multivariable Cox proportional hazards model.

Results—Patients with first kidney graft survival of >5 years had better second graft survival compared to patients with first graft survival of 30 days-5 years ($p<0.01$). Patients with first

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kidney graft survival less than 30 days had similar second kidney graft outcomes(p=0.50) as those with >5 year first kidney graft survival, demonstrating that very early first graft loss is not associated with poor second transplant outcome. Patients 15-20 years of age at second transplant have lower second graft survival compared to other age groups; p<0.01, regardless of other recipient/donor characteristics and recurrent disease.

Conclusions—Poor second transplant outcomes are identified among patients with previous pediatric kidney transplant with first graft survival >30 days, but < 5 years, and those receiving second transplants at a high risk age category (15-20 years). These groups may benefit from increased attention both pre- and post-transplant.

Keywords

kidney; graft; survival; retransplant; pediatric

Introduction

Patients with end stage renal disease (ESRD) benefit most from kidney transplantation, whether at initial or subsequent transplant.[1-3] Over the last decade, the number of patients relisted after failed kidney transplant has risen.[4-6] However, transplant rates for repeat transplants are lower than for first transplants, in part, due to a relative enrichment of anti-HLA antibody sensitized patients within the retransplant group.[4] Among pediatric patients undergoing initial renal transplant, many will eventually require retransplantation due to their relatively young age and typically fewer exclusionary co-morbid conditions.[1,7,8] In the U. S., pediatric patients retain priority for subsequent transplants under the United Network for Organ Sharing(UNOS)SHARE-35 policy for donors <35 years of age.[9-11] Therefore, retransplantation performed in pediatric years (age <18) can occur at any age under this policy provided that the patient was relisted prior to turning age 18. Consequently, candidates awaiting repeat transplantation are notably younger compared to all registrants on the waiting list, leading to the fact that 52.7% of all repeat kidney transplant candidates are <50 years of age, with more than 20% awaiting retransplant <18 years of age.[4, 12]

Age at transplant is associated with outcome after first kidney transplant. Reports of patients 13-25 years of age demonstrate inferior graft outcomes when transplanted with high quality deceased donor organs compared to recipients of all other ages, and thus are at risk for requiring early repeat organ transplant.[9,13,14] Younger patients(age <10 years) have superior first kidney graft and patient survival compared to those undergoing primary transplant at older pediatric ages.[9,15,16] Whether age at second transplant is associated with graft outcome, even after accounting for previous transplant experience, is unclear. The advancement of pediatric kidney transplantation practices, surgical technique, and immunotherapy, has revealed substantial improvements in first kidney graft and patient survival.[17,18] Despite these changes, some groups of pediatric kidney recipients continue to demonstrate poor graft outcomes regardless of donor quality.[9] Since this group attains the greatest survival benefit from longest graft survival, it is of interest to identify factors associated with high risk for poor outcomes so that intervention may be targeted to these patients.

Renal allograft survival is generally superior for first transplants compared with repeat transplants with decrease in 5-year survival by 5% among adults.[4] Overall organ utility may therefore be impacted by increasing rates of repeat transplantation.[4,5] We report that poor primary renal graft survival among pediatric recipients is associated with inferior second transplant graft survival and that retransplantation within the known higher risk age (15-20 years) group is associated with inferior outcomes regardless of initial graft survival. Identifying modifiable risk factors among these young high risk groups will lend opportunities for developing better interventions to improve allograft survival in the future.

Results

Study Population

Of 415,613 listed subjects, there were 2,281 who received a first kidney transplant at age <18 years and second kidney transplant from October 1987 through May 2009. There were 707 subjects whose second KT graft failed (31.0%). Of these subjects, 574 (81.2%) received a third kidney transplant, accounting for 25.2% of the total study population.

First versus Second Transplant—Group comparisons between first and second transplant are shown in Table1. Theproportion of patients with peak panel-reactive antibody (%PRA) of >80 increased between first and second kidney transplant from 2.2% to 28.2%, p<0.01, while the number of haplo-identical or human leukocyte antigen (HLA) well-matched (3-6 of 6 antigen matched) patients at second transplant decreased from 1,414 (63.5%) to 1,096 (48.4%), p<0.01. We also determined that better first HLA matching correlated with lower peak %PRA level at second transplant (coeff = -0.14; p<0.01). Patients who received second kidney transplant had longer waiting times(median 376 vs 147 days; p<0.01), longer pre-transplant dialysis duration(median 886 vs 320 days; p<0.01), and received more organs with cold ischemia time of >12 hours (54.7% vs 40.2%; p<0.01) compared to their first transplant experience. Evidence of delayed graft function (DGF) after first and second kidney transplant remained relatively constant, 14.1% and 16.6%, respectively, belying the high quality of the donors used in general. (SDC, Table 1) Finally, the majority of first kidney transplants were received from living donors(56.6%), while fewer(36.1%) patients received living donor kidneys at second transplant,(p<0.01) regardless of era at transplant.

