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Enhanced Significance of Donor–Recipient Age Gradient as a Prognostic Factor of Graft Outcome in Living Donor Kidney Transplantation

Milljae Shin · Jae Berm Park · Choon Hyuck David Kwon · Jae-Won Joh · Suk-Koo Lee · Sung-Joo Kim

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Abstract

Background Successful kidney transplantation (KT) increases survival and improves quality of life for patients with end-stage renal disease. Donor age is an important factor influencing graft outcomes. We evaluated the relationship between the donor–recipient age gradient (DRAG) and graft outcomes after living-donor kidney transplantation (LDKT). Additionally, we analyzed graft survival in patients receiving kidneys from age-mismatched donors.

Methods From February 1995 to March 2011, a series of 968 consecutive adult LDKT recipients were enrolled in our study. Graft survival and laboratory data for each patient were retrospectively collected. DRAG values were divided into four groups: ≤ -21, -20 to -1, 0–20, and ≥ 21 years.

Results Higher DRAG had negative effects on graft rejection episodes and serum creatinine levels beyond the first month post-transplantation. A DRAG of more than 20 years was significantly correlated with worse 10-year graft survival. Kidneys from donors older than 55 years of age showed significantly compromised graft outcomes when transplanted into recipients younger than 30 years of age, but not in older recipients. Graft survival in transplants using old-to-old allocation was not different from that of young-to-young allocation. In cases of older donors, a lower DRAG between older donors and older recipients showed more favorable graft outcomes than a higher DRAG between older donors and younger recipients.

Conclusions This study demonstrated that DRAG may serve as a prognostic factor for predicting graft outcomes after LDKT. Additionally, we showed that transplantation of older donor kidneys via living donation is justified in appropriately chosen age-matched recipients.

Abbreviations

DRAG	Donor–recipient age gradient
KT	Kidney transplantation

Introduction

It is well established that kidney transplantation (KT) is the treatment of choice for patients with end-stage renal disease. Transplant recipients have been shown to have a survival advantage and higher health survey scores than patients remaining on dialysis [1–3]. Although a successful KT increases survival rates and improves quality of life for these patients, this advantage may be distorted by several contributing factors over extended periods of time. An important factor that influences graft outcomes is donor age [4]. The effects of donor age on the short- and long-term outcomes of living donor KT have been evaluated in many studies, and most have demonstrated that advanced donor age is a negative independent predictor of graft function and survival [5–9]. Recipient age also affects graft survival, as elderly recipients have been shown to have a significantly lower graft survival and higher incidence of death with a functioning graft compared to younger KT recipients [10, 11]. One large study reported that older recipient age is an independent risk factor for the development of chronic allograft failure [12].

M. Shin · J. B. Park · C. H. D. Kwon · J.-W. Joh · S.-K. Lee · S.-J. Kim (✉)
Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Irwon-dong, Gangnam-gu, Seoul 135-710, Republic of Korea
e-mail: kmhyj.kim@samsung.com

M. Shin
e-mail: milljae.shin@gmail.com

While it is well established that both donor and recipient age affect graft survival following living donor KT, it remains unclear whether the influences of donor age on transplant outcomes were increased or decreased according to the relative age of the recipient. Some investigators have argued that recipient age is an important modifier of the relationship between donor age and graft survival [7]. Older recipient age has been associated with decreased influence of donor age on acute rejection and death-censored graft survival. Thus, the effects of donor and recipient age in combination may be important in predicting renal transplant outcomes [13, 14].

In the present study we evaluated the impact of the donor–recipient age gradient (DRAG) on long-term graft outcomes in patients receiving living donor kidney transplants (LDKT), and determined the value of the DRAG as a predictive factor of graft outcomes. We also analyzed graft survival in age-mismatched living donors by comparing older donor to younger recipient transplant pairs with young-to-young or old-to-old transplant pairs.

Patients and methods

Patient population

From February 1995 to March 2011, a total of 1,542 KTs were performed at our institution. To limit possible confounding factors, recipients under the age of 18 ($n = 48$) and patients who received deceased donor KTs ($n = 526$) were excluded from the analysis. A series of 968 consecutive adult (>18 years of age) LDKT recipients were included in this study. Post-transplant observation was continued until June 2012. All of the patients were followed for at least 1 year. Additionally, there was no policy at our center to disqualify older-aged donors if they passed a careful preoperative assessment.

