

Adult Living-Donor Kidney Transplantation, Donor Age, and Donor–Recipient Age



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Introduction: Owing to organ shortage, the number of kidney transplantation (KT) involving older adult living donors is increasing. We aimed to investigate the effects of living-donor age and donor-recipient age differences on KT outcomes.

Methods: This single-center, retrospective cohort study involved 853 adult LDKTs performed between January 2008 and December 2018. Recipients were stratified into the following 5 groups based on donor age and donor-recipient age difference: donor age, 30 to 49 years and age difference, –10 to 15 years; donor age, 50 to 69 years and age difference, –10 to 15 years; donor age, 50 to 69 years and age difference, 15 to 40 years; donor age, 70 to 89 years and age difference, –10 to 15 years; and donor age, 70 to 89 years and age difference, 15 to 40 years (groups 1, 2, 3, 4, and 5, respectively). As a primary outcome, the risk of graft loss was investigated. The secondary outcomes were postoperative estimated glomerular filtration rates (eGFRs) and mortality rates of recipients.

Results: Group 4, representing KT between older adult donors and older adult recipients, had the highest graft loss risk and mortality. The eGFRs of the recipients from donors aged 70 to 89 years (groups 4 and 5) were significantly lower than those from donors in the other groups. Although the differences in the eGFR between groups 4 and 5 were not significant, the eGFR of group 4 was lower than that of group 5 at 6 months post-KT.

Conclusion: LDKTs from older adult donors to older adult recipients resulted in the worst graft survival and mortality rates.

Kidney Int Rep (2021) 6, 3026–3034; <https://doi.org/10.1016/j.ekir.2021.10.002>

KEYWORDS: donor age; donor-recipient age difference; graft biopsy; graft loss; living-donor kidney transplantation; mortality

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Owing to organ shortage, the number of LDKTs from marginal donors is increasing.^{1–3} Marginal donor factors include age (>65 years) and comorbidities, such as hypertension, glucose intolerance, dyslipidemia, and obesity.^{3,4} Although many previous reports have referred to KT from older adult living donors, older adult living-donor age has been defined as that between 55 and 65 years based on the previously limited numbers of living donors aged >70 years.^{5–11} The population of older adult living donors

aged >70 years is gradually increasing; therefore, the effects of grafts on LDKTs from these donors require elucidation. Nevertheless, only 1 study has investigated LDKT outcomes from living donors aged >70 years.¹² Postnephrectomy survival of living donors aged >70 years has been reported to be significantly better than that of matched healthy controls.¹² Nevertheless, the graft-loss rate among the recipients was significantly higher than that among recipients from living donors aged 50 to 59 years.¹² Furthermore, a donor-recipient age difference of >30 years has been reported to increase the risk of graft loss within 12 months post-transplantation relative to an age difference of 10 to 20 years.¹³ This finding indicates that evaluating recipient outcomes according to donor age is insufficient; the age of the donor and the recipient, including the age difference between donor and

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Received 20 July 2021; revised 30 September 2021; accepted 4 October 2021; published online 14 October 2021

