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Living Donor Age and Kidney Transplant Outcomes

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We assessed the relationship between living donor (LD) age and kidney survival in 1063 adults transplanted between 1980 and 2007. Increasing LD age was associated with lower kidney function (GFR) before and after transplantation and loss of GFR beyond 1 year. Increasing LD age was also associated with low-moderate proteinuria posttransplant (151–1500 mg/day, $p < 0.0001$). By univariate analysis, reduced graft survival related to lower GFR at 1 year [HR = 0.925 (0.906–0.944), $p < 0.0001$], proteinuria [HR = 1.481 (1.333–1.646), $p < 0.0001$] and increasing LD age [HR = 1.271 (1.219–1.326), $p = 0.001$]. The impact of LD age on graft survival was noted particularly >4 years posttransplant and was modified by recipient age. Thus, compared to a kidney graft that was within 5 years of the recipient age, younger kidneys had a survival advantage [HR = 0.600 (0.380–0.949), $p = 0.029$] while older kidneys had a survival disadvantage [HR = 2.217 (1.507–3.261), $p < 0.0001$]. However, this effect was seen only in recipients <50 years old. By multivariate analysis, the relationship between LD age and graft survival was independent of GFR but related to proteinuria. In conclusion, LD age is an important determinant of long-term graft survival, particularly in younger recipients. Older kidneys with reduced survival are identifiable by the development of proteinuria posttransplant.

Key words: Donor age, graft survival, living donor kidney transplantation, proteinuria

Abbreviations: ANOVA, analysis of variance; CI, confidence interval; DGF, delayed graft function; D-Rage, the difference between donor and recipient age; DoR, donor was more than 5 years older than the recipient; DR, donor was within ±5 years of the recipient age; DyR, donor was at least 5 years younger than the recipient; HR, hazard ratio; LD, living donor; MDRD, Modification of Diet in Renal Disease; SBP, systolic blood pressure.

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Introduction

Donor age is considered to be a strong determinant of death-censored graft survival at least among recipients of deceased donor kidneys (1). It is interesting to note that in the early transplant literature (before 1990) the impact of deceased donor age on kidney graft survival was not appreciated (2). However, increasing success of transplantation led to longer observation times and the recognition that increasing deceased donor age is an important determinant of death-censored graft survival (3), particularly beyond 5 years posttransplant (4). The reason(s) behind this relationship are likely complex but it has been suggested that at least in part it relates to the biology of the older kidney which limits its capacity to tolerate injury (5). In apparent conflict with this hypothesis, the relationship between living donor (LD) age and graft survival is less clear (6,7). In part, this may be due to the difficulty of separating the relationship between LD age and graft survival from other important variables including, (1) the progressive decline in kidney function associated with aging (8,9); and (2) the fact that kidneys from older donors are more frequently transplanted into older recipients thus potentially confounding the impact of donor age.

Recipient age is an important modifier of the relationship between donor age and graft survival. Compared to younger recipients, older recipients are more likely to receive kidneys from older donors and are also more likely to have a shorter posttransplant survival. This shorter follow-up time of older recipients may have the effect of 'protecting' the allograft from death-censored graft failure. Thus, increasing recipient age is associated with worse patient survival but better death-censored graft survival (10). These observations have been applied in the clinic by assigning older deceased donor kidneys to older recipients (11). However, a similar practice has not been generally adopted in LD transplantation. These data suggest that to fully understand the possible impact of LD age on graft survival we need to consider age of the recipient in the analysis particularly relative to the age of the donor. Furthermore, the definition of 'younger' or 'older' donor needs to be considered relative to the recipient age. This strategy was employed in this and in previous studies (12).

Over the last decade there has been a progressive increase in the use of LD organs. Furthermore, the characteristics of the LD have changed, particularly with the acceptance of progressively older LD. The goal of this study was to examine the relationship between LD age, graft function and graft survival in a large cohort of LD recipients who received their allograft over the past three decades in one institution.

Methods

Patient population

The study cohort included all adult (older than 18 years of age) first kidney allograft recipients of a LD kidney transplanted at Mayo Clinic, Rochester, MN, USA, between January 1980 and December 2007. Recipients of nonrenal solid organs or bone marrow transplants before, after or at the time of the kidney transplant and recipients of ABO-incompatible and/or positive crossmatch transplants were excluded from these analyses. After application of these selection criteria, 1063 candidates qualified for the study. Recipient and donor clinical and laboratory information were obtained from electronic medical records. The institutional review board approved this study and the collection of data.