First Kidney Graft Survival—Patients grouped by first kidney graft survival were compared. Table2. As expected, patients who were young at first kidney transplant and experienced graft failure within 30 days remained young when they received their second kidney, while those with >5 years of first kidney graft survival were older at second transplant. Primary ESRD diagnosis at first transplant demonstrate more patients with glomerulonephritis (GN; >22%) in the 30 days-1 year and 1-5 year survival groups and more patients with Uropathy/Congenital renal disease (>34%) in the 0-30 days and >5 year survival groups (p<0.01).

The causes of graft failure after first transplant varied. Chronic rejection was more common among patients whose first kidney survivals were 1-5 years and >5 years, while hyperacute/ acute rejection and graft thrombosis/complication was more common for patients whose first

graft survivals were 30 days-1 year and <30 days, respectively; p<0.01. A greater proportion of patients whose first graft survival was 30 days–1 year and 1-5 years had higher %PRA levels(80+), longer pre-transplant dialysis time, and longer waiting times (>36 months) at second transplant compared to other groups, p<0.01. Additionally, patients with first kidney survival of >5 years had a higher proportion of older (>30 years, 53.8%) and living (47.1%) donors at second transplant; p<0.01.(SDC, Table 2)

Recipient Age at Second Transplant—Of patients that were grouped by recipient age at second transplant, 258 (11.3%) were 0-10 years, 280 (12.3%) were 11-14 years, 795 (34.9%) were 15-20 years, and 948 (41.6%) were >20 years of age. The majority of recipients had a low %PRA level (0-20) at second transplant p<0.01. Most patients received deceased grafts at second transplant, although a larger proportion of deceased grafts were reported for the two youngest age groups (<15 years-old; p<0.01) and those with early first graft loss (<30 days; p<0.01). The majority of pediatric patients undergoing repeat kidney transplant had shorter waiting times (p<0.01) and shorter median pre-transplant dialysis days (p<0.01). (SDC, Table 3)

Second Kidney Graft Outcomes

Association with First Kidney Graft Survival—We analyzed second kidney graft survival comparing categories of first graft survival. Figure 1. Patients whose first kidney transplant survival lasted 30 days–1 year also had significantly worse second kidney graft outcomes [log-rank p<0.01; hazard ratio (HR) =1.82; 95% CI 1.32-2.51; p<0.01; Table3], with median survival time of 5.8 [Inter-Quartile Range (IQR) 1.4-11.4] years, p<0.01. A similar effect was seen for recipients whose first graft survived 1-5 years, demonstrating worse second kidney graft survival of 5.8 (IQR 2.6-11.5) years with HR=1.50 (95% CI 1.21-1.87); p<0.01. Conversely, patients with < 30 days of first graft survival experienced a median second graft survival of 9.0 years (IQR 3.4-18.1) years and HR=1.13 (95% CI 0.80-1.59; p=0.50), revealing no difference in survival from the reference population (first graft survival >5 years), with a second kidney survival of 9.4 (IQR 4.6-NA) years.

Association with Recipient Age at Transplant—We then analyzed second kidney graft survival by groups of recipient age at second transplant. Figure 2. Independent of first graft survival, recipients 15-20 years of age at second transplant had worse second kidney graft survival (log rank p<0.01),with median survival of 5.8 (IQR 2.3-13.3) years and an increased risk for graft failure [HR=1.70; 95% CI 1.31-2.20; p<0.01]. Table3. Compared to recipients aged 15-20, median graft survivals for patients age 0-10, 11-14, and >20 years were significantly higher: median survival 10.2 (IQR 4.7-13.6), 9.5 (IQR 4.0-18.4) and 8.6 (IQR 4.2-NA) years, p<0.01, respectively. Patients age 11-14 (p=0.70) and >20 years (p=0.59) had no difference in second transplant graft survival compared to the reference [aged 0-10].

