Kidney Transplantation From Elderly Donor

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ABSTRACT

Aim. In recent years, there has been an increase in usage of grafts from advanced-age donors because of the shortage of organ availability. Acceptance of elderly living-kidney donors remains controversial due to the higher incidence of comorbidity and greater risk of postoperative complications. The objective of this study was to evaluate the graft function and patient survival using kidneys from living-related and unrelated donors who were older than 65 years of age.

Materials and Methods. From December 2008 until December 2013 we compared the outcomes of 294 patients (mean age, 47.67 ± 12.4 years; range, 16 to 74 years old) who received grafts from donors ≥65 years old to 2339 patients who received grafts from donors who were younger than 65 years old.

Results. We observed no significant differences in sex, time on dialysis, or cold ischemia time between the groups. The recipient ages between two groups were similar. For survival analysis we used the Kaplan-Meier survival estimator. Patient survival at 1, 2, and 3 years was 91.1%, 89.1%, and 88.5%, respectively, for patients transplanted with kidneys from donors ≥65-years-old vs 96.7%, 95.9%, and 95.0%, respectively, in the <65-year-old donor group. Multivariate analysis showed the variables associated with patient survival to be donor age at time of transplantation in years (hazard ratio [HR], 1.65; 95% confidence interval [CI], 1.59–1.71; $P < .05$), time on dialysis in months (HR, 1.22; 95% CI, 1.21–1.23; $P = .002$). Graft survival rates at 1, 2, and 3 years censored for death with functional graft at was 97.6%, 96.4%, and 94.1%, respectively, for patients transplanted with kidneys from donors older than 65 years vs 97.5%, 96.8%, and 95.2%, respectively, in the <65-year-old donor group. Multivariate analysis, HLA-DR mismatches (HR, 1.23; 95% CI, 1.12–1.55; $P = .050$), delayed graft function (HR, 1.77; 95% CI, 1.53–2.07; $P = .021$), and perhaps acute rejection (HR 1.14; 95% CI, 0.82–1.95; $P = .093$) were the variables associated with graft survival.

Conclusion. We concluded that the use of kidneys from donors older than 65 years of age allows us to increase the rate of renal transplantation to approximately 15 to 20 per million population, with good graft and patient survivals provided that the protocol for expanded criteria organs ensured proper macroscopic and microscopic evaluation of the organ for transplantation.

KIDNEY transplantation is the preferred therapy for patients with end-stage renal disease, and most importantly it offers better quality of life, cardiovascular stability, and improved survival [1–3]. More than 20,000

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patients currently await deceased-donor kidney transplantation in Turkey, many of whom will die before a suitable organ becomes available [4]. Because of the limited supply and the increased demand, donor criteria for accepting kidneys have been extended. Living-donor kidney transplantation in the elderly mostly from elderly donors has increased in the past 20 years. Based on Organ Procurement Transplant Network/United Network for Organ Sharing (OPTN/UNOS) data, the proportion of living-donor transplantations performed in patients older than 65 years has increased from 3.1% in 1996 to 13.3% in 2014 in the United States. To increase the donor pool in our center, we began to perform renal transplantations from elderly donors in 2008.

The aim of the present study was to analyze retrospectively the results of renal transplantation among recipients whose donors were ≥65 years old and compare them with results of recipients whose donors <65 years old.

PATIENTS AND METHODS

All 2700 consecutive kidney transplantations from living-related and unrelated donors (approved by the local ethical committee of our city) performed in our unit from December 2008 to December 2013 were included in the study. Data regarding recipients, donors, and transplants were collected from an electronic database. Recipient data included age, gender, time on dialysis, and original disease that caused end stage renal failure. Donor data included age, gender, and follow-up creatinine levels. Transplant variables included warm and cold ischemia times, immediate renal function, rejection episodes, and serum creatinine levels. The glomerular filtration rate was estimated using the abbreviated Modification of Diet in Renal Disease equation (estimated glomerular filtration rate [mL/min/1.73 m^2]).

Continuous variables are expressed as mean ± SD and categorical ones as percentages. Group comparisons were performed using variance analysis and Kruskal-Wallis tests for parametric and nonparametric continuous data, respectively. The χ^2 test was used to compare categorical variables. Survival data were assessed with the Kaplan-Meier method and the Cox proportional hazard regression model (univariate and multivariate). A 2-tailed *P* value of .05 was considered to be statistically significant.

RESULTS

For recipients whose kidneys were from ≥65-year-old donor group (group 1), there were 165 male and 129 female patients whose median age at transplantation was 48 years. The mean time on dialysis was 26 months. The initial immunosuppression was a tacrolimus-based (194 patients) cyclosporine-based (75 patients), or a calcineurin inhibitor–free (25 patients) regimen (Table 1).

For patients who received kidneys from donors <65 years old (group 2), the median age at transplantation was 43 years, and female/male ratio was 935/1404. The mean time on dialysis was 23 months. The initial immunosuppression was 1357 with tacrolimus-based regimen, 645 with cyclosporine-based regimen, and 337 patients who were on calcineurin inhibitor–free regimen (Table 1). We observed no significant differences in sex ($P = .313$), time on dialysis ($P = .216$), or cold ischemia time ($P = .634$) between the groups. The recipient ages for the two groups were similar ($P = .582$). Patient survival rates at 1, 2, and 3 years was 91.1%, 89.1%, and 88.5%, respectively, for group 1 vs 96.7%, 95.9%, and 95.0%, respectively, in group 2 ($P < .05$). Multivariate analysis showed the variables associated with patient survival to be donor age at transplantation in years (hazard ratio [HR], 1.65; 95% confidence interval [CI], 1.59–1.71; $P < .05$), time on dialysis in months (HR, 1.22; 95% CI, 1.21–1.23; $P < .05$).