The selection of an LD in our program is guided primarily by the health of the donor and not by donor age or HLA matching. Donor GFR prior to donation was measured by nonradiolabeled iothalamate clearance (13). Potential LDs were excluded if their iothalamate clearance was less than the 5 percentile of the normal according to age and/or had significant proteinuria (urine protein more than 150 mg/day or urine albumin more than 30 mg/day). All donor nephrectomies were done by the hand-assisted laparoscopic technique. Kidney allograft function posttransplant was assessed by serum creatinine, estimated GFR using the Modification of Diet in Renal Disease (MDRD) equation (14) and iothalamate clearance. Changes in allograft function over time were assessed as the slope of the reciprocal of serum creatinine by simple linear regression method. GFR slopes were analyzed at three intervals: first 5 days, from day 5 to 365 and from 1 to 5 years. Delayed graft function (DGF) was defined as the need for dialysis during the first week posttransplant. Urinary protein excretion was measured in 24-h urine samples at 1-year posttransplant.

Immunosuppression consisted of induction with antithymocyte globulin in 610 patients (69.6%), anti-CD25 antibodies in 85 (9.7%), alemtuzumab in 45 (5.2%), and OKT3 in 2 (0.2%). One hundred and thirty-four (15.3%) patients did not receive induction immunosuppression. In 187 patients information on induction was not available. Maintenance immunosuppression during the first year posttransplant most commonly included tacrolimus, mycophenolate mofetil and corticosteroids (N = 649, 64.3%). Cyclosporine was used instead of tacrolimus in 230 patients (22.8%) and sirolimus instead of either calcineurin inhibitor in 59 (5.8%). Seventy-two patients (7.1%) received prednisone and azathioprine during the first year posttransplant. Overall, 23.7% of patients received azathioprine instead of mycophenolate mofetil during the first year posttransplant.

Data analysis

Data were expressed as percentage for categorical variables and as mean and standard deviation for continuous variables unless otherwise stated. Proportions between two groups were compared by chi-square. Numerical differences between two groups were assessed by Student's *t*-test or Wilcoxon if the data were not uniformly distributed. Analysis of variance (ANOVA) and Kruskal–Wallis were used for comparison of data among several groups. Patient and graft survival were compared by Kaplan–Meier plots and Cox regression. LD age was analyzed as a continuous variable, in decade intervals or as the difference between LD and recipient age (D-Rage). All reported p values are two-sided. A p value of less than 0.05 was considered to indicate statistical significance.

Table 1: Patient characteristics

Parameter	Value (%)
Number of patients	1063
Recipient age (years)	48.0 ± 15.4
Recipient sex (% males)	725 (68.2)
Recipient race (% Caucasian)	892 (93.1)
Donor age (years)	42.2 ± 12.0
Donor sex (% males)	491 (46.2)
Donor race (% Caucasian)	99.4%
Donor type, number (%):	
Living related	761 (71.6)
Living unrelated	302 (28.4)
Primary renal disease, number (%)	
Glomerular disease	401 (41.3)
Diabetes mellitus	137 (14.1)
Polycystic kidney disease	129 (13.3)
Hypertension	106 (10.9)
Unknown	48 (4.9)
Others	150 (15.5)
Preemptive transplant[1]	44.6%
HLA mismatches (median)	2.8 ± 1.7 (3)
Follow-up time in months, (median)	97.5 ± 70.7 (77)

[1]Percentage of patients receiving no dialysis prior to the transplant.

Results

Characteristics of study population (Table 1)

This population included a high proportion of Caucasians among both LD (99.4%) and recipients (93.1%), a racial distribution representative of geographic location of this transplant program. A relatively large proportion of transplant recipients in this cohort (44.6%) received preemptive kidney transplants, that is, without receiving pretransplant dialysis.