Study design

Donor–recipient age gradient was defined as the value of the recipient age subtracted from the donor age, and ranged from negative to positive numbers. All recipients were divided into four groups based on the computed DRAG: group 1, DRAG ≤ -21 years ($n = 160$); group 2, DRAG -20 to 1 year ($n = 379$); group 3, DRAG 0 to 20 years ($n = 311$); and group 4, DRAG ≥ 21 years ($n = 118$). Patients were considered "old" at an age of 55 years or older and "young" at an age of 30 years or younger [15]. To further investigate the effects of age matching on graft survival, four additional subgroups were created with respect to donor and recipient age at the time of transplantation. The donor–recipient combinations included: old-to-old group, donors and recipients ≥ 55 years ($n = 24$); old-to-young group, donors ≥ 55 years and recipients ≤ 30 years ($n = 30$); young-to-old group, donors ≤ 30 years and recipients ≥ 55 years ($n = 31$); and young-to-young group, donors and recipients ≤ 30 years ($n = 41$).

Data collection, clinical follow-up, and outcome variables

Clinical data from donors and their corresponding recipients were retrospectively collected from electronic medical records. Post-transplant allograft function was assessed according to serum creatinine levels. The serum creatinine of the recipient was recorded daily for the first 7 days post-transplantation; on day 14; at the end of months 1, 3, 6, and 12; and annually thereafter. Graft outcomes analyzed included the incidence of biopsy-proven graft rejection, serum creatinine levels, and graft survival rates. Both death-censored and uncensored 1-, 3-, 5-, and 10-year graft survivals were examined. Overall graft survival was calculated from the date of transplantation until death, return to dialysis, or the end of the study period. Death-censored graft survival was censored for death with a functioning graft.

Transplant surgery and immunosuppressive regimen

All surgeries during the study period were performed by the same transplant team. Immunosuppression was primarily initiated with a triple regimen that consisted of a calcineurin inhibitor, mycophenolate mofetil (CellCept; Roche), and glucocorticoids. Calcineurin inhibitors such as cyclosporine (Neoral; Novartis Pharma) and tacrolimus (Prograf; Astellas Pharma Inc.) were used in 472 (48.8 %) and 496 (51.2 %) patients, respectively. Among them, 100 (10.3 %) patients switched the type of calcineurin inhibitor used during the study period. A total of 1.5 g (750 mg twice daily) of mycophenolate mofetil was provided for 825 (85.2 %) patients the day after transplantation. This dose was adjusted according to the occurrence of hematologic or gastrointestinal side effects. Additionally, 64 (6.6 %) patients received azathioprine (Azathioprine Pharmachemie) and 8 (0.8 %) patients received sirolimus (Rapamune; Astellas Pharma Inc.). A total of 500 mg of methylprednisolone was injected into all patients during the anhepatic period. After 1 week, oral methylprednisolone at a dosage of 16 mg twice daily was provided, and this dose was tapered over time. Since May 2004, two single doses of basiliximab (Simulect; Novartis Pharma) were routinely given for immune induction therapy on days 0 and 4. This was alternated with anti-thymocyte globulin (ATGAM; Pharmacia) in 42 (4.3 %) patients. The immunosuppression protocol and dose of immunosuppressive

drugs were not adjusted according to recipient age. Prophylactic antibiotics were administrated systemically. Biopsy-proven rejections were initially treated with pulsed steroids followed by a steroid taper.

Statistical analysis

Categorical variables are expressed as the number of cases or as percentages. Comparisons between DRAG groups with specific demographic characteristics or graft rejection episodes were made using the Pearson's Chi square test. Continuous variables were reported as mean values and SD. Differences between groups in baseline characteristics and serum creatinine levels were calculated with one-way analysis of variance (ANOVA) and repeated measures ANOVA, respectively. Both death-censored and uncensored graft survival were estimated by the Kaplan–Meier method and compared with log rank tests. Data analysis was performed with SPSS 18.0 software (SPSS, Chicago, IL). Two-tailed p values <0.05 were considered to be statistically significant.