All clinically and statistically relevant factors associated with second kidney graft failure are listed. (SDC, Table 4). Primary diagnoses for ESRD associated with second kidney graft failure include: Drug/Other [HR=1.73; 95% CI 1.12-2.66; p=0.01], and other potentially recurrent diseases (Focal Segmental Glomerulosclerosis/Systemic Lupus Erythematosis/

Hemolytic Uremic Syndrome; FSGS/SLE/HUS) [HR=2.01; 95% CI 1.29-3.13; p<0.01]. Peak %PRA level >80 at second transplant revealed a significant hazards for failure [HR=1.31; 95% CI 1.04-1.66; p=0.02]. Although most patients received dialysis at some point prior to second kidney transplantation, there was a small number of patients (n=107; 4.7%) who underwent pre-emptive repeat transplantation, which conferred a protective effect with HR=0.22 (95% CI 0.09-0.54); p<0.01. As seen in first kidney transplantation, living donor transplantation favored better second kidney graft survival, HR=0.70 (95% CI 0.52-0.95), p=0.02, compared to deceased donor grafts. Although patients in this cohort received organs mostly from donors age 31-50, we found that grafts from older donors (>50 years-old) were significantly associated with increased hazards for graft failure, HR=2.13 (95% CI 1.55-2.92), p<0.01, but showed no association with degree of sensitization (p=0.36). In an analysis of deceased donor recipients alone, we found a similar HR=2.28 (95% CI 1.59-3.26), p<0.01, indicating that older (>50 years) living donors are not contributing significantly to the excess risk of graft loss compared to the entire cohort. Finally, secondary renal grafts from deceased donors less than 50 years of age are not associated with increased graft loss.

Living Versus Deceased Donor Grafts—Upon examining living versus deceased donor grafts and second transplant outcomes, we found that patients with longer first transplant survival times were more likely to have a second transplant from a living donor. Meanwhile, the association between first kidney graft survival time or age at second transplant and second graft outcomes remained the same, regardless of donor type. When deceased donor graft recipients were examined separately, patients with >5 years of first kidney graft survival revealed a significant drop in second graft survival (18.1% decline), but not enough to differentially influence graft survival across groups defined by first graft survival. Therefore, while deceased donor grafts yields yielded inferior survival on average compared to live donor grafts among second kidney recipients, it does not differentially impact graft survival across groups defined by first kidney graft survival.

Upon analyzing living donor second kidney graft recipients alone, median donor age was 37 years (IQR 27-46 years) and the majority of living donors were biologically related (78.2%). There was no association between living donor age or %PRA and graft survival. However, better HLA matching (3-6 antigen match) was associated with favorable graft outcomes (HR=0.67; p=0.04). Exploring this further, among those with at least haplo-identical matched (3+) antigens, 87.0% were blood related (parent/sibling/child) to their donor. This accounted for 32.4% of the total donor population within the entire cohort. Finally, we found that patients whose first kidney survival was 30 days–1 year continued to reflect poorer second kidney outcomes (HR=2.75; p<0.01). Conversely, patients 15-20 years-old had comparable survival compared to other retransplanted age groups with a living donor. Living donor retransplantation was the only identified factor that potentially mitigated poorer outcomes among 15-20 year-old recipients.

FSGS, SLE, HUS Patients—A separate analysis of patients with FSGS, SLE and HUS revealed no difference in second kidney graft survival independently, log-rank p=0.36, so they were analyzed as a single group that are at higher risk of primary disease recurrence.

This group had relatively poorer second kidney graft survival (median survival 5.9 vs 8.3 years <0.01) compared to first graft survival. Using the same modeling strategy as the primary study, this subgroup analysis revealed that differences in hazards among patients grouped by first kidney graft survival time and age at second transplant coincided with outcomes as mentioned in our full model, despite poorer second graft outcomes as a whole group. (*SDC, Results*)

Discussion

Among all pediatric first transplant recipients who receive a second kidney transplant, we found that survival time of the first kidney and recipient age at second transplant are key factors associated with second graft outcomes. While increased risk of graft loss among 18-23 year-olds is known[19], this report of national retransplant data highlights the importance of the first transplant experience and its impact on second transplant outcomes. These factors add to known prognostic cofactors including cause of ESRD, cause of first graft failure, highly recurrent diseases (FSGS, SLE, HUS), and degree of sensitization (%PRA>80).[20,21] In our analysis, the adjusted HR for second graft failure based on first graft survival was more significant in this population than these more well-established risk factors.[20-22] Therefore, the approach to repeat kidney transplantation involves many considerations including the previous transplant experience, even within a pediatric population where the benefit of transplantation is assumed relative to other options of renal replacement therapy.[7]

In our cohort, despite using high quality donor grafts at second transplant, [11, 14, 20] graft survival was negatively affected if first kidney graft survival time was 30 days-5 years (5.8 years) versus 0-30 days and >5 years (9.0 and 9.4 years, respectively). These results suggest that poorer than expected outcomes after first transplant are associated with inferior outcomes after second transplant. Although those with very early first graft loss of <30 days may have experienced technical complications with their initial graft, their loss did not portend poorer second graft outcomes. In a recent study examining the likelihood of retransplantation among patients in the Scientific Registry of Transplant Recipients, pediatric patients with longer previous graft survival and prior preemptive transplantation have increased rates of retransplantation, but the association of initial transplant factors such as graft survival time and age at transplant with survival outcomes of subsequent transplants is not demonstrated as it is here.[21]