The age of LD increased progressively from 1980 to 2007 ($r = 0.221$, $p < 0.0001$). Thus, mean donor age was 36.6 ± 12.7 years between 1980 and 1989; 40.8 ± 11.5 between 1990 and 1999; and 43.8 ± 11.6 between 2000 and 2007. Between 1980 to 1985, 100% of LD in this cohort were blood relatives of their recipient while between 2002 and 2007 this figure declined to 59.5%.

LD age, graft function and proteinuria

Increasing LD age related to progressively lower predonation GFR and lower graft function, 1-year posttransplant measured as higher serum creatinine, lower estimated GFR and lower iothalamate clearance ($p < 0.0001$, Table 2). To further examine the reasons for the lower posttransplant GFR observed in recipients of older LD we estimate the change in GFR during three posttransplant periods: (1) During the first 5 days posttransplant, older LD

Table 2: Donor age, donor GFR and kidney graft function posttransplant

Parameter	Donor age (decades)					p
	18–30	31–40	41–50	51–60	>60	
Number of patients (%)	168 (16%)	290 (27%)	330 (31%)	186 (18%)	89 (8%)	
Donor: GFR[1] predonation	110.9 ± 16.1	106.0 ± 15.2	102.1 ± 14.1	95.9 ± 13.9	87.5 ± 12.3	< 0.0001[3]
Recipient[5]						
Serum creatine (mg/dL)	1.39 ± 0.64	1.41 ± 0.40	1.50 ± 0.44	1.66 ± 1.45	1.72 ± 0.61	0.0002[3]
Estimated GFR[2]	61.3 ± 18.9	55.7 ± 14.3	52.4 ± 13.5	49.9 ± 12.2	43.6 ± 12.2	< 0.0001[3]
GFR[1]	65.4 ± 19.7	59.6 ± 16.4	57.2 ± 16.9	55.6 ± 15.8	44.5 ± 13.3	< 0.0001[3]
GFR slopes						
0–5 days (mL/min/day)	13.3 ± 6.2	12.0 ± 5.7	11.5 ± 5.8	10.2 ± 4.8	9.3 ± 5.2	< 0.0001[4]
5–365 days (mL/min/mo)	0.38 ± 1.81	0.32 ± 1.70	0.16 ± 1.68	0.24 ± 1.35	0.15 ± 1.66	0.148[4]
1–5 years (mL/min/mo)	0.03 ± 0.45	0.01 ± 0.35	–0.02 ± 0.43	–0.02 ± 0.35	–0.15 ± 0.34	0.016[4]

[1]Iothalamate GFR in ml/min/1.73 m^2.
[2]Estimated GFR by Modification of Diet in Renal Disease (MDRD) equation.
[3]ANOVA.
[4]Kruskal–Wallis nonparametric test.
[5]Kidney function measured 1 year posttransplant.

kidneys had a slower rate of increase in GFR compared to younger LD (Table 2). This observation was also confirmed in a subgroup of patients who did not have DGF posttransplant (data not shown). The incidence of DGF in recipients of LD younger than 60 years old was 2.5% and in recipients of LD older than 60 years old was 6.8% ($p = 0.03$); (2) From day 5 to 365, average GFR slopes were positive and did not relate significantly to LD age although they were numerically lower in older donors (Table 2); (3) From year 1 to 5, GFR slopes were significantly more negative as LD age increased. In summary, compared to younger LD kidneys, older LD kidneys had a lower baseline GFR, did not achieve as much function following transplantation and started a more rapid decline in GFR after the first year posttransplant.

Increasing LD age related to increasing levels of proteinuria at 1-year posttransplant ($N = 754$, $p < 0.0001$, Kruskal–Wallis). This relationship remained unchanged when patients treated with sirolimus were excluded from the analysis. The percentage of recipients with normal levels of protein in the urine (<150 mg/day) decreased progressively from 67.7% in recipients of LD younger than 30 years old to 44.4% in recipients of LD older than 60 years old (Figure 1). Conversely, increasing LD age was associated with an increased percentage of recipients with low (151–500 mg/day) and moderate (501–1500 mg/day) levels of proteinuria ($p = 0.021$). In contrast, the percentage of recipients with higher levels of proteinuria (>1500 mg/day) did not relate to LD age.