Results

Baseline characteristics of the study population

The median ages of donors and recipients were 40 years (range 18–68 years) and 42 years (range 18–72 years), respectively. The median DRAG value was -2, and ranged from -41 to 43 years (mean 11.8 years). Of the 968 adult LDKT recipients enrolled, 539 (55.7 %) received kidneys from donors whose age was greater than their own. Demographic data of donors and recipients stratified by DRAG group is shown in Table 1. The total number of HLA mismatches was calculated as the sum of the mismatches in the A, B, and DR loci. In group 1, which includes younger donors and older recipients, a higher proportion of donors were male. Otherwise, the four DRAG groups had similar baseline demographics.

Effects of DRAG on allograft rejection and serum creatinine levels

Donor–recipient age gradient was associated with an increased incidence of allograft rejection ($p = 0.003$). The percentage of recipients that experienced rejection increased progressively from 5.0 % in recipients with a DRAG ≤ -21 years to 18.6 % in recipients with a DRAG $\geq$ 21 years. The increasing DRAG had a negative effect on graft function as measured by post-transplant serum creatinine ($p = 0.014$). Although differences in serum creatinine levels were not significant between groups 2 and 3, they were significantly higher in group 4 (DRAG $\geq$ 21 years) compared with the other groups at all time points beyond the first month post-transplantation. Conversely, group 1 consistently had the lowest serum creatinine levels after KT. Comparisons of data for allograft rejection episodes and mean serum creatinine levels according to DRAG group are shown in Table 2 and Fig. 1.

Effects of DRAG on overall and death-censored graft survival

After a median follow-up period of 75 months (range 1–208 months), a total of 89 grafts (9.2 %) failed during the study period. 19 (2.0 %) patients died with functioning grafts. Reasons for graft loss before death included chronic allograft nephropathy in 34 patients, rejection in 22 patients (acute, 15; chronic, 7), recurrence of primary renal disease in 9 patients, renal artery occlusion in 4 patients, and BK virus associated nephropathy in 1 patient. Overall graft survival and death-censored graft survival curves for the four DRAG groups are shown in Fig. 2a, b, and survival rates at 1, 3, 5, and 10 years are depicted in corresponding numerical tables below the Kaplan–Meier plots. At and beyond 3 years post-transplant, both overall and death-censored long-term graft survival of group 4 (DRAG $\geq$ 21 years) were significantly decreased compared with those of groups 2 and 3. Although there was no statistical difference in overall graft survival between groups 1 and 4, graft survival after censoring for death with a functioning graft was substantially different between the two groups. Differences in overall and death-censored graft survival between groups 1, 2, and 3 were not observed. Thus, a DRAG of $\geq$21 years correlated with decreased 10-year graft survival, particularly death-censored graft survival.

Effects of DRAG on overall and death-censored graft survival in age-mismatched donor–recipient pairs

Of the 968 KT recipients enrolled, 120 (12.4 %) were $\geq$55 years of age and 179 (18.5 %) were $\leq$30 years of age at the time of transplantation. Of recipients $\geq$55 or $\leq$30 years of age, 54 (18.1 %) received kidneys from older donors ($\geq$55 years) and 72 (24.1 %) received kidneys from younger donors ($\leq$30 years). Therefore, 126 LDKT were performed using the concept of partiality to donor and recipient age. To assess the effects of DRAG on graft survival among different age-matched allocations, overall and death-censored graft survival curves for the age combination subgroups were compared (Fig. 3).

