Research Article

Old-for-Old Age Matching in Living Donor Kidney Transplantation: A Single-Center Experience

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Abstract

The impact of donor age, especially from older donors (≥ 60 years), on recipient outcomes in living donor kidney transplantation were retrospectively evaluated in 181 consecutive primary kidney transplant recipients. Patients were categorized according to donor age: age ≤ 39 (n=15), 40–49 (n=28), 50–59 (n=71), and ≥ 60 years (n=67). Cox proportional hazard multivariate analysis was used to calculate the relative risk of patient and graft survival. Cox analysis showed that donor age, as a continuous variable, was not a risk factor for patient or graft survival. Death-uncensored (65.4%) and censored (73.1%) graft survival rates in the oldest donor group were lowest, although the differences did not reach statistical significance (p=0.086 and 0.127, respectively). Mean estimated glomerular filtration rates one year after transplantation in these 4 groups were 63.1 ± 13.9, 60.4 ± 18.5, 49.2 ± 15.4 and 42.6 ± 11.4 ml/min/1.73 m^2, respectively (p < 0.001). Subdivision by age of recipients of kidney donors ≥ 60 years into those aged, ≤ 39, (n=31), 40-59, (n=25) and ≥ 60 (n=11) years, showed optimal results in old for old combination transplants. The death-uncensored graft survival rates in the 3 subgroups were 64.5%, 76.0% and 90.9%, respectively (p=0.869), whereas their mean estimated glomerular filtration rates 1 year after transplantation were 40.7 ± 7.4, 41.0 ± 10.7 and 51.4 ± 14.3 ml/min/1.73 m^2, respectively (p=0.025). Age-matching may be beneficial when performing living donor kidney transplantation from older donors.

Keywords: Living donor kidney transplantation; Donor age; Clinical outcome; Old-for-old age-matching

Introduction

Kidney transplantation is often the treatment of choice for patients with end-stage renal disease, regardless of age. Deceased donor kidney transplantation is rare in Japan, for social and religious reasons, so most kidney transplants are from living donors. Japan has no living donor exchange program for kidney transplantation for ethical reasons. The growing number of candidates for kidney transplantation and the aging population has led to the increased use of organs from living elderly individuals. Advanced donor age is considered an important risk factor for poor post-transplant outcomes, at least among recipients of deceased donor kidneys [1,2]. Many changes occur as kidney age, including structural alterations, functional decline and modification of immunogenicity [3].

To evaluate the impact of living donor age on post-transplant outcomes, we retrospectively analyzed outcomes of kidney transplantation based on donor age in our center. We also analyzed the effects of the recipient and donor age on clinical outcomes in transplant recipients.

Patients and Methods

This study included 181 adult kidney transplant recipients, ≥16 years of age, who underwent living donor kidney transplantation at our center between November 1988 and July 2013. These patients were followed up at our outpatient clinic until the end of the observation period in July 2014. Recipients of second kidney transplants (n=10) and ABO blood type incompatible transplant (n=41) were excluded from this study.

According to the policy of our center, all donor candidates are admitted for several days to evaluate their suitability as kidney donors. Donor selection is determined by consensus of the nephrologists, transplant surgeons, anesthesiologists, and if necessary, psychiatrists at our center.

The maintenance immunosuppressive regimen given to recipients included a calcineurin inhibitor, mycophenolate mofetil, azathioprine or mizoribine and steroids. Steroids were discontinued in patients who maintained stable graft function 2 years after transplantation. Since 2002, basiliximab has been used for induction therapy. Data on transplant recipients were collected from the medical records of our institution and analyzed.

Two methods of statistical analysis were used to assess the effects of age on clinical outcomes. Cox proportional hazard univariate and multivariate models used 12 clinical factors as variables; recipient age and sex, waiting time, cause of the end-stage renal disease, donor age and sex, estimated glomerular filtration rate (eGFR) before donation, calculated using the MDRD equation modified for Japanese individuals [4], human leukocyte antigens (HLA) mismatches, cytomegalovirus (CMV) serostatus, year of transplantation (1988-2001 versus 2002–2013), acute rejection episode (AR) and CMV infection within 1 year after transplantation. In this analysis, recipient and donor ages were considered continuous variables. Variables with p<0.2 on univariate analysis were entered into the multivariate analysis.

The second method of statistical analysis was a comparison of four recipient groups stratified by donor age at the time of transplantation, with Group 1, 2, 3, and 4 consisting of recipients from donors aged <40 (n=15, 8.3%), 40–49 (n=28, 15.5%), 50–59 (n=71, 39.2%), and ≥ 60 (n=67, 37.0%) years, respectively.