Increasing LD age was associated with increasing levels of systolic blood pressure (SBP) in the recipient 1-year posttransplant. However, by multivariable analysis this relationship was explained by the fact that recipients of older LD kidneys were also older (see later). LD age did not relate significantly to diastolic BP or with the incidence of acute rejection or polyoma virus nephropathy during the first year posttransplant (data not shown). Finally, LD age did not relate to the percentage of patients with anti-HLA class I or anti-HLA class II antibodies pretransplant (data available in most patients transplanted since 1/1/2000, $N = 498$).

LD age, patient and death-censored graft survival

During a follow-up period of 97.5 ± 70.7 months, 176 recipients (16.6%) died with a functioning graft and 134 (12.6%) lost their allograft not due to patient death. By univariate analysis increasing LD age related to worse patient survival [HR = 1.232 (1.088–1.394) for every decade increase in LD age, $p = 0.001$]. However, this relationship was explained by the fact that recipients of older LD kidneys were also older. Thus, by multivariate analysis reduced patient survival in this cohort related to increasing recipient age [HR = 1.916 (1.837–1.998) for every decade increase in recipient age, $p < 0.0001$] and to the diagnosis of diabetes pretransplant [HR = 2.573 (1.797–3.580), $p < 0.0001$], but did not relate significantly to LD age.

By univariate analysis, increasing LD age related to reduced death-censored graft survival [HR = 1.271 (1.219–1.326) for every decade increase in LD age, $p = 0.001$] (Figure 2). Compared to recipients of kidneys from LD younger than 30 years old, the risk of graft failure in recipients of kidneys between 31 and 40 years was not significantly increased [HR = 1.107 (0.635–1.930), $p = 0.720$]. However, as LD age increased beyond 40 years the risk of graft failure increased progressively: LD age between 41 and 50 years [HR = 1.777 (1.052–3.002), $p = 0.032$]; LD age between 51 and 60 years [HR = 1.796 (0.986–3.273), $p = 0.056$]; and LD older than 60 years [HR = 2.611 (1.311–5.199), $p = 0.006$]. Most kidney grafts were lost when they were relatively young. Thus, at the time of graft loss the median age of the kidney was 50 (mean 49.9 ± 12, range 20–75).

Increasing LD age related to increasing recipient age ($r = 0.182$, $p < 0.0001$). However, as suggested by this

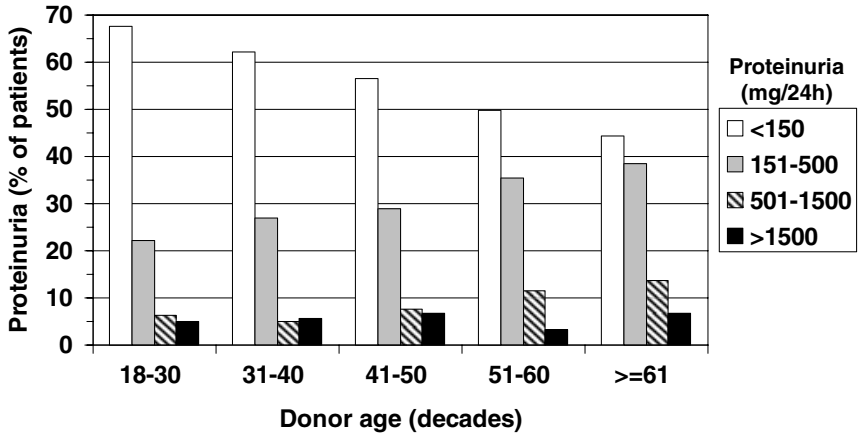

Figure 1: Urine protein levels measured in 24-h urine samples collected one year posttransplant. Open bars: proteinuria <150 mg/day (normal range); gray bars: proteinuria between 151 and 500 mg/day; stripped bars: proteinuria between 501 and 1500 mg/day; black bars: proteinuria greater than 1500 mg/day.