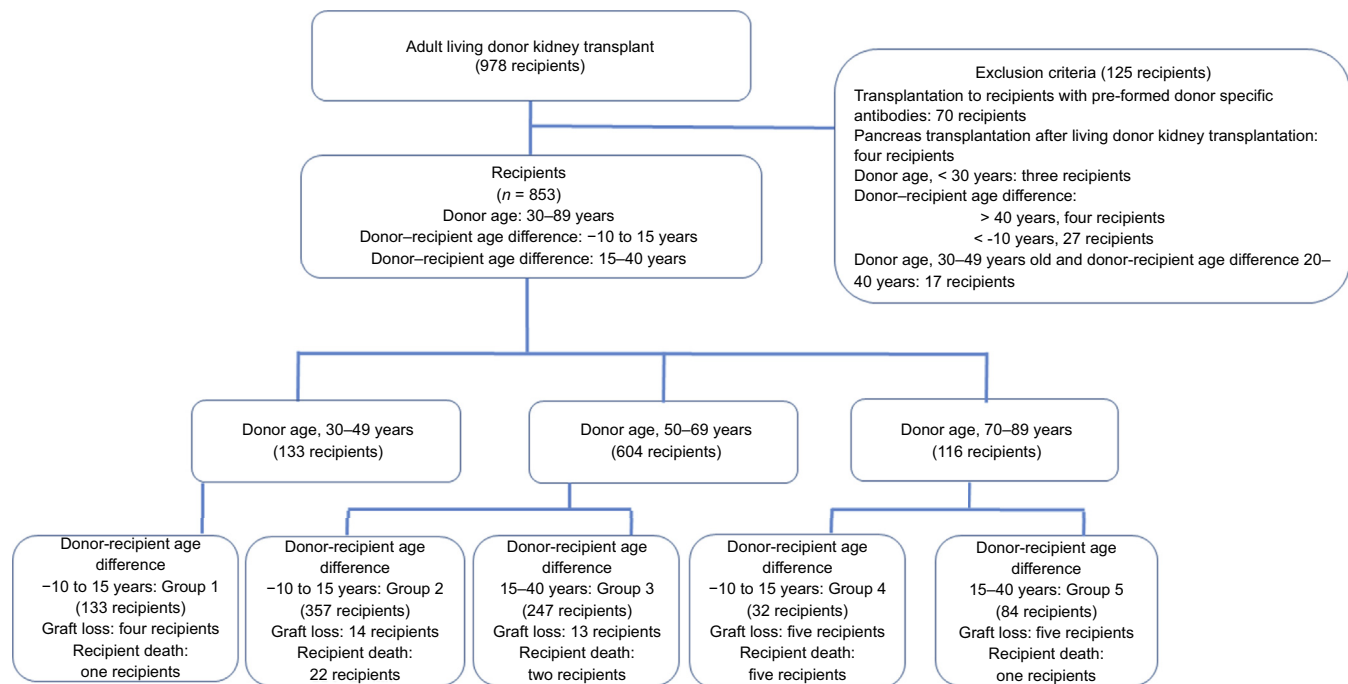


Figure 1. Patient flow chart.

recipient, should be investigated. Donor age and donor-recipient age difference should be investigated simultaneously to more fully elucidate the effects of grafts from older adult living donors on recipient outcomes.

This study aimed to investigate the effects of living donors' age > 70 years and donor-recipient age differences on KT recipient outcomes.

METHODS

Study Design

This retrospective cohort study was approved by the Institutional Review Board of the Nagoya Daini Red Cross Hospital (Aichi, Japan; approval number, 1416) and was conducted according to the principles of the Declaration of Helsinki. LDKTs were performed according to the Declaration of Istanbul. Recipients were stratified into the following 5 groups based on donor age and donor-recipient age difference: donor age, 30 to 49 years and age difference, –10 to 15 years; donor age, 50 to 69 years and age difference, –10 to 15 years; donor age, 50 to 69 years and age difference, 15 to 40 years; donor age, 70 to 89 years and age difference, –10 to 15 years; and donor age, 70 to 89 years and age difference, 15 to 40 years (denoted as groups 1, 2, 3, 4, and 5, respectively, [Figure 1](#) and [Supplementary Figure S1](#)). This approach allows the classification of LDKT based on donor-recipient pairs, in which donors and recipients have similar ages and in which donors are older and recipients are younger. As a primary outcome, the risk of graft loss was compared among the 5 groups. The secondary outcomes compared the

postoperative eGFRs and mortality rates of the recipients among the 5 groups. This study was reported in accordance with Strengthening The Reporting of OBServational studies in Epidemiology guidelines.

Follow-Up Assessments

Recipient postoperative assessments were undertaken fortnightly for the first 3 months and monthly thereafter.

Participants

All consecutive recipients who had undergone adult LDKT at our hospital between January 2008 and December 2018 were recruited. Patients were followed up until June 2020. We excluded recipients with pre-formed donor-specific antibodies (70 recipients); pancreas transplantation after LDKT (4 recipients); donor age < 30 years (3 recipients); donor-recipient age differences > 40 years (4 recipients) or ≤ 10 years (27 recipients); and donor age of 30 to 49 years and donor-recipient age difference of 20 to 40 years (17 recipients). The number of recipients that were classified in the latter group was considered too small compared with the number of adult LDKTs performed, probably because of the exclusion of pediatric recipients. Pediatric recipients were excluded from the analysis because of differences from adult recipients in terms of causes of graft loss, such as nonadherence to treatment and eGFR evaluation.^{14–17} In total, 853 recipients were enrolled in this study. All donor and recipient data were retrospectively collected from medical records and analyzed anonymously; therefore, the requirement for informed consent was waived.

Living Donors

Living donors were selected according to the living kidney donor guidelines in Japan^{4,18} and were analyzed in terms of surgical outcomes, graft quality, adverse events, and operation methods of donor nephrectomy. Surgical outcomes included kidney side, kidney weight, warm ischemic time, operating time, and operation blood loss. Graft quality included arterial length, number of preserved arteries, venous length, number of preserved veins, ureter length, and number of preserved ureters. Furthermore, adverse events included arterial injury, venous injury, open conversion, and intraoperative bleeding.