While the four age combination subgroups were not statistically different, overall graft survival for young recipients was strikingly different depending on the age of the donor grafts. In contrast, when the two groups of older

Table 1 Baseline characteristics of the study population grouped according to DRAG

Characteristic	DRAG (years)				Total ($n = 968$)	p value
	≤ -21 ($n = 160$)	-20 to -1 ($n = 379$)	0 to 20 ($n = 311$)	≥ 21 ($n = 118$)		
Donor gender						
Male	113 (70.6)	187 (49.3)	163 (52.4)	50 (42.4)	513 (53.0)	0.000
Female	47 (29.4)	192 (50.7)	148 (47.6)	68 (57.6)	455 (47.0)	
Donor age (years)	26.5 ± 5.7	38.1 ± 8.9	43.2 ± 8.3	53.9 ± 5.4	39.8 ± 10.9	0.000
Median donor age, years (range)	27, (18–44)	38, (18–62)	44, (21–66)	54, (43–68)	40, (18–68)	
Donor history of diabetes	0 (0.0)	1 (0.3)	1 (0.3)	0 (0.0)	2 (0.2)	0.841
Donor history of hypertension	0 (0.0)	0 (0.0)	2 (0.6)	0 (0.0)	2 (0.2)	0.237
Recipient gender						
Male	84 (52.5)	234 (61.7)	163 (52.4)	71 (60.2)	552 (57.0)	0.057
Female	76 (47.5)	145 (38.3)	148 (47.6)	47 (39.8)	416 (43.0)	
Recipient age (years)	53.3 ± 6.2	44.4 ± 8.6	37.8 ± 8.2	27.1 ± 5.2	41.6 ± 10.8	0.000
Median recipient age, years (range)	53, (40–72)	45, (24–64)	37, (19–58)	28, (18–44)	42, (18–72)	
Previous kidney transplant	4 (2.5)	15 (4.0)	14 (4.5)	0 (0.0)	33 (3.4)	0.110
Positive recipient hepatitis B serostatus	6 (3.8)	19 (5.0)	17 (5.5)	1 (0.8)	43 (4.4)	0.185
Positive recipient hepatitis C serostatus	3 (1.9)	7 (1.8)	4 (1.3)	0 (0.0)	14 (1.4)	0.490
Positive B cell FCXM	3 (1.9)	4 (1.1)	2 (0.6)	0 (0.0)	10 (1.0)	0.234
Number of HLA mismatches	3.0 ± 0.8	3.3 ± 1.5	3.1 ± 1.6	2.9 ± 0.8	3.2 ± 1.4	0.192
0	0 (0.0)	24 (6.3)	32 (10.3)	2 (1.7)	58 (6.0)	
1	7 (4.4)	17 (4.5)	20 (6.4)	3 (2.5)	47 (4.9)	
2	24 (15.0)	48 (12.7)	34 (10.9)	23 (19.5)	129 (13.3)	
3	102 (63.8)	118 (31.1)	81 (26.0)	75 (63.6)	376 (38.8)	
4	19 (11.9)	94 (24.8)	83 (26.7)	13 (11.0)	209 (21.6)	
5	6 (3.8)	49 (12.9)	53 (17.0)	1 (0.8)	109 (11.3)	
6	2 (1.3)	29 (7.7)	8 (2.6)	1 (0.8)	40 (4.1)	
Peak PRA (%)	4.1 ± 15.9	1.9 ± 10.8	4.5 ± 16.8	1.1 ± 8.9	3.0 ± 13.7	0.682
0–30	150 (93.8)	366 (96.6)	290 (93.2)	116 (98.3)	922 (95.2)	
30–50	2 (1.3)	4 (1.1)	7 (2.3)	1 (0.8)	14 (1.4)	
50–80	3 (1.9)	5 (1.3)	6 (1.9)	0 (0.0)	14 (1.4)	
80–100	5 (3.1)	4 (1.1)	8 (2.6)	1 (0.8)	18 (1.9)	
Cold ischemic time (min)	72.9 ± 40.8	67.5 ± 31.9	68.1 ± 37.9	64.1 ± 26.4	68.2 ± 35.0	0.083
Anastomosis time (min)	31.6 ± 12.6	34.7 ± 14.0	34.8 ± 11.5	34.5 ± 12.1	34.2 ± 12.9	0.062
Pretransplant dialysis						
No (pre-emptive)	34 (21.3)	59 (15.6)	47 (15.1)	20 (17.0)	160 (16.5)	0.347
Yes	126 (78.8)	320 (84.4)	264 (84.9)	98 (83.1)	808 (83.5)	
Pre-transplant time on dialysis (months)	22.6 ± 37.8	26.4 ± 40.6	24.2 ± 36.4	14.0 ± 19.5	23.6 ± 36.9	0.063
Follow-up time (months)	64.1 ± 46.4	79.3 ± 50.3	78.7 ± 50.0	76.2 ± 49.7	76.2 ± 49.7	0.054