statistically weak association, there were significant age differences between LD and recipient age in this cohort. To assess the impact of these differences donor/recipient pairs were divided into following groups: (1) 477 pairs (45%) where the donor was at least 5 years younger than the recipient (DyR); (2) 379 pairs (35%) where the donor was within ±5 years of the recipient age (DR); and (3) 207 pairs (20%) where the donor was more than 5 years older than the recipient (DoR) (Table 3). The DyR group included older recipients who received kidneys from younger donors. In contrast, the DoR included younger recipients who received kidneys from relatively older donors. Compared to the DR group, recipients in the DyR group had a significant graft survival advantage [HR = 0.600 (0.380–0.949), p = 0.029] while recipients in the DoR group had a significant graft survival disadvantage [HR = 2.217 (1.507–3.261), p < 0.0001] (Figure 3A). The impact of the difference between donor and recipient age (D-Rage) on graft survival was noted particularly in younger recipients (Figure 3B). Thus, in recipients younger than 50 years (approximate median age of the recipient population, N = 570) D-Rage had a significant impact on graft survival [HR = 1.030 per 1 year difference in donor/recipient age (1.017–1.043), p < 0.0001]. In contrast, in recipients older than 50 years old (N = 493) there was no significant relationship between D-Rage and death-censored graft survival [HR = 1.017 (0.989–1.045), p = 0.227] (Figure 3C). It should be noted that in recipients older than 50 years old the DoR group was quite small (N = 16).

In addition to donor age, the following variables related to death-censored graft failure by univariate analysis: donor GFR pretransplant [HR = 0.971 (0.958–0.985), p < 0.001], recipient age [HR = 0.975 (0.963–0.987), p < 0.001], months on dialysis pretransplant [HR = 1.001 (1.000–1.001), p = 0.007], DGF [HR = 4.661 (2.393–9.080), p < 0.001], HLA mismatches [HR = 1.246 (1.106–1.405), p < 0.001], GFR at 1 year posttransplant [HR = 0.925 (0.906–0.944), p < 0.001] and proteinuria at 1 year posttransplant [HR = 1.481 (1.333–1.646), p < 0.001]. In contrast, the following variables were found to be not significantly related

Table 3: Donor and recipient characteristics classified according to the age difference between LD and recipients

	Donor-recipient age difference[1]			
Variables	DyR	DR	DoR	p
Number of patients (%)	477 (45%)	379 (35%)	207 (20%)	
Donor demographics				
Age (years)	36.7 ± 9.7	44.4 ± 12.1	51.1 ± 9.8	0.0001[3]
% Males	47%	46%	43%	NS[4]
BMI (kg/m^2)	27.6 ± 5.1	27.8 ± 5.0	27.4 ± 4.3	NS[3]
GFR[2] pretransplant	105.7 ± 15.9	101.5 ± 15.4	95.6 ± 14.6	0.0001[3]
Recipient demographics				
Age (years)	58.1 ± 11.4	44.7 ± 12.1	31.0 ± 10.5	0.0001[3]
% Males	69%	68%	67%	NS[4]
BMI (kg/m^2)	28.4 ± 5.6	27.2 ± 5.8	25.5 ± 5.7	0.0001[3]

[1]DyR: donor at least 5 years younger than recipient; DR: donor within ±5 years of recipient age; DoR: donor at least 5 years older than recipient.
[2]GFR in mL/min/1.73 m^2.
[3]ANOVA.
[4]Chi square
NS, nonsignificant.

to death-censored graft survival: donor gender, donor BMI, donor type (living related vs. living unrelated), recipient gender, recipient BMI, pretransplant diabetes, preemptive transplant, acute rejection during 1 year posttransplant, induction therapy, immunosuppressive regimens and year of transplant.

We next analyzed other variables that could explain the relationship between D-Rage and death-censored graft survival. A multivariate analysis including all of the pretransplant variables related to graft survival (except recipient age since it is highly related to D-Rage) is shown in Table 4, Model 1 (581 patients included in this analysis). In this model, D-Rage remained significantly related to death-censored graft survival and in particular this relationship was independent of the LD GFR pretransplant.

Table 4 also displays two additional multivariate models including posttransplant variables related to death-censored graft survival. The first of these models (Table 4, Model 2, 504 patients included in this analysis) showed that D-Rage is related to graft survival independently of all other posttransplant variables in this analysis, including graft function at 1 year. Additional models were constructed including rather than GFR at 1 year, the slope of the reciprocal of the serum creatinine at different time intervals. All of those models (results not shown) confirmed the result of Model 2, that is the relationship between D-Rage and graft survival is statistically independent of graft function. In contrast to these findings, in a final statistical model including posttransplant variables (Table 4, Model 3, 413 patients included in this analysis) the relationship between D-Rage and graft survival was noted to be not independent from the presence of proteinuria 1 year posttransplant.