Table 1. Characteristics of the Patients According to Donor Age

	<65-year-old Donors	≥65-year-old Donors	*P*
Age, y	43	48	.582
Gender (M/F)	1404/935	165/129	.313
Time on dialysis (mo)	23	26	.216
Delayed graft function (%)	4.5	4.9	.778
Early rejection (%)	12.4	13.5	.115
Immunosuppression			
TAC	1357	194	.481
CsA	645	75	
CNI free	337	25	
Patient survival (%)			
1-y	96.7	91.1	<.05
2-y	95.9	89.1	
3-y	95	88.5	
Graft survival censored with death (%)			
1-y	97.5	97.6	.471
2-y	96.8	96.4	
3-y	95.2	94.1	

Abbreviations: TAC, tacrolimus; CsA, cyclosporine; CNI, calcineurin inhibitors.

Graft survival censored for death with functional graft at 1, 2, and 3 years was 97.6%, 96.4%, and 94.1%, respectively, for group 1 and 97.5%, 96.8%, and 95.2%, respectively, in group 2 ($P = .471$). Multivariate analysis, HLA-DR mismatches (HR, 1.23; 95% CI, 1.12–1.55; $P = .050$), delayed graft function (HR, 1.77; 95% CI, 1.53–2.07; $P = .021$), and acute rejection (HR 1.14; 95% CI, 0.82–1.95; $P = .093$) were the variables associated with graft survival. Donor follow-up data related with creatinine at 1, 2, and 3 years was 1.28 mg/dL, 1.41 mg/dL, and 1.45 mg/dL, accordingly. One donor had broken his leg. No death was encountered in donors from group 1 (Table 1).

DISCUSSION

According to our results, patient survival at 1, 2, and 3 years was 91.1%, 89.1%, and 88.5%, respectively, for group 1 vs 96.7%, 95.9%, and 95.0%, respectively, in group 2 ($P < .05$). Graft survival censored for death with functioning graft at 1, 2, and 3 years was 97.6%, 96.4%, and 94.1%, respectively, for group 1 vs 97.5%, 96.8%, and 95.2%, respectively, in group 2 ($P = .471$). Patient survival rates for group 1 were less than that for group 2 and statistically significant ($P < .05$), but when graft survival was censored for death with functioning graft, there was no statistical significance (Table 1). In other words, patients died with functioning grafts. Considering diseases causing patient deaths and the ratio of them, there

was no statistical significant difference between groups ($P = .421$ and $P = .572$, respectively). Most mortality was due to cardiovascular system diseases (40%), infectious etiologies (35%), and other reasons (hepatic insufficiency, pulmonary embolism, etc). When we compared the two groups categorized by donor age, no differences were observed in the time on dialysis ($P = .216$), the prevalence of delayed graft function ($P = .778$), rejection episodes ($P = .115$), or in the initial immunosuppression ($P = .481$).

Our results were excellent compared with other studies and OPTN/UNOS data. According to OPTN/UNOS data, for living-related donors ≥65 years of age, patient survivals at 1, 3, and 5 years vary at 89.3%, 78.1%, and 68.3%, respectively; graft survival rates at 1, 3, and 5 years also vary at 81.1%, 64.3%, and 49.6%, accordingly.

In a study performed by Berger et al, older living-donor allograft recipients' (>70 years old age) graft loss was significantly higher than matched 50- to 59-year-old live-donor allografts but similar to matched non-extended criteria donors for 50- to 59-year-old deceased-donor allografts. Mortality among living kidney donors aged >70 years was no higher than healthy matched controls drawn from the NHANES-III cohort; in fact, mortality was lower, probably reflecting higher selectivity among older live donors than could be captured in National Health and Nutrition Examination Survey III [5].

In another study that included 73 older living donors (older than 60 years), Young et al reported no statistically significant difference in graft loss (both all-cause and death-censored) but a counter intuitive 2.7-fold higher risk of recipient death [6]. Another that included 117 donors older than 60 years (with 25 donors older than 70 years) concluded that death-censored graft loss was not associated with donor age, using a multivariate model in which almost no coefficient was statistically significant [7].

There are other studies in the literature that found encouraging results with elderly living-donor transplantations [8–10]. Graft survival, patient survival, degree of hypertension, and renal function were similar in elderly and young living-donor transplantation groups. In a latest study done by Englum et al using the UNOS database, 250,827 kidney transplantations between 1994 and 2012, 92,646 were living-donor kidneys, with 4.5% of these recipients (n = 4186) transplanted with elderly (≥70 years old) living-donor kidneys. According to their results, overall survival among kidney transplant recipients from older living donors was similar to or better than standard criteria donors' recipients, better than extended criteria donors' recipients, but worse than younger living-donor recipients [11].

In contrary to these results, a systematic review of transplantation outcomes for recipients of living-donor kidneys from 1980 to June 2008 showed that recipients of kidneys from older living donors (>60 years of age) have poorer 5-year patient and graft survival than recipients of kidneys from younger donors [12].

In conclusion, our data show that transplanted kidneys from elderly living donors display excellent short- and long-term graft outcomes.

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