Values are expressed as number (%) or mean ± SD

FCXM flow cytometry crossmatch

recipients were compared, no differences in overall graft survival were detected with respect to donor age. Similarly, kidneys from older donors severely compromised graft survival only when transplanted into young recipients. Overall graft survival in old-to-old transplant allocation was not different from that of young-to-young transplants. Older recipients of transplants from older donors had a graft survival advantage, while young recipients of older donor kidneys had a significant disadvantage in graft survival. In cases of older donors, the lower DRAG between an older

Table 2 Differences in allograft rejection episodes and mean serum creatinine levels grouped according to DRAG

Outcomes	DRAG (years)				Total ($n = 968$)
	≤−21 ($n = 160$)	−20 to 1 ($n = 379$)	0–20 ($n = 311$)	≥21 ($n = 118$)	
Allograft rejection*	8 (5.0)	37 (9.8)	37 (11.9)	22 (18.6)	104 (10.7)
Acute rejection	6 (3.8)	32 (8.4)	36 (11.6)	21 (17.8)	95 (9.8)
Chronic rejection	2 (1.3)	5 (1.3)	1 (0.3)	1 (0.8)	9 (0.9)
Serum creatinine (mg/dL)					
Pre-transplant	6.54 ± 2.24	7.68 ± 2.62	7.43 ± 3.02	8.27 ± 3.31	7.49 ± 2.83
1 week	1.08 ± 0.62	1.27 ± 0.90	1.27 ± 0.68	1.40 ± 1.13	1.25 ± 0.83
2 weeks	1.04 ± 0.59	1.30 ± 0.98	1.27 ± 0.80	1.42 ± 1.02	1.26 ± 0.88
1 month	1.02 ± 0.32	1.48 ± 1.24	1.29 ± 0.65	1.66 ± 1.15	1.36 ± 0.97
3 months	1.15 ± 0.72	1.26 ± 0.33	1.25 ± 0.32	1.52 ± 0.91	1.27 ± 0.52
6 months	1.20 ± 0.50	1.32 ± 0.48	1.30 ± 0.29	1.61 ± 1.09	1.33 ± 0.56
1 year	1.15 ± 0.36	1.34 ± 0.93	1.29 ± 0.29	1.53 ± 0.93	1.32 ± 0.71
2 years	1.04 ± 0.31	1.26 ± 0.48	1.25 ± 0.36	1.59 ± 1.11	1.27 ± 0.56
3 years	1.16 ± 0.76	1.29 ± 0.58	1.28 ± 0.37	1.81 ± 1.93	1.33 ± 0.86
4 years	1.22 ± 1.02	1.45 ± 1.18	1.30 ± 0.47	2.03 ± 2.31	1.44 ± 1.21
5 years	1.34 ± 1.50	1.60 ± 1.62	1.43 ± 0.64	2.19 ± 2.17	1.59 ± 1.50