Discussion

This analysis confirms previous observations that the median age of LD and the use of living unrelated donors have increased significantly over the last three decades. The increasing use of older LD emphasizes the relevance of assessing the relationship between LD age, graft function and/or survival. These results showed clearly that increasing LD age is associated with reduced death-censored graft survival. However, it is important to note that the reduction in survival is apparent particularly after 4 years posttransplant. This observation is consistent with previous studies in deceased donors (4) showing that the relationship of donor age and graft survival is evident after long periods of follow-up. This observation likely explains why some studies have found no significant association between LD age and graft survival over relatively short periods of follow-up (7).

These results showed that the magnitude of the impact of LD age on graft survival is conditioned in large part by the age of the recipient. In older recipients, patient survival is the main limitation to length of graft survival. In contrast, in younger recipients death-censored graft survival is the main limitation of the success of kidney transplantation. In practical terms, these results indicate that selecting an LD based on donor age would have little impact on the success of kidney transplantation in older recipients.

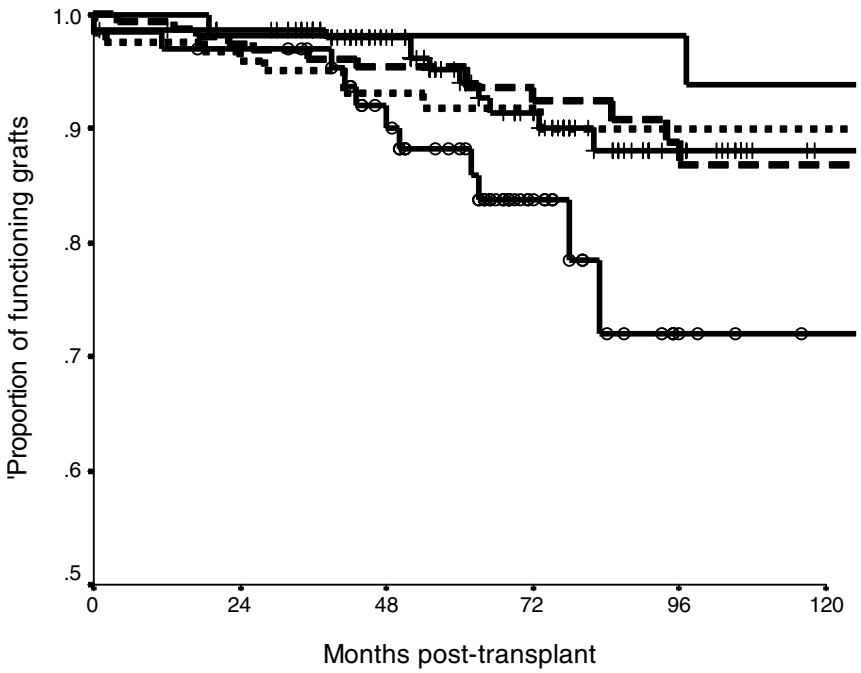

Figure 2: Relationship between donor age (in decades) and death-censored graft survival. Groups include donors between 18 and 30 years old (—); donors between 31 and 40 years old (– – –); donors between 41 and 50 years old (+ — +); donors between 51 and 60 years old (. . .) and donors older than 60 years old (—) ($p = 0.014$, Log Rank).