Second transplants among 15-20 year-olds have inferior outcomes independent of initial graft survival duration[9, 19, 21], %PRA at second transplant, duration of waiting time, and pre-transplant dialysis duration. We also demonstrated an inverse correlation between HLA matching at first transplant and Peak %PRA level prior to second transplant. Therefore, it is clear that those patients who are better matched in previous transplants are less sensitized, facilitating access to subsequent transplant over those who were previously less well-matched. This fact should be carefully considered before accepting poorly matched deceased donor primary grafts for pediatric patients who are likely to require second transplants later in life. We suspect that the poorer outcomes in this age group are multi-factorial, but poor medical adherence is a likely contributor to early graft loss[22, 23] since recurrence of primary

disease and sensitization were controlled for in our model. This indicates that favorable first graft survival at a young age does not ensure favorable second graft outcomes when transplants are done in recipients in the high risk age group.[19, 21]

We also found that deceased donation yields inferior graft outcomes on average compared to living donation among second kidney transplant recipients, a fact well documented for primary transplants. However, it did not differentially impact graft survival across groups defined by first kidney graft survival category. We also observed that retransplant outcomes in recipients aged 15-20 years were equivalent to other age groups when a live donor allograft was used. Whether this is due to the graft quality itself or whether recipients of live donor second transplants have access to better social support, health-sensitive environments, and systems of care, cannot be ascertained in the current data. These data point to one possible method to address poorer outcomes of second transplants in recipients aged 15-20 - pursue living donor transplantation.[24] In a secondary analysis of donor type at second transplant, pre-emptive transplantation is favored over deceased donor transplantation and dialysis.[24-27] Finally, HLA-matching (3+) mostly due to blood-related donation among living donor recipients, conferred a protective effect on graft survival.[28]

This study has some limitations. Since UNOS data exists from October 1987 onward, we could not analyze patients with exceedingly long first kidney graft survival that have not yet received or been eligible for repeat kidney transplant, and those who experienced first graft failure and were medically/socially deemed unsuitable candidates for repeat transplantation. Large registry data relies heavily on data coding and reporting. Variables such as CMV and hepatitis Cserologies, immunosuppression protocols, desensitization, and warm ischemia time had >30% missing data and were not included in this study. Medication/follow-up adherence, growth and development data cannot be assessed with national data and this limited our ability to assess possible impact on graft failure. Finally, primary ESRD diagnosis at second transplant of “retransplant” is coded for most patients, limiting us from exploring true probability of graft failure associated with diagnosis.

The intent of this study is not to discourage retransplantation in children, adolescents, and young adults, who are generally expected to derive substantial transplant benefit, but rather to stratify risk and target interventions to this group which may have a higher risk of graft failure than has been initially perceived. Patients undergoing repeat kidney transplantation necessitate careful evaluation given their significantly different risks versus patients undergoing first transplantation.[7] Recognition of this phenomenon is crucial in determining an effective approach to the management of these patients. Because the benefits of transplantation only last as long as the graft functions, new approaches to patient/family support, medication adherence, and encouragement to utilize live donor and better-matched deceased donor grafts should be taken with pediatric recipients.

Materials and Methods

Patient Selection

Of 415,613 patients listed in the national dataset, we identified 49,611 repeat kidney transplant recipients registered with UNOS from October 1, 1987, to May 12, 2009. All

subjects with first transplant occurring at <18 years of age (n=3,807) and second transplant at any age were selected. Patients missing key data (age, transplant date, and graft survival) or transplanted after the follow-up period were excluded, leaving 2,281 patients for analysis.[29] (SDC, Figure 1)

Variables and Subject Characteristics

Subject level variables included first kidney graft survival time, transplant performed after SHARE-35 policy implementation (September 28, 2005), recipient age, recipient ethnicity, cause of ESRD or primary diagnosis, pre-transplant diabetes, recipient CMV and Hepatitis C serostatus at transplant, peak %PRA level and HLA match level at first and second transplant, waiting times, pre-emptive transplant (no renal replacement therapy), cold and warm ischemia times, cause of first graft failure, donor variables (deceased vs living, gender, age, ethnicity, CMV serostatus), dialysis duration, and presence of delayed graft function (DGF). DGF was defined as need for dialysis within one week after transplantation. To control for time period differences with respect to available immunosuppression, we included time interval data: era at first and second kidney transplant (1988-1994, 1995-1999, 2000-2005, 2006-2009).(*SDC, Materials and Methods*) First kidney graft survival time groups were defined as 0-30 days, 30 days-1 year, 1-5 years, and >5 years. Age groups at second transplant were defined: 0-10, 11-14, 15-20, and >20 years.