Statistical analysis was performed using SPSS Version 17.0. Categorical data were compared using the chi-square test and continuous data were compared using one-way analysis of variance. Patient and graft survival rates in each group were calculated using the Kaplan-Meier method and compared using log-rank tests. A p value below 0.05 was considered statistically significant.

Results

Risk factors for patient and graft survival

Independent risk factors for patient and graft survival were summarized in (Table 1). The multivariate proportional-hazard models showed that recipient age was the only independent risk factor for patient survival. AR, CMV infection and donor sex (male) were risk factors for death-censored graft survival, whereas AR, eGFR before donation, donor sex (male) and CMV infection were risk factors for death-uncensored graft survival.

Donor age was not a significant risk factor for patient or graft survival. The univariate proportional-hazard model showed that donor age did not significantly affect patient survival (relative risk [RR]=1.044; 95% confidence interval [CI], 0.974 – 1.118; p=0.226). Although the univariate proportional-hazard model of death-censored graft survival showed that donor age was a significant risk factor (RR=1.038; 95% CI, 1.001–1.075; p=0.042), multivariate analysis, after adjustment with other important variables, such as AR, CMV infection, and donor sex, showed that donor age was not independent risk factor (RR=1.044; 95% CI, 1.001 – 1.0089; p=0.059). Similarly, donor age was a significant risk factor for death-uncensored graft survival on the univariate (RR=1.039; 95% CI, 1.007 – 1.003; p=0.018), but not on multivariate (RR=1.030; 95% CI, 0.995 – 1.066; p=0.090), analysis.

Other factors, such as recipient sex, waiting time, cause of the end-stage renal disease, HLA mismatch numbers, CMV serostatus and year of transplantation, did not affect patient or graft survival.

Baseline patient characteristics

Patients were evaluated for a mean duration of 8 years and 2 months ± 5 years and 11 months (median, 6 years and 10 months). The pre-transplant variables that differed significantly among the four groups are shown in (Table 2). The mean pre-donation eGFR was significantly lower in recipients who received transplants from Group 4 donors. The mean recipient age in the elderly donor group was the highest among the groups, indicating that older kidneys were more likely to be donated to older recipient. There were no differences in other pre-transplant variables among the 4 groups, including donor and recipient sex, etiology of renal disease, waiting time, CMV serology of the recipient and donor, year of transplantation (1988-2001 versus 2002-2013), or HLA mismatches.

Recipient outcomes in each group

Both patient and graft survival rates tended to be lower in recipients who received from donors aged ≥ 60 years than those in the other three donor group, although these differences were not statistically significant. The rates of AR and CMV infection within 12 months after transplantation were the same among the four donor age groups. Mean eGFR one year after transplantation was highest in Group 1 and lowest in Group 4. Because mean pre-donation eGFR differed significantly among the 4 groups, we calculated the difference between pre-donation eGFR and that of recipients one year post-transplant (δeGFR). Similar to mean eGFR, mean δeGFR was lowest in Group 1 and highest in Group 4, indicating that grafts from elderly donors showed a greater functional decline 1 year after transplantation than grafts from the other three donor age groups (Table 3).

Analysis of subgroups of the elderly donor group

To examine the interaction of donor and recipient age on transplant outcome, especially older donors, patients who received grafts from individuals aged ≥ 60 years (Group 4) were divided into three age groups: aged < 40 (Group A, n=31, 46.3%), 40–59 (Group B, n=25, 37.3%) and ≥ 60 (Group C, n=11, 16.4%) years. There were no significant differences in patient or graft survival rates among these three subgroups. The frequency of AR during the first year following transplantation was the lowest in Group C, although the difference was not statistically significant. The rate of CMV infection in each of three subgroups was comparable. Mean eGFR one year after transplantation was the highest in Group C. Because mean pre-donation eGFRs of these three subgroups were approximately equal, mean δeGFR was lower in Group C than in the other two groups (Table 4).

variables	relative risk	95% confidence interval	p
Patient survival			
recipient age	1.054	1.009 - 1.102	0.019
Death-censored graft survival			
acute rejection	2.928	1.466 - 5.851	0.002
cytomegalovirus infection	2.457	1.048 - 5.764	0.039
donor sex (male)	1.894	0.975 - 3.681	0.047
Death-uncensored graft survival			
acute rejection	2.103	1.160 - 3.813	0.014
donor eGFR before donation	0.978	0.959 - 0.998	0.029
donor sex (male)	1.874	1.056 - 3.325	0.032
cytomegalovirus infection	2.110	1.047 - 4.255	0.037

Table 1: Risk factors for patient and graft survival on multivariate analysis.