Recipients

Among the recipients, operation results, postoperative eGFR, baseline biopsy findings 1 hour post-transplantation, graft loss, and mortality were investigated. The operation results included cold ischemic time and perioperative adverse events, such as delayed graft function, surgical site infection, arterial thrombosis, urine leakage, ureteral necrosis, ureteral stenosis, lymphocele, incisional hernia, and postoperative bleeding requiring reoperation. Postoperative eGFR was adjusted for recipient sex, transplantation from a first-degree relative donor, dialysis vintage, preoperative sensitization, human leukocyte antigen (HLA)-AB mismatch, HLA-DR mismatch, and preoperative conditioning. Baseline biopsy findings 1-hour post-transplantation were defined as the presence of interstitial fibrosis and tubular atrophy >5% and the presence of glomerulosclerosis or arteriosclerosis according to the 2007 Banff classification system as determined by a transplant pathologist. The risk of graft loss was investigated using recipient, donor, and operative factors. Recipient factors included donor age and donor-recipient age difference group; recipient age; age difference between donor and recipient; recipient sex; recipient body mass index; body weight difference between donor and recipient; height difference between donor and recipient; transplantation from a first-degree relative donor; dialysis vintage; preoperative sensitization, such as transfusion, pregnancy, and transplantation; HLA-AB mismatch; HLA-DR mismatch; preoperative panel reactive antibodies class I positive ($\geq 5\%$); preoperative panel reactive antibodies class II positive ($\geq 5\%$); ABO-incompatible transplantation; and preoperative conditioning, such as rituximab administration, splenectomy, double filtration plasmapheresis, and plasmapheresis. Donor factors included donor age; donor sex; donor body mass index; baseline biopsy findings 1 hour post-transplantation (presence of interstitial fibrosis and tubular atrophy >5%); any glomerulosclerosis or arteriosclerosis according to the 2007 Banff classification system as

determined by a transplant pathologist; >1 preoperative comorbidity; smoking history; and preoperative eGFR. Operation factors included kidney side, kidney weight, warm ischemic time, donor operation time, donor operation blood loss, donor nephrectomy operation methods, and cold ischemic time.

Statistical Analysis

Statistical analyses of donor and recipient characteristics were performed using the Kruskal-Wallis test for continuous variables and the χ^2 test for categorical variables. Normal distribution of recipient eGFR data was confirmed using histograms. Linear mixed-model analysis was used to evaluate whether donor age and donor-recipient age difference groups (groups 1, 2, 3, 4, and 5) affected eGFRs over time, where “case” was a random factor, “time” was a repetitive factor, and “groups 1, 2, 3, 4, and 5” and “interaction with time” (defined as “time \times groups 1, 2, 3, 4, and 5”) were fixed factors. To adjust for confounding factors, recipient sex, transplantation from a first-degree relative donor, dialysis vintage, preoperative sensitization, HLA-AB mismatch, HLA-DR mismatch, and preoperative conditioning were included as covariates. The repeated-measures covariance structure was a compound symmetry. The estimated marginal means and their standard errors and 95% CIs were calculated and compared with those of groups 1, 2, 3, 4, and 5 at each time point. The Benjamini-Hochberg method (false discovery rate method) was used to adjust for multiple comparisons. The incidence of graft biopsy findings was analyzed using logistic regression analysis adjusted for donor sex. A Fine-Gray competing risk regression model was used to evaluate the risk factors for graft loss. The variables with $P < 0.05$ were used for the multivariate analysis. For the Fine-Gray competing risk regression model, the proportional hazard assumption was confirmed using a log-log plot. No interaction effects between the variables were identified in the models using the interaction items. The cumulative survival rate was calculated using the Kaplan-Meier method. All statistical analyses were performed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corporation, Armonk, NY) and SAS 9.4 (SAS Institute Inc., Cary, NC) software. For all analyses, $P < 0.05$ were considered statistically significant.

RESULTS

Study Population

A total of 978 adult LDKTs were performed at our hospital during the study period, of which 125 transplantations