Values are expressed as number (%) or mean ± SD

* $p = 0.003$, Pearson's Chi square test

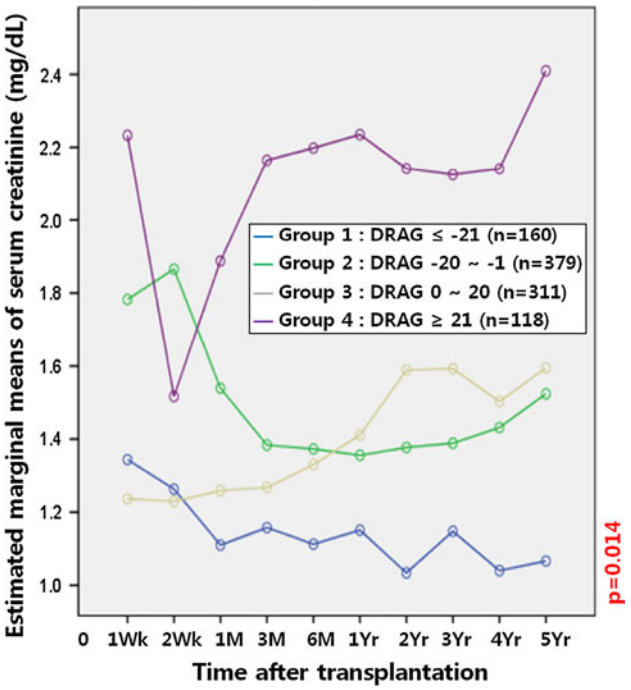


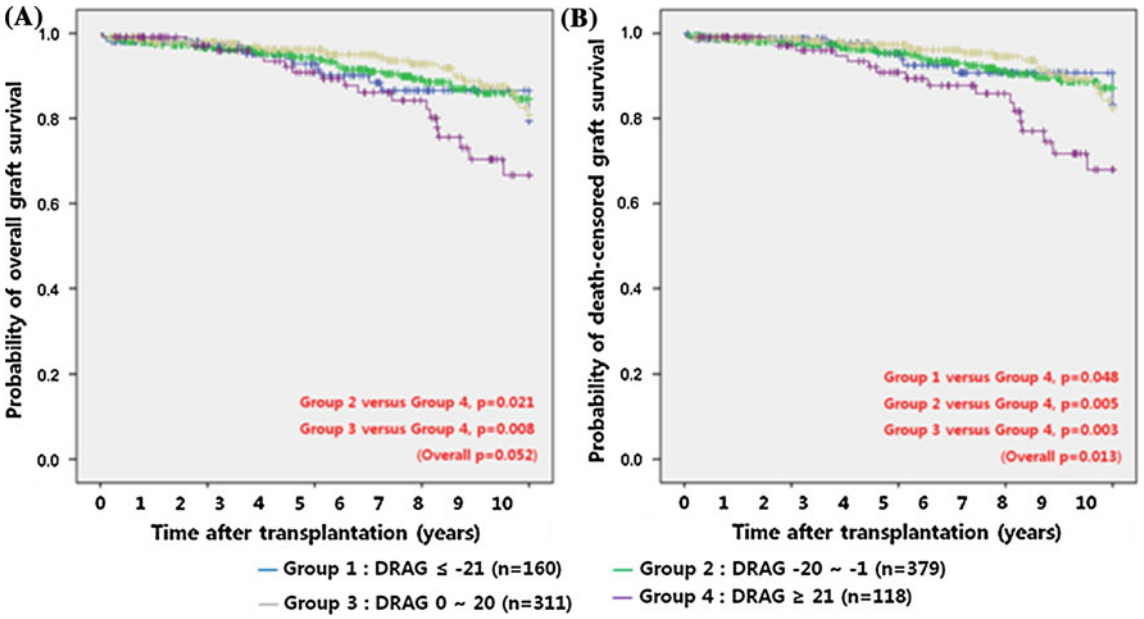
Fig. 1 Changes in mean serum creatinine levels during the first 5 years post-transplantation grouped according to DRAG ($p = 0.014$, repeated measures ANOVA)

donor and an older recipient was more favorable for overall graft survival than the higher DRAG between an older donor and a younger recipient. Thus, DRAG, in combination with age-matched allocation, appears to influence overall graft survival, with similar differences noted for death-censored graft survival.

Discussion

The use of grafts from older donors has been associated with inferior graft function, increased episodes of acute rejection, and reduced short- and long-term graft survival [5–9, 16]. Advanced donor age has been identified as a major factor contributing to unfavorable transplant outcomes after LDKT. Increased graft loss of older donor kidneys could be due to various physiologic and immunologic factors. For example, functional nephron mass is decreased in older kidneys [17], which may lead to hyperfiltration injury [18]. Older grafts have also been shown to have increased susceptibility to prolonged ischemic damage [19] and acute rejection episodes [20, 21]. One retrospective study proposed that older kidneys are more immunogenic to antigens expressed in injured tissue, and that increased immune recognition increases the incidence of acute interstitial rejection [22]. In a recent animal study, P16INK4a expression was increased in older kidneys, which is reflective of somatic cell senescence, the state in which cells have lost their capacity for repair and replication [23].