Characteristic	Group 1	Group 2	Group 3	Group 4	p
Number	15	28	71	67	
Donor age, mean ± SD (years)	32.5 ± 4.9	45.3 ± 2.8	55.0 ± 2.5	65.0 ± 4.0	<0.001
Pre-donation eGFR, mean ± SD (mL/min/1.73 m²)	90.2 ± 13.8	76.8 ± 15.8	77.2 ± 17.4	71.9 ± 11.9	<0.001
Recipient age, mean ± SD (years)	42.4 ± 11.8	33.4 ± 13.8	36.9 ± 14.1	43.4 ± 12.2	0.002

Table 2: Patient demographics in each group.

	Group 1	Group 2	Group 3	Group 4	p
Patient survival (%)	93.3	96.4	94.4	92.5	0.696
Death-uncensored graft survival (%)	93.3	82.1	76.1	73.1	0.127
Death-censored graft survival (%)	86.7	78.6	70.4	65.4	0.086
Acute rejection within 12 months after transplantation (%)	33.3	14.3	38	31.3	0.200
Cytomegalovirus infection within 12 months after transplantation (%)	6.7	14.3	16.9	17.9	0.741
eGFR 1 year after transplantation, mean ± SD (mL/min/1.73 m^2)	63.1 ± 13.9	60.4 ±18.5	49.2± 15.3	42.6 ± 11.4	<0.001
δeGFR, mean ± SD (mL/min/1.73 m^2)	26.5 ± 14.8	18.4 ±16.5	29.4± 18.6	29.7 ± 13.2	0.016

Table 3: Clinical outcomes of recipients in the four groups.

	Group A	Group B	Group C	p
Number	31	25	11	
Patient survival (%)	93.5	92.0	90.9	0.450
Death-uncensored graft survival (%)	64.5	76.0	90.9	0.869
Death-censored graft survival (%)	58.1	68.0	81.8	0.997
Acute rejection within 12 months after transplantation (%)	35.5	36.0	9.1	0.221
Cytomegalovirus infection within 12 months after transplantation (%)	22.6	8.0	27.3	0.263
eGFR 1 year after transplantation, mean ± SD (mL/min/1.73 m^2)	40.7 ± 9.4	41.0 ±10.7	51.4± 14.3	0.025
δeGFR, mean ± SD (mL/min/1.73 m^2)	31.6 ± 10.0	29.5 ±15.1	25.4± 16.0	0.450

Table 4: Outcomes of recipients who received kidneys from elderly donors according to recipient age.

Discussion

Donor age is an important predictor of short- and long-term outcomes in deceased donor kidney transplantation. The use of kidneys from deceased donors of an advanced age is associated with an increased likelihood of delayed graft function and AR [1,2]. The negative effects of advanced age are lower for living than for deceased donor transplants, perhaps because rates of delayed graft function are much lower in living than in deceased donor transplantation. Of the 181 recipients in the present study, only one required hemodialysis after transplantation. Thus, in agreement with previous findings [5,6], we found that older age of living donors had only a marginal impact on graft survival following transplantation but could result in deterioration of graft function.

When we divided the recipients of organs from older donors into subgroups by age, we found that the best outcome occurred in recipients aged ≥ 60 years. Superior graft function one year after transplantation was observed in the old-for-old combination group, owing in part to the low incidence of AR in this group. Only one of 11 recipients experienced AR within the first year after transplantation. Although the concept of age matching between donors and recipients is derived from the deceased donor kidney allocation system, it remains unclear whether old-for-old age matching yields optimal results in deceased donor kidney transplantation [2,7-9]. There are few studies that have evaluated the benefit of age matching in living kidney transplantation. To our knowledge, only one previous study reported excellent results for old-for-old combination in living donor kidney transplantation [10]. Our findings are in good agreement with those of this earlier study, suggesting the necessity of age-dependent immunosuppressive protocols for these combinations.

This study had several limitations, including the small number of enrolled patients for relatively long periods, its retrospective design, and the absence of an analysis of etiology. The use of kidneys from older living donors who were selected using the present criteria is reasonable and our findings suggest that age-matching may be beneficial when performing living donor kidney transplantation if the transplants are from elderly donors.

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