Statistical Analysis

ANOVA, Kruskal Wallis, and Chi-Square tests were used to compare group characteristics, as appropriate. Our primary outcome, second kidney graft survival, was defined as time from second kidney transplant to second kidney graft failure (return to dialysis, pre-emptive retransplant), patient death, loss to follow-up, or censoring by date of last follow up or death with functioning graft.[30,31]

Second kidney graft survival was analyzed using Kaplan-Meier point estimates and log-rank tests. A multivariable Cox regression model was built assessing variables that met nominal significance ($p<0.20$)[30,32] or had clinical relevance and were retained if statistically significant($p<0.05$).[32] Variables removed from the model were tested for evidence of confounding and effect modification using percent hazard difference (>15%) and the likelihood ratio tests (p < or equal to 0.05), respectively.[32,33] The Groennesby and Borgan test determined final model adequacy and the Schoenfeld test of residuals confirmed proportionality of hazards for the final multivariable model.[34,35] All statistical analyses were performed using STATA 12.0/IC statistical software.[36,37] For further details on methods used to conduct this study including variables and statistical methods, please refer to *SDC, Materials and Methods*.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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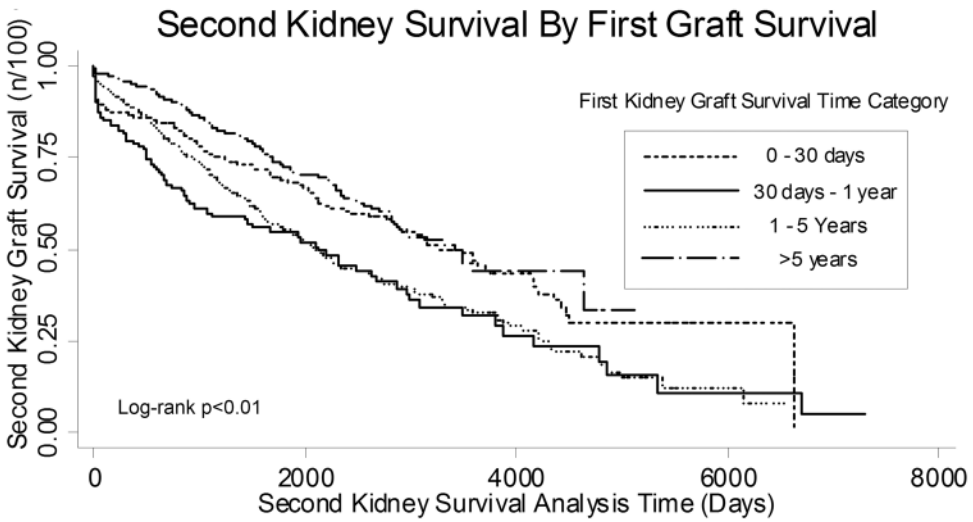
Abbreviations

ANOVA	analysis of variance
CI	confidence interval
CMV	cytomegalovirus
DGF	delayed graft function
ESRD	end stage renal disease
FSGS	focal segmental glomerulosclerosis

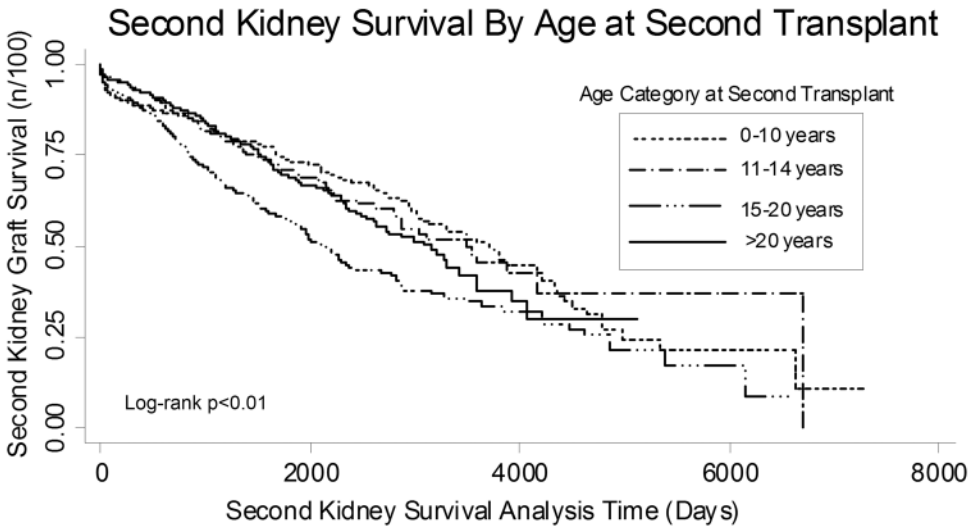
GN	glomerulonephritis
HLA	human leukocyte antigen
HR	hazards ratio
HUS	hemolytic uremic syndrome
IQR	inter-quartile range
OPTN	Organ Procurement and Transplantation Network
%PRA	panel reactive antibody
SLE	systemic lupus erythematosis
UNOS	United Network for Organ Sharing