Despite significant age-related effects on graft outcomes, advanced donor age alone does not have a negative impact on corresponding kidney transplant recipients. Rather, other coexisting pre- and post-transplant risk factors result in



	Overall graft survival rate (%)				Death-censored graft survival rate (%)			
	1yr	3yr	5yr	10yr	1yr	3yr	5yr	10yr
Group 1	98.1	97.2	92.8	86.6	98.7	97.7	95.2	90.7
Group 2	97.8	96.3	94.7	86.0	98.6	97.4	95.8	88.6
Group 3	98.7	97.6	95.6	87.5	98.7	98.3	96.7	89.2
Group 4	99.2	96.0	90.8	70.4	99.2	96.0	90.8	71.7

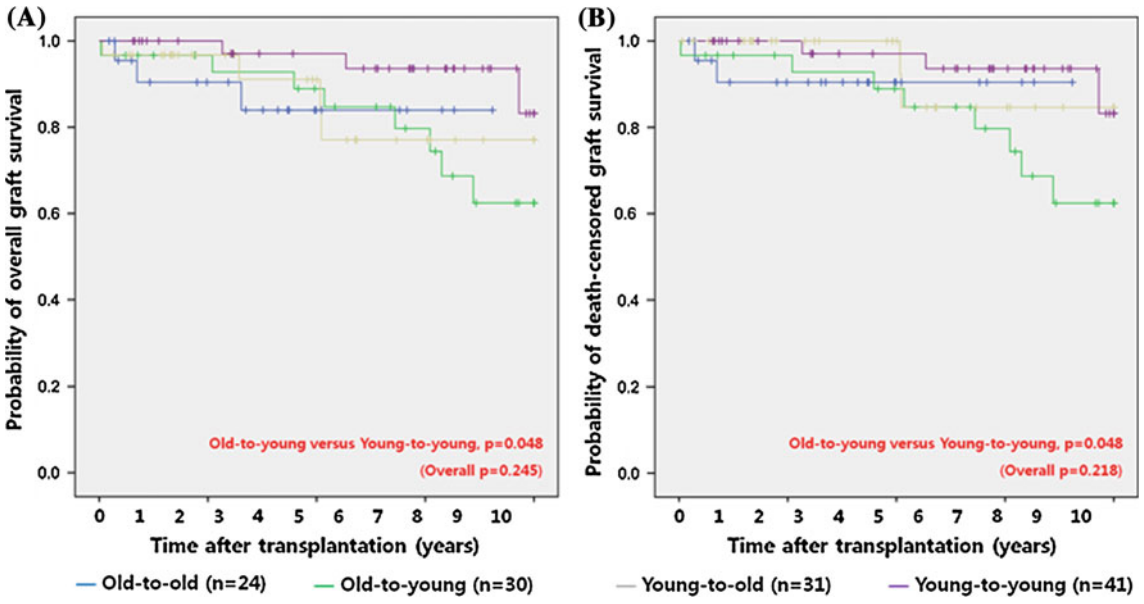
(yr, year)

Fig. 2 Graft survival analysis among recipients in different DRAG groups: **a** overall graft survival (overall $p = 0.052$, log rank test). **b** death-censored graft survival (overall $p = 0.013$, log rank test)

impaired graft outcomes [24, 25]. Several publications have defined donor age as an effect modifier, reporting that negative effects on graft function among recipients of older kidneys were attenuated depending on donor gender (male) [8], recipient race (African American) [26], donor glomerular filtration rate and recipient body weight [27], acute rejection episodes [8], degree of HLA mismatch [9], size of the transplant center [24], and age of the recipient. Numerous conflicting results regarding the impact of recipient age on graft survival have been reported. Decreases in graft survival benefit among older recipients have been consistently shown [28], whereas some investigators have demonstrated an increase in the relative risk of elderly donor organs in younger recipients that was absent in older recipients [7].