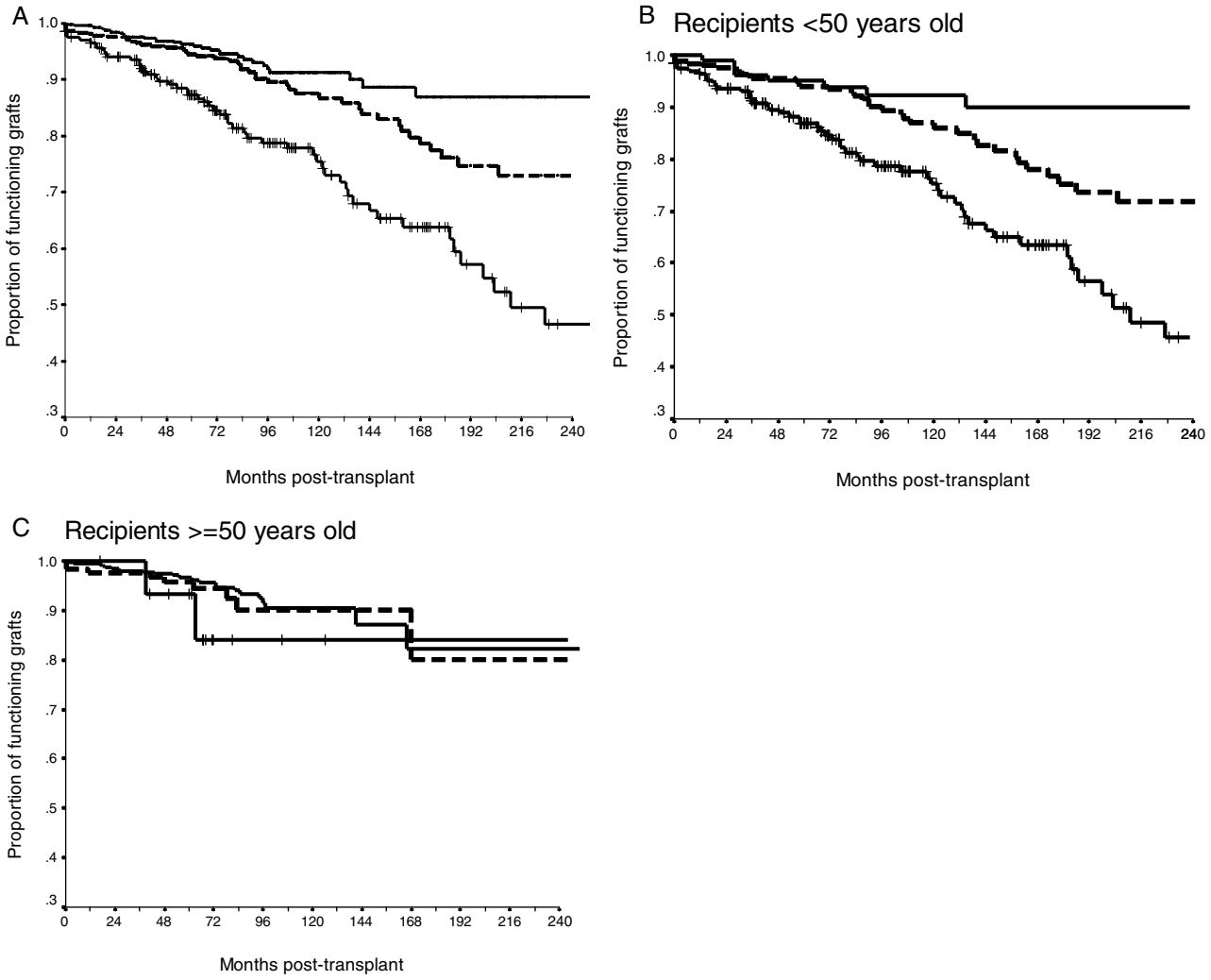

Figure 3: Death-censored graft survival in patients classified according to the age difference between donor and recipient. (A) All recipients in the cohort (N = 1063, p < 0.0001, Log Rank); (B) recipients younger than 50 years old (N = 552, p < 0.0001); (C) recipients 50 years old or older (N = 511, p = 0.500). DyR, donor younger than recipient by at least 5 years (—); DR donor within ±5 years of the recipient age (– – –); DoR, donor older than the recipient by at least 5 years (+—+).

Table 4: Relationship between death-censored graft survival, donor-recipient age difference (D-Rage) and other variables

	Model 1: Pretransplant variables		Model 2: Posttransplant variables		Model 3: Posttransplant variables	
Variables	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
D-Rage (years)	1.019 (1.002, 1.037)	0.031	1.020 (1.005, 1.036)	0.008	1.009 (0.988, 1.031)	0.389
Donor GFR[1]	0.976 (0.945, 0.998)	0.034	–	–	–	–
HLA mismatch	1.258 (1.053, 1.504)	0.012	–	–	–	–
Months on dialysis	1.000 (1.000–1.001)	0.302	–	–	–	–
DGF	–	–	2.895 (0.893, 9.384)	0.076	3.782 (0.856, 16.709)	0.079
GFR[1] at 1 year	–	–	0.92 (0.907, 0.946)	<0.0001	0.936 (0.910, 0.962)	<0.0001
Proteinuria at 1 year (grams/day)	–	–	–	–	1.520 (1.291, 1.789)	<0.0001

[1]GFR in mL/min/1.73 m^2.