Median Second Kidney Graft Survival by First Kidney Survival Time

First Kidney Survival Time Category	Median Graft Survival Time
0-30 days	9.0 years
30 days-1 year	5.8 years
1-5 years	5.8 years
>5 years	9.4 years

Figure 1.



Median Second Kidney Graft Survival by Age at Second Transplant

Age Category at Second Transplant	Median Graft Survival Time
0-10 years	10.2 years
11-14 years	9.5 years
15-20 years	5.8 years
>20 years	8.6 years

Figure 2.

Table 1
Baseline Characteristics at First and Second Kidney Transplant

Recipient Characteristics		First Kidney	Second Kidney	P
		N(%)	N(%)	
Gender, Male		1291(66.6)	1291(66.6)	0.99
Age Category at Transplant				<0.01
	0 - 5 yrs	445(19.5)	80(3.5)	
	6 - 10 yrs	478(21.0)	178(7.8)	
	11 - 14 yrs	620(27.2)	280(12.3)	
	15 – 20 yrs[1]	738(32.3)	795(34.8)	
	> 20 yrs	NA	948(41.6)	
Ethnicity				
	White	1466(64.3)	1466(64.3)	0.99
	Black	419(18.4)	419(18.4)	
	Hispanic	315(13.8)	315(13.8)	
	Other[2]	81(3.55)	81(3.5)	
Era at Transplant				
	1988-1994	1299(57.0)	179(7.8)	<0.01
	1995-1999	660(28.9)	461(20.2)	
	2000-2005	265(11.6)	966(42.5)	
	2006-2009	57(2.5)	675(29.5)	
Share 35 Status, N Post Policy		36(1.6)	719(31.5)	<0.01
ESRD Diagnosis at Transplant		N=2208	N=2263	<0.01
	Drug/Other[3]	413(18.7)	171(7.6)	
	Glomerulonephritis	411(18.6)	132(5.8)	
	FSGS/SLE/HUS	323(14.6)	185(8.2)	
	Uropathy/Congenital	729(33.0)	271(12.0)	
	PCKD	133(6.0)	63(2.8)	
	Metabolic Disease	99(4.5)	48(2.1)	
	Retransplant	NA	1345(59.4)	
	Autoimmune Disease	100(4.5)	48(2.1)	
Peak %PRA Category		N=1088	N=1817	<0.01
	0 - 20	978(89.9)	757(41.7)	
	21 - 79	86(7.9)	547(30.1)	
	80+	24(2.2)	513(28.2)	
HLA Match Level		N=2228	N=2263	<0.01
	0 - 2	814(36.5)	1167(51.6)	
	3 - 6	1414(63.5)	1096(48.4)	
Cause of Graft Failure		N=1,859	N=683	<0.01
	Infection/BK Virus/Other	359(19.3)	140(20.5)	
	Hyperacute/Acute Rejection[4]	264(14.2)	137(20.1)	
	Primary Failure	64(3.4)	34(5.0)	

Recipient Characteristics		First Kidney	Second Kidney	P
	Graft Thrombosis/Complication	187(10.1)	45(6.6)	
	Recurrent Disease	117(6.3)	46(6.7)	
	Chronic Rejection	868(46.7)	281(41.1)	
Donor Type				<0.01
	Living	1290(56.6)	824(36.1)	
	Deceased	990(43.4)	1457(63.9)	

ESRD = End-stage renal disease, CMV = cytomegalovirus, FSGS = Focal Segmental Glomerulosclerosis, SLE= Systemic Lupus Erythematosis, HUS = Hemolytic Uremic Syndrome, PCKD = Polycystic Kidney Disease, HLA = Human Leukocyte Antigen, PRA = Panel-Reactive Antibody;

[1]15-20 yrs: All patients listed in the 15-20 year category at first transplant were age 15-17 by inclusion criteria;

[2]Other includes: Asian, American Indian/Alaska Native, Native Hawaiian/other Pacific Islander, Multiracial, Unknown;

[3]Other includes: nephrotoxicity, hypertension, diabetes, malignancy or hematologic disease, and trauma;

[4]Hyperacute/Acute Rejection: Due to low prevalence of hyperacute rejection (n=8), these patients were included in the same group as those who experienced acute rejection.