Table 1. Donor and recipient characteristics

	Donor age 30–49 yr		Donor age 50–69 yr		Donor age 70–89 yr		P value
	Donor-recipient age difference, –10 to 15 yr		Donor-recipient age difference, –10 to 15 yr		Donor-recipient age difference, 15–40 yr		
	Group 1	Group 2	Group 3	Group 4	Group 5		
	n = 133	n = 357	n = 247	n = 32	n = 84		
Donor							
Donor age, yr, mean (SD)	43.4 (4.7)	59.6 (5.6)	61.1 (4.8)	72.6 (2.2)	72.9 (2.3)		<0.001
Donor sex (male), n (%)	45 (33.8)	119 (33.3)	76 (30.8)	23 (71.9)	28 (33.3)		<0.001
Smoking history, n (%)	62 (46.6)	150 (42.0)	102 (41.3)	21 (65.6)	31 (36.9)		0.059
Preoperative comorbidities ≥1, n (%)	66 (49.6)	259 (72.5)	205 (83.0)	29 (90.6)	71 (84.5)		<0.001
Hypertension, n (%)	6 (4.5)	93 (26.1)	87 (35.2)	17 (53.1)	41 (48.8)		<0.001
Dyslipidemia, n (%)	50 (37.6)	214 (59.9)	162 (65.6)	24 (75.0)	54 (64.3)		<0.001
Glucose intolerance, n (%)	24 (18.0)	104 (29.1)	89 (36.0)	14 (43.8)	39 (46.4)		<0.001
Obesity—body mass index ≥ 30 kg/m ² , n (%)	6 (4.5)	1 (0.3)	0	0	0		<0.001
Donor body mass index (kg/m ²), mean (SD)	22.9 (3.6)	22.7 (3.0)	22.8 (2.7)	23.1 (2.3)	22.6 (2.9)		0.638
Preoperative eGFR (ml/min per 1.73 m ²), mean (SD)	81.5 (14.8)	72.5 (12.5)	73.0 (11.1)	67.9 (9.7)	67.8 (12.5)		<0.001
Baseline biopsy 1 h post-transplantation, n (%)	26 (19.5)	197 (56.3)	145 (59.2)	25 (78.1)	70 (84.3)		<0.001
Glomerulosclerosis, % (SD)	3.2 (5.1)	10.1 (10.5)	10.0 (10.3)	16.2 (14.1)	15.1 (12.8)		<0.001
ci 0, n (%)	127 (95.5)	311 (88.9)	221 (90.2)	24 (75.0)	70 (84.3)		<0.001
ct 0, n (%)	116 (87.2)	224 (64.0)	154 (62.9)	15 (46.9)	41 (49.4)		<0.001
ah 0, n (%)	92 (69.2)	179 (51.1)	118 (48.2)	10 (31.3)	42 (50.6)		<0.001
Recipient							
Recipient age (y), mean (SD)	44.7 (6.1)	60.1 (6.5)	33.6 (6.3)	69.5 (4.7)	44.3 (4.5)		<0.001
Age difference between donor and recipient (y), mean (SD)	–1.2 (4.2)	–0.5 (4.2)	27.6 (3.8)	3.3 (4.0)	28.7 (3.9)		<0.001
Recipient sex (male), n (%)	91 (68.4)	238 (66.7)	162 (65.6)	10 (31.3)	58 (69.0)		0.001
Recipient body mass index (kg/m ²), mean (SD)	23.3 (3.9)	22.5 (3.4)	22.1 (4.2)	21.2 (2.2)	22.2 (3.8)		0.003
Body weight difference between donor and recipient (kg), mean (SD)	–4.4 (19.0)	–2.7 (15.7)	–3.1 (15.9)	8.9 (12.6)	–6.5 (13.7)		<0.001
Height difference between donor and recipient (cm), mean (SD)	–4.2 (13.6)	–4.7 (12.8)	–6.5 (10.6)	5.9 (12.9)	–10.3 (10.2)		<0.001
Recipient follow-up period (mo), mean (SD)	76.7 (39.2)	69.6 (38.2)	79.8 (37.3)	50.7 (35.3)	69.0 (38.4)		<0.001
Transplantation from a first-degree relative donor (%)	32 (24.1)	53 (14.8)	235 (95.1)	1 (3.1)	80 (95.2)		<0.001
Dialysis vintage (mo), mean (SD)	22.3 (49.0)	35.9 (62.5)	17.9 (41.1)	32.1 (50.5)	21.3 (47.7)		<0.001
Preoperative sensitization—transfusion, pregnancy, transplantation; n (%)	40 (30.1)	159 (44.6)	74 (30.0)	25 (78.1)	28 (33.3)		<0.001
HLA-AB mismatch, mean (SD)	2.8 (0.9)	2.9 (1.0)	1.8 (0.5)	3.0 (0.8)	1.8 (0.7)		<0.001
HLA-DR mismatch, mean (SD)	1.6 (0.6)	1.6 (0.6)	0.9 (0.4)	1.6 (0.6)	1.0 (0.4)		<0.001
Preoperative PRA class I (positive, ≥5%), n (%)	7 (5.3)	40 (11.2)	23 (9.3)	4 (12.5)	9 (10.7)		0.364
Preoperative PRA class II (positive, ≥5%), n (%)	5 (3.8)	14 (3.9)	9 (3.6)	1 (3.1)	5 (6.0)		0.909
ABO-incompatible transplantation, n (%)	43 (32.3)	151 (42.3)	54 (21.9)	15 (46.9)	19 (22.6)		<0.001
Preoperative conditioning (preoperative rituximab administration or splenectomy, preoperative double filtration plasmapheresis, or plasmapheresis, n (%))	43 (32.3)	151 (42.3)	61 (24.7)	16 (50.0)	20 (23.8)		<0.001
Graft loss, n (%)	4 (3.0)	14 (3.9)	13 (5.3)	5 (15.6)	5 (6.0)		0.039
Recipient death, n (%)	1 (0.8)	22 (6.2)	2 (0.8)	5 (15.6)	1 (1.2)		<0.001

ah, arteriolar hyaline thickening; ci, interstitial fibrosis; ct, tubular atrophy; eGFR, estimated glomerular filtration rate; HLA, human leukocyte antigen; PRA, panel reactive antibody. Bold font indicates statistically significant results.