However, in younger recipients LD age becomes a very important determinant of length of graft survival and selecting an LD that is younger than the recipient will have important beneficial consequences for the recipient. For example, as displayed in Figure 3B, recipients younger than 50 years old whose donor is more than 5 years younger have a greater than 90% death-censored graft survival at 10 and 20 years posttransplant. In contrast, it should be noted that in our program up to 20% of younger recipients receive relatively older donors and thus have a graft survival disadvantage. Indeed, age is a continuous variable so the arbitrary definition of younger or older was adopted here simply to facilitate the analysis and illustrate the point.

Most kidney grafts are not lost due to their longevity but due to other circumstances that require investigation. Thus, the median age of the kidney graft when lost was 50 years. These analyses showed that LD age was an important determinant of two additional variables that relate to graft survival: graft function and proteinuria. In normal individuals increasing age is associated with a decline in kidney function (8,9). Increasing LD age not only relates to lower kidney function prior to donation but also to lower graft function after transplantation. Several previous studies showed that graft function strongly relates to death-censored graft survival (15). Thus, it could be postulated that the reduced survival of older kidneys is due to their reduced function. However, these results showed conclusively that this is not the case as the relationship between LD age and graft survival is statistically independent of kidney function. In addition to the effect of aging, older LD grafts have a slow recovery of function immediately following transplantation (i.e. lower GFR slope first 5 days posttransplant) an observation noted in previous studies (16). In addition, older LD kidneys have a tendency to lose function after the first year posttransplant. The more rapid loss of function observed in recipients of older LD cannot be explained by their lower baseline GFR because in both native kidneys (8,9) and in allografts (17) the rate of loss of kidney function does not relate to the baseline GFR. These observations beg the question, why do some older LD kidneys lose function progressively after transplantation and consequently have a shorter survival? The associations noted here between LD age, proteinuria and graft failure we postulated provide a possible explanation for these findings.

Posttransplant proteinuria is a strong and independent covariate of graft survival (18–21). The pathogenesis of this association is likely complex and it is better understood considering two levels of proteinuria: First, high levels of proteinuria (>1500 mg/day) are most often indicative of glomerular pathology, either recurrent or *de novo* (21) which is associated with poor graft survival (22). The lack of relationship between LD age and high level proteinuria showed here (see Figure 1) indicates that the incidence of these glomerular pathologies does not vary with LD age. Second, recipients with low (151–500 mg/day) or moderate (501–1500 mg/day) levels of proteinuria also have reduced graft survival (19–21) but these grafts most often have nonglomerular and nonspecific pathology. However, in kidney recipients even low levels of proteinuria are frequently associated with albuminuria, suggesting abnormal glomerular permeability (21). Of interest, this study showed that low-to-moderate levels of proteinuria are highly associated with LD age. Furthermore, the presence of proteinuria explained statistically the association between LD age and death-censored graft survival. That is, those LD grafts, particularly from older donors, that develop proteinuria have reduced survival. Conversely, older LD kidneys that do not develop proteinuria posttransplant have a survival that is comparable to that of younger LD kidneys.

Donor age is classified among the nonmodifiable factors that relate to graft survival. We dispute the implications of this classification because in fact most kidney grafts are lost at a relatively young age. Perhaps a more constructive approach to this issue would be to ask why kidney grafts deteriorate functionally after transplantation and why age apparently accelerates this process. Age is indeed a nonmodifiable factor. However, recognition of the variables that cause allograft deterioration and the study of the responses of the kidney to injury may suggest preventive and therapeutic measures that may prolong graft survival. We postulate that the shorter life span of kidney grafts is not inevitable and, in fact, it can be successfully modified. These results indicate that LD age is quite relevant to long-term death-censored graft survival, particularly in younger individuals and suggest that the biology of the older LD graft determines important functional abnormalities that are progressive and eventually lead to the graft's premature failure.

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Disclosure

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

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