Significance: p-value<0.05.

Table 2

Baseline Characteristics at Second Transplant Grouped by First Kidney Graft Survival Time

Recipient Characteristics		0-30 days	30 days-1 yr	1-5 years	>5 years	P
		N(%)	N(%)	N(%)	N(%)	
		N=300	N=154	N=687	N=1,140	
Gender, Male		177(59.0)	93(60.4)	353(51.4)	668(58.6)	0.01
Age Category						<0.01
	0 - 10 yrs	111(37.0)	32(20.8)	70(10.2)	45(4.0)	
	11 - 14 yrs	55(18.3)	29(18.8)	81(11.8)	115(10.1)	
	15 - 20 yrs	117(39.0)	61(39.6)	287(41.8)	330(29.0)	
	> 20 yrs	17(5.7)	32(20.8)	249(36.3)	650(57.0)	
Ethnicity						<0.01
	White	177(59.0)	86(55.8)	386(56.2)	818(71.6)	
	Black	63(21.0)	37(24.0)	167(24.3)	152(13.3)	
	Hispanic	52(17.3)	26(16.9)	101(14.7)	137(12.1)	
	Other[1]	8(2.7)	5(3.3)	33(4.8)	33(2.9)	
Era at Transplant						<0.01
	1988-1994	64(21.3)	36(23.4)	71(10.3)	8(0.7)	
	1995-1999	96(32.0)	42(27.3)	180(26.2)	143(12.4)	
	2000-2005	93(31.0)	51(33.1)	268(39.0)	554(48.6)	
	2006-2009	47(15.7)	25(16.2)	168(24.5)	435(38.2)	
Share 35 Status, N Post Policy		51(17.0)	27(17.5)	181(26.4)	460(40.4)	<0.01
ESRD Diagnosis at First Transplant		N=295	N=151	N=665	N=1097	<0.01
	Drug/Other[2]	70(23.7)	29(19.2)	118(17.7)	196(17.9)	
	Glomerulonephritis	46(15.6)	34(22.5)	150(22.6)	181(16.5)	
	FSGS/SLE/HUS	40(13.6)	30(19.9)	113(17.0)	140(12.8)	
	Uropathy/Congenital	101(34.2)	29(19.2)	186(28.0)	413(37.6)	
	PCKD	14(4.8)	13(8.6)	34(5.1)	72(6.5)	
	Metabolic Disease	10(3.4)	12(7.9)	28(4.2)	49(4.5)	
	Retransplant	NA	NA	NA	NA	
	Autoimmune Disease	14(4.7)	4(27)	36(5.4)	46(4.2)	

Recipient Characteristics		0-30 days	30 days-1 yr	1-5 years	>5 years	P
Cause of First Kidney Failure		N=299	N=151	N=657	N=752	<0.01
	Infection/BK Virus/Other	47(15.7)	38(25.2)	152(23.1)	122(16.2)	
	Hyperacute/Acute Rejection	59(19.7)	48(31.8)	101(15.4)	56(7.5)	
	Primary Nonfunction	32(10.7)	1(0.7)	10(1.5)	21(2.8)	
	Graft Thrombosis/Complication	154(51.5)	17(11.3)	9(1.4)	7(0.9)	
	Recurrent Disease	5(1.7)	23(15.2)	55(8.4)	34(4.5)	
	Chronic Rejection	2(0.7)	24(15.9)	330(50.2)	512(68.1)	
Peak %PRA Category at Second Transplant		N=254	N=124	N=575	N=864	<0.01
	0 - 20	120(47.2)	48(38.7)	202(35.1)	387(44.8)	
	21-79	70(27.6)	29(23.4)	184(32.0)	264(30.6)	
	80+	64(25.2)	47(37.9)	189(32.9)	213(24.7)	
HLA Match Level at Second Transplant						<0.01
	0 - 2	175(58.5)	92(60.9)	372(54.2)	528(46.9)	
	3 - 6	125(41.5)	59(39.1)	315(45.9)	598(53.1)	
Cause of Second Kidney Failure		N=116	N=76	N=278	N=213	<0.01
	Infection/BK Virus/Other	28(24.1)	11(14.5)	52(18.7)	49(23.0)	
	Hyperacute/Acute Rejection[3]	31(26.7)	21(27.6)	48(17.3)	37(17.4)	
	Primary Nonfunction	4(3.5)	2(2.6)	16(5.7)	12(5.6)	
	Graft Thrombosis/Complication	15(12.9)	7(9.2)	12(4.3)	11(5.2)	
	Recurrent Disease	4(3.5)	5(6.6)	24(8.6)	13(6.1)	
	Chronic Rejection	34(29.3)	30(39.5)	126(45.3)	91(42.7)	
Donor Type						<0.01
	Living	60(20.0)	36(23.4)	191(27.8)	537(47.1)	
	Deceased	240(80.0)	118(76.6)	496(72.2)	603(52.9)	