were excluded; the remaining 853 recipients were included in the study. The 853 recipients were followed up between January 2008 and June 2020 (median observation period: 69.0 [interquartile range, 40.0–105.0] months) and were included in the final analysis.

Recipient Results

Descriptive Data Concerning Donors and Recipients Among Donor Age and Donor-Recipient Age Difference Groups

Table 1 reveals both the donor and recipient characteristics among the 5 groups. Regarding donor characteristics, there were significant differences in donor age, donor sex, preoperative comorbidities, preoperative eGFR, and baseline biopsy findings. Regarding recipient characteristics, there were significant differences in recipient age; age difference between donor and recipient; recipient sex; recipient body mass index; body weight difference between donor and recipient; height difference between donor and recipient; recipient follow-up period; transplantation from a first-degree relative donor; dialysis vintage; preoperative sensitization; HLA-AB mismatch; HLA-DR mismatch; ABO-incompatible transplantation; preoperative conditioning, including rituximab, splenectomy, double filtration plasmapheresis, or plasmapheresis; graft loss; and recipient death. Regarding donor surgery, there was a significant difference in the kidney weight and arterial length. Regarding recipient surgery, there was a significant difference in the incidence of lymphocele (Supplementary Table S1).

eGFR Changes Among Donor Age and Donor-Recipient Age Difference Groups

There were significant differences in eGFRs between the groups, except for those between groups 2 and 3 and between groups 4 and 5 (Figure 2 and Supplementary Table S2). Although the differences in eGFR between groups 4 and 5 were not significant, the eGFR of group 4 was lower than that of group 5 at 6 months post-KT.

Pathologic Findings of Baseline Biopsy 1 Hour After Reperfusion Among Donor Age and Donor-Recipient Age Difference Groups

The incidence of pathologic changes significantly increased with donor age. Accordingly, there was no significant difference between groups 4 and 5 ($P = 0.224$; odds ratio, 0.524; 95% CI, 0.185–1.484; Table 2).

Risk Factors for Graft Loss as a Primary Outcome

The 5-year graft survival for each group was 97.0%, 97.5%, 97.2%, 84.2%, and 96.3%, respectively. In the univariate Fine-Gray competing risk regression model analysis, group 4 (hazard ratio [HR], 8.304; 95% CI, 2.246–30.700; $P = 0.002$), recipient sex (HR, 2.351; 95% CI, 1.086–5.090; $P = 0.030$), and preoperative

sensitization (HR, 0.444; 95% CI, 0.212–0.933; $P = 0.032$) were significant risk factors for graft loss (Supplementary Table S3). In the multivariate Fine-Gray competing risk regression model analysis, group 4 (HR, 16.230; 95% CI, 4.439–59.370; $P < 0.001$) was a significant risk factor for graft loss (Table 3).

Causes of Graft Loss

There was no significant difference in causes of graft loss among the 5 groups ($P = 0.260$, Table 4).

Clinical Events of Recipients Post-KT

The clinical events, including infection and cardiovascular events, were most frequent in group 4 (Table 4).

Recipient Mortality

Recipient mortality rates are found in Figure 3 and Supplementary Table S4. The mortality rate was significantly higher in group 4 than in the other 4 groups (Supplementary Table S4). In total, 31 recipients died. Especially, 25 recipients with functioning grafts died for the following reasons: a traffic accident ($n = 1$) in group 1; acute myocardial infarction ($n = 3$), heart failure ($n = 3$), lung cancer ($n = 2$), and post-transplant lymphoproliferative disorder, thoracic aortic aneurysm rupture, liver failure, arrhythmia, pneumocystis pneumonia, accident, cerebral bleeding, unknown cause, brain cancer, cryptococcal meningitis, and suicide (all $n = 1$) in group 2; pancreatic cancer ($n = 1$) in group 3; pancreatic cancer, drowning, and traumatic subarachnoid bleeding (all $n = 1$) in group 4; and heart failure ($n = 1$) in group 5. The remaining 6 deaths occurred after graft loss for the following reasons: acute aortic dissection, heart failure, and sepsis after acute cellulitis (all $n = 1$) in group 2; cerebral bleeding ($n = 1$) in group 3; and pneumocystis pneumonia and aspiration pneumonia (all $n = 1$) in group 4.