Given these data as background for our study, we used a DRAG to evaluate the effects on graft function and survival in LDKT. This study revealed that higher DRAG was associated with an increased incidence of graft rejection, elevated serum creatinine levels beyond the first month post-transplantation, and poorer long-term death-censored and uncensored graft survival. Using DRAG as a prognostic factor for predicting graft outcome after living donor KT is worthwhile as it produced results of greater significance than use of donor age alone. Noppakun et al. suggested that living donor age has little impact on the success of KT in older recipients. Donor age does, however, become a very important determinant of length of graft survival in younger recipients [7]. These results are consistent with previously reported observations in deceased donor KTs [14], which demonstrated that the combination of donor and recipient age is critical in determining host immunoresponsiveness, and that increased age is associated with improved transplant survival, lower rejection rates, and superior outcomes for older donor organs. Given that donor and recipient age appear to modulate each other, DRAG may be an important determinant of graft survival.

Because age plays an important role in selecting both the donor graft and recipient, the function of the graft appears to change in a complementary manner depending on the functional requirements of the recipient [29]. Older donor grafts show a gradual loss of functional nephron mass [30] and limited capacity to respond appropriately to physiologic challenges [31, 32], ultimately resulting in lower physiologic



	Overall graft survival rate (%)				Death-censored graft survival rate (%)			
Allocation	1yr	3yr	5yr	10yr	1yr	3yr	5yr	10yr
Old-to-old	90.4	90.4	84.0	84.0	90.4	90.4	90.4	-
Old-to-young	96.7	92.8	88.9	62.4	96.7	92.8	88.9	62.4
Young-to-old	96.8	91.1	84.1	77.1	97.0	97.0	92.3	84.6
Young-to-young	97.1	97.1	93.6	83.2	97.1	97.1	93.6	83.2

(yr, year)

Fig. 3 Graft survival analysis among recipients in different donor–recipient age combination groups: **a** overall graft survival (overall $p = 0.245$, log rank test), **b** Death-censored graft survival (overall $p = 0.218$, log rank test)

renal reserves. When older grafts are transplanted into younger recipients with increased metabolic demands, functional reserves are insufficient compared with transplantation into older recipients. In addition, elderly recipients exhibit differences in immune function, including reduced naive T cells [14], increased regulatory T cells [33], impaired function of antigen-presenting cells such as dendritic cells [34], and altered cytokine profiles [35].

To satisfy the metabolic needs and immunologic differences of the recipients, older kidneys are best matched to older recipients. In patients undergoing deceased donor transplants, several studies have found that age-matching may improve outcomes of KT using older donor grafts [32, 36–38]. Likewise, younger patients with older grafts have the poorest graft survival [39]. In 1999, the Eurotransplant Senior Program (ESP) was developed to preferentially allocate kidneys from older donors to older recipients [40]. The program allows for expansion of the older donor pool [41], less delayed graft function [42], and acceptable levels of graft survival [43, 44]. Although these data were obtained from deceased donor KT studies, taken collectively with our results, donor and recipient age matching could affect graft outcomes in LDKT. These data are consistent with other previous studies that describe an absence of negative effects of advanced living-donor age in older recipients [45, 46] that remains present in younger recipients [7]. In reality, older recipients have a reduced post-transplantation life expectancy, higher incidence of death with functioning grafts, and satisfactory actual graft survival despite a shorter graft half-life. Allocating younger donor grafts to older recipients could be interpreted as an inefficient use of resources. It is possible, however, to optimize allocation by selecting living donors according to donor age as well as DRAG.

Conclusions

Our results show that increased DRAG is associated with development of graft rejection, increased post-transplant serum creatinine levels, and reduced overall and death-censored graft survival. This suggests that DRAG may serve as a prognostic factor for predicting graft outcomes after LDKT. Furthermore, transplantation of older kidneys

via living donation is justified in appropriately chosen age-matched recipients. Thus, the DRAG, rather than a fixed age limit, provides a clinically useful tool that may help with organ allocation when there is more than one potential donor.

Conflict of interest The authors of this manuscript have no conflicts of interest to disclose.

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