ESRD = End-stage renal disease, CMV = cytomegalovirus, FSGS = Focal Segmental Glomerulosclerosis, SLE= Systemic Lupus Erythematosis, HUS = Hemolytic Uremic Syndrome, PCKD = Polycystic Kidney Disease, HLA = Human Leukocyte Antigen, PRA = Panel-Reactive Antibody;

[1]Other includes: Asian, American Indian/Alaska Native, Native Hawaiian/other Pacific Islander, Multiracial, Unknown;

[2]Other includes: nephrotoxicity, hypertension, diabetes, malignancy or hematologic disease, and trauma;

[3]Hyperacute/Acute Rejection: Due to low prevalence of hyperacute rejection (n=8), these patients were included in the same group as those who experienced acute rejection.

Significance: p-value<0.05

Table 3
Multivariable Cox Regression Model of Second Kidney Graft Failure

Variable Name	HR(CI)	P
First Graft Survival Time		
0-30 days	1.13(0.80-1.59)	0.50
30 days-1 yr	1.82(1.32-2.51)	<0.01
1-5 years	1.50(1.21-1.87)	<0.01
>5 years	Reference	
Age at Second Transplant		
0-10 years	Reference	
11-14 years	1.06(0.77-1.47)	0.70
15-20 years	1.70(1.31-2.20)	<0.01
>20 years	1.10(0.81-1.49)	0.59
Ethnicity		
White	Reference	
Black	1.15(0.92-1.43)	0.21
Hispanic	1.06(0.81-1.39)	0.66
Other[1]	0.98(0.64-1.50)	0.93
Era at Second Transplant (Year)		
1988-1994	Reference	
1995-1999	1.12(0.87-1.46)	0.38
2000-2005	0.81(0.61-1.08)	0.16
2006-2009	0.76(0.51-1.15)	0.20
ESRD Diagnosis at First Transplant		
Polycystic Kidney Disease	Reference	
Other[2]/Drug	1.73(1.12-2.66)	0.01
Glomerulonephritis	1.45(0.94-2.23)	0.09
FSGS/SLE/HUS	2.01(1.29-3.13)	<0.01
Uropathy/Congenital	1.48(0.98-2.25)	0.07
Metabolic Disease	1.55(0.90-2.69)	0.12
Autoimmune Disease	1.74(1.00-3.03)	0.05
Cause of First Kidney Graft Failure		
Other/Infection/BK Virus	Reference	
Hyperacute/Acute Rejection	1.21(0.92-1.59)	0.18
Primary Non-Function	1.24(0.72-2.16)	0.44
Graft Thrombosis/Complication	0.83(0.59-1.19)	0.32
Recurrent Disease	1.39(0.96-2.01)	0.08
Chronic Rejection	1.04(0.82-1.31)	0.76
Peak %PRA Category at Second Transplant		
0-20	Reference	
21-79	1.15(0.92-1.43)	0.22
80+	1.31(1.04-1.66)	0.02

Variable Name	HR(CI)	P
Unknown	1.10(0.83-1.47)	0.48
HLA Match Level at Second Transplant		
0-2	Reference	
3-6	0.87(0.73-1.04)	0.13
Pre-emptive Transplant	0.22(0.09-0.54)	<0.01
Cold Ischemia Time At Second Transplant		
<12 hr	Reference	
12-24 hr	1.04(0.81-1.35)	0.73
>24 hr	1.22(0.92-1.62)	0.17
Donor Type at Second Transplant		
Deceased	Reference	
Living	0.70(0.52-0.95)	0.02
Donor Age Category at Second Transplant		
0-5 yrs	1.31(0.77-2.23)	0.31
6-10 yrs	0.80(0.47-1.36)	0.41
11-14 yrs	1.03(0.66-1.62)	0.89
15-20 yrs	Reference	
21-30 yrs	0.96(0.72-1.27)	0.77
31-50 yrs	1.28(1.00-1.64)	0.05
>50 yrs	2.13(1.55-2.92)	<0.01
Donor Ethnicity at Second Transplant		
White	Reference	
Black	1.26(0.97-1.65)	0.08
Hispanic	0.82(0.61-1.12)	0.21
Other	1.51(0.92-2.48)	0.10

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[1]Other includes: Asian, American Indian/Alaska Native, Native Hawaiian/other Pacific Islander, Multiracial, Unknown;

[2]Other includes: nephrotoxicity, hypertension, diabetes, malignancy or hematologic disease, and trauma;

Significance: p-value<0.05