DISCUSSION

This study investigated the effects of donor and recipient ages on adult LDKT. Donor age and donor-recipient age difference affected the postoperative eGFR of recipients; however, recipient surgical results were not affected. LDKT from donors aged 70 to 89 years to recipients with a donor-recipient age difference of -10 to 15 years was found to be an independent risk factor for graft loss and presented the highest risk factor for recipient mortality.

A previous study found that LDKTs from donors aged >70 years were a risk factor for graft loss compared with LDKTs from donors aged 50 to 59 years.¹² To our knowledge, this is the only previous study referring to LDKT from donors aged >70 years. Nevertheless, that study did not investigate the donor-recipient age difference. A univariate analysis by

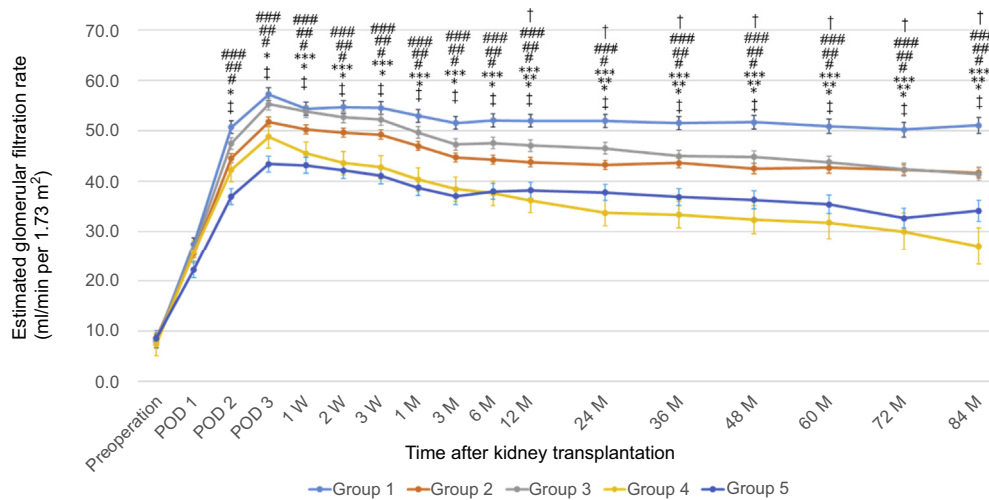


Figure 2. eGFR changes in recipients post-transplantation. Error bars indicate SDs. eGFR was adjusted for recipient sex, transplantation from a first-degree relative donor, dialysis vintage, preoperative sensitization, HLA-AB mismatch, HLA-DR mismatch, and preoperative conditioning. The Benjamini–Hochberg method (FDR method) was used for multiplicity adjustment. **P* < 0.05, group 4 versus group 1; ***P* < 0.05, group 4 versus group 2; ****P* < 0.05, group 4 versus group 3. #*P* < 0.05, group 5 versus group 1; ##*P* < 0.05, group 5 versus group 2; ###*P* < 0.05, group 5 versus group 3; †*P* < 0.05, group 3 versus group 1; ‡*P* < 0.05, group 2 versus group 1. eGFR, estimated glomerular filtration rate; FDR, false discovery rate; HLA, human leukocyte antigen; M, postoperative month; POD, postoperative day.

Ferrari *et al.*¹³ found that an LDKT donor-recipient age difference of ≥30 years, but not 10 to 20 years, was a risk factor for graft loss within 12 months post-operatively. Nevertheless, a multivariate analysis using Cox regression models indicated that donor-recipient age difference was not associated with increased graft loss or serum creatinine levels.¹³ No previous studies have investigated the effects of donor-recipient age difference on LDKT. This is likely because of donor age and donor-recipient age differences not having been considered simultaneously. This study is the first to have simultaneously investigated donor age and donor-recipient age differences in consecutive populations to evaluate the effects of age on LDKT. Concerning the donor characteristics, although smoking history was similar among the groups, preoperative comorbidities except for obesity increased with donor age. This may have resulted in the significantly increased pathologic findings in the baseline biopsy 1 hour post-transplantation and ultimately, in the lowest

preoperative donor eGFR in groups 4 and 5, which was the transplantation from donors aged 70 to 89 years. A declining eGFR with age was previously observed and attributed to the increasing incidence of sclerotic glomeruli in the general population,^{19,20} which may have been amplified because of comorbidities.²¹

The donor age and donor-recipient age difference groups had similar recipient surgical results, except for lymphocele, kidney weight, and arterial length. Although the incidence of lymphocele was significantly higher in group 5, the patients were treated successfully postoperatively. The significant difference in the arterial length and kidney weight did not affect postoperative results because recipient perioperative adverse events were similar except for lymphocele. Postoperative lymphocele, arterial length, and kidney weight did not affect graft function or increase graft loss. In a previous study, delayed graft function was more frequent in recipients grafted from older adult donors.²² In this study, only one delayed graft function

Table 2. Logistic regression analysis of graft biopsy findings 1-hour post-kidney transplantation defined as the presence of interstitial fibrosis and tubular atrophy, glomerulosclerosis, or arteriosclerosis

	Unadjusted					Adjusted for donor sex				
	<i>n</i> (%)	OR	95% CI		<i>P</i> value	<i>n</i> (%)	OR	95% CI		<i>P</i> value
Group 1	26 (19.5)	0.045	0.022	0.094	<0.001	26 (19.5)	0.043	0.021	0.089	<0.001
Group 2	197 (56.3)	0.239	0.128	0.448	<0.001	197 (56.3)	0.234	0.124	0.440	<0.001
Group 3	145 (59.2)	0.269	0.141	0.513	<0.001	145 (59.2)	0.269	0.141	0.514	<0.001
Group 4	25 (78.1)	0.663	0.238	1.851	0.433	25 (78.1)	0.524	0.185	1.484	0.224
Group 5	70 (84.3)	1.000			Ref	70 (84.3)	1.000			Ref

OR, odds ratio; Ref, reference. Bold font indicates statistically significant results.

Table 3. Multivariate Fine-Gray competing risk regression model analysis for graft loss

	P value	Hazard ratio	95% CI	
			Lower limit	Upper limit
Recipient characteristics				
Age difference group between donor and recipient	<0.001	(for all categories)		
Group 1	Ref	1.000		
Group 2	0.460	1.524	0.500	4.647
Group 3	0.330	1.748	0.567	5.390
Group 4	<0.001	16.230	4.439	59.370
Group 5	0.210	2.321	0.615	8.764
Recipient sex (vs. female)	0.074	2.313	0.921	5.811
Preoperative sensitization (transfusion, pregnancy, transplantation) (vs. negative)	0.180	0.533	0.213	1.335

Ref, reference.

Bold font indicates statistically significant results.

was identified in group 1, without any significant differences found among the 5 groups. Consequently, 1 graft loss owing to thrombosis was identified in group 3. To the best of our knowledge, there have been no previous studies reporting recipient eGFR changes postoperatively stratified according to donor age and donor-recipient age difference. A previous study investigating the effects of donor-recipient age difference on mean serum creatinine levels at 1-, 5-, and 10-years post-transplantation did not report any

significant differences.⁶ Nevertheless, in this study, significant differences were found in recipient eGFRs between groups, except for the comparisons between groups 2 and 3 and between groups 4 and 5, which were comparisons of recipients transplanted from the same donor age stratification. This implied that the pathologic findings in the baseline biopsy 1-hour post-transplantation might have affected the recipient postoperative eGFR over a long period of time. Interestingly, the difference in eGFR ran in parallel over time in groups 1 to 3. Nevertheless, the eGFR of group 4 was lower than that of group 5 at 6 months postoperatively, which might explain the highest graft loss risk found in group 4. A previous study found no significant difference in the risk of graft loss between different donor-recipient age difference groups in a multivariate Cox regression model.⁶ That study had limitations in the study design, as it did not consider donor age.⁶ In our study, we identified a novel finding in that group 4, which represented LDKT between older adult donors and older adult recipients, had the highest risk of graft loss. Because group 4 comprised older adult recipients, the graft loss in this group could have been because of postoperative clinical events, such as infection and cardiovascular events.^{10,23,24} The mortality of recipients in group 4 was the highest, followed by group 2. The obtained results concerning recipient mortality were unsurprising because

Table 4. Clinical outcomes of recipients' post-transplantation

	Donor age 30–49 yr		Donor age 50–69 yr		Donor age 70–89 yr		P value
	Donor-recipient age difference, –10 to 15 yr		Donor-recipient age difference, –10 to 15 yr		Donor-recipient age difference, 15–40 yr		
	Group 1	Group 2	Group 3	Group 4	Group 5		
	n = 133	n = 357	n = 247	n = 32	n = 84		
Clinical events, n (%)	53 (39.8)	190 (53.2)	118 (47.8)	22 (68.7)	36 (42.9)		0.009
Biopsy proven rejection, n (%)	16 (12.0)	46 (12.9)	21 (8.5)	4 (12.5)	7 (8.3)		0.449
Biopsy proven recurrent nephritis, n (%)	3 (2.3)	6 (1.7)	4 (1.6)	0	0		0.673
Infection, n (%)	46 (34.6)	161 (45.1)	106 (42.9)	20 (62.5)	31 (36.9)		0.030
Cardiovascular events, n (%)	2 (1.5)	9 (2.5)	0	2 (6.3)	2 (2.4)		0.048
Death, n (%)	1 (0.8)	22 (6.2)	2 (0.8)	5 (15.6)	1 (1.2)		<0.001
Death with functioning graft, n (%)	1 (0.8)	19 (5.3)	1 (0.4)	3 (9.4)	1 (1.2)		<0.001
Graft loss, n (%)	4 (3.0)	14 (3.9)	13 (5.3)	5 (15.6)	5 (6.0)		0.039
Causes of graft loss							0.260
Rejection, n (%)	3 (2.3)	3 (0.8)	7 (2.8)	2 (6.3)	2 (2.4)		
Recurrent nephritis, n (%)	1 (0.8)	2 (0.6)	3 (1.2)	0	0		
Chronic allograft nephropathy, n (%)	0	2 (0.6)	1 (0.4)	0	3 (3.6)		
Cardiovascular events, n (%)	0	3 (0.8)	0	2 (6.3)	0		
Infection, n (%)	0	3 (0.8)	2 (0.8)	1 (3.1)	0		
Thrombosis, n (%)	0	1 (0.3)	0	0	0		
Graft survival period (mo), mean (SD)	75.7 (39.2)	68.8 (38.4)	78.4 (37.3)	48.6 (32.3)	67.1 (37.5)		<0.001

Bold font indicates statistically significant results.

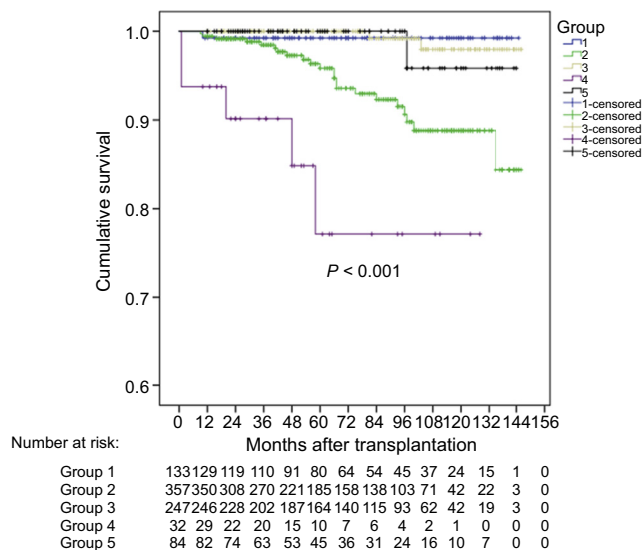


Figure 3. Mortality rate among recipients post-transplantation.

recipient mortality increased with the average age of the groups. Although the KTs between older donors (>70 years) to older recipients could lead to poor graft outcomes when compared with other groups, the 5-year graft survival rate of 84.2% was considered reasonably good. Post-nephrectomy survival of living donors aged >70 years has been reported to be significantly better than that of matched healthy controls.¹² These observations and the substantially improved quality of life for the rest of the older donor's and older recipient's life after KTs might indicate that KTs between older donors and older recipients are acceptable in the clinical practice.^{25,26}

The impact of donor age on the outcomes of younger recipients could be evaluated by comparison of groups 1, 3, and 5. When eGFRs were compared among these 3 groups, the eGFR declined significantly as the donor age increased. The HR for graft loss in groups 1, 3, and 5 increased as the donor age increased, although there were no significant differences. Nevertheless, the mortality rates were similar among these 3 groups. These observations implied that although the lower graft function in the younger recipients who received a transplant from elderly donors could lead to worse graft survival than those from younger donors, LDKTs from the elderly donors to younger recipients could be a favorable life-saving treatment for chronic kidney diseases in clinical practice.

The limitations of this study included its retrospective design and the small number of patients classified into group 4 with wide CIs. Before this study's findings can be adopted in clinical practice, a prospective investigation of the effects of donor age and donor-recipient age differences on LDKT in a large population over a longer observational period is warranted.

In conclusion, LDKT from older adult donors to older adult recipients carries a high risk of graft loss and recipient mortality. The eGFRs of recipients with transplants from donors aged >70 years were significantly lower than those of recipients with transplants from younger donors.

DISCLOSURE

All the authors declared no competing interests.

AUTHOR CONTRIBUTIONS

TH designed, acquired data, interpreted the results, and drafted the manuscript; TT, MO, YM, AT, and TK acquired data; KF, NG, TI, and SN interpreted the results; and KU and YW approved the final version of the manuscript.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1. Distribution of donor and recipient age and classification of recipient groups. Recipients were classified into 5 groups based on donor age and donor-recipient age difference.

Table S1. Donor and recipient operation results.

Table S2. Recipient eGFR changes.

Table S3. Univariate Fine-Gray competing risk regression model analysis for graft loss.

Table S4. Log-rank test for the mortality of recipients.

STROBE Statement (PDF).

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