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The Impact of Time-Zero Biopsy on Early Graft Outcomes After Living Donor Kidney Transplantation

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ABSTRACT

Background. In contrast with deceased donor transplantation, the clinical significance of pathologic findings in time-zero biopsies after living donor kidney transplantation are rarely reported, due to the expectation that histologic findings and renal function are normal. The aim of this study was to identify subclinical pathologic findings in living donors and examine the effect on early graft renal function.

Methods. Between December 2006 and July 2011, 146 living-donor kidney transplant recipients were enrolled in this study. We retrospectively analyzed donor and recipient-related clinical parameters, and post-transplant 6 months and 1 year estimated glomerular filtration rate (eGFR) as early graft renal function. Time-zero biopsies were evaluated using the 2007 Banff criteria.

Results. Most abnormal histologic findings were of mild degree as determined by Banff scores. Global glomerulosclerosis (GS, 35.6%), tubular atrophy (CT, 36.3%), interstitial fibrosis (CI, 20.5%), vascular fibrous intimal thickening (CV, 4.1%), arteriolar hyaline thickening (AH, 14.4%), interstitial inflammation (I, 3.4%) were pathologic findings in time-zero biopsies. The univariate analysis revealed that donor age and gender were significantly associated with eGFR at post-transplant 6 months and at 1 year ($P < .05$). Furthermore, GS and CT were significantly associated with early graft renal function ($P < .05$). However, multivariate linear regression analysis showed only donor age was significantly associated with early graft renal function ($P = .001$).

Conclusion. A mild degree of subclinical, pathologic findings on time-zero biopsy did not affect early graft renal function in living-donor kidney transplantation.

THE CLINICAL and histologic statuses of donors are known to influence graft outcome after kidney transplantation, especially after deceased donor kidney transplantation.[1–4] Many authors have reported on the importance of time-zero biopsy. Time-zero biopsies could predict allograft renal function in deceased donor kidney transplantation.[5] Sometimes, unsuspected renal pathology was reported in donor kidney, although all donors were fully studied and all of them accepted the guideline criterion as healthy kidney donors.[6,7] The aim of this study was to identify subclinical, pathologic findings in living donors and examine the effect on early graft renal function.

MATERIALS AND METHODS

Patient Selection

One hundred forty-six living-donor kidney transplant recipients were enrolled in this study between December 2006 and July 2011 at Severance Hospital, Yonsei University Health System. The clinical characteristics and histologic findings of time-zero biopsies were analyzed. This study was approved by our institutional review board.

Clinical Data

We used estimated glomerular filtration rate (eGFR) at post-transplant 6 months and 1 year as parameters of early graft outcomes. The values of eGFR were calculated using with the

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Table 1. Clinical Characteristics of Donors and Recipients

Clinical Characteristics	Mean ± SD or %
Donors	
Age (y)	40.7 ± 11.4
Gender (male/female)	65/81
Body mass index (kg/m^2)	23.1 ± 3.0
Systolic blood pressure (mm Hg)	125.6 ± 15.1
Diastolic blood pressure (mm Hg)	77.3 ± 10.6
Serum creatinine (mg/dL)	0.93 ± 0.18
Creatinine clearance (mL/min/1.73 m^2)	98.6 ± 31.3
Recipients	
Age (y)	43.8 ± 10.8
Gender (male/female)	87/59
Body mass index (kg/m^2)	22.5 ± 3.4
History of diabetes	20 (13.7%)
Human leucocyte antigen mismatch	
0–1	33 (22.6%)
2–4	100 (68.5%)
5–6	13 (8.9%)
Mian immunosuppressant	
Cyclosporine	65 (44.5%)
Tacrolimus	81 (55.5%)

SD, standard deviation.

Modification of Diet in Renal Disease (MDRD) formula. Graft loss was defined as death or conversion to maintenance dialysis. Time-zero biopsies were performed using an 18-G needle gun on the upper kidney pole before reperfusion. Paraffin-embedded permanent sections were stained with hematoxylin and eosin with Masson trichrome, and read by a pathologist specializing in transplantation. Histopathologic findings were rated using the 2007 Banff scoring system.[8,9]

Statistics

All statistical analyses were performed using SPSS 18.0 for Windows (SPSS, Chicago, IL). Univariate analysis was performed using the independent *t*-test or analysis of variance and the chi-square-test or linear regression analysis. Multivariate linear regression analysis was performed with adjustment for recipient and donor clinical parameters. Kaplan-Meier survival curves were used for graft survival analysis. A two-sided $P < .05$ was considered to be significant.

RESULTS

Patient Characteristics

Mean donor age was 40.7 ± 11.4 years. Mean serum creatinine and creatinine clearance values were 0.93 ± 0.18 mg/dL and 98.6 ± 31.3 mL/min/1.73 m^2. Recipients had a mean age of 43.8 ± 10.8 years. Almost all recipients received calcineurin inhibitor based immunosuppressive therapy. Basiliximab was used as an induction therapy (Table 1).

Hisotologic Findings in Time-Zero Biopsy

The mean number of glomeruli measured in time-zero biopsies was 14.0 ± 6.8. Immunoglobulin (Ig) A nephritis was detected incidentally in 6 biopsies (5 cases in subclass I, 1 case in subclass II by the Haas classification).[10] Abnormal histologic findings were obtained in 61.6% of the 146 biopsies. Glomerulosclerosis (GS), tubular atrophy (CT), interstitial fibrosis (CI), arteriolar hyaline thickening (AH), vascular fibrous intimal thickening (CV), and interstitial inflammation (I) were observed in 35.6%, 36.3%, 20.5%, 14.4%, 4.1%, and 3.4%, respectively, of 135 the donor kidneys. The majority of histologic findings were of mild degree according to the Banff criteria (grade I).[8,9]

Post-transplant Outcomes

Mean eGFRs at post-transplant 6 months and 1 year were 60.2 ± 17.6 and 62.3 ± 18.7 mL/min/1.73 m^2. Mean follow-up duration after transplantation was 33 ± 18.8 months, and

Table 2. Univariate Analysis of the Association Between Histologic Parameters and Graft Outcome

Banff Score (n = 146)	eGFR at 6 Months	*P*	eGFR at 1 year	*P*
Glomerulosclerosis		.016		.018
0% (n = 94; 64.4%)	62.76 ± 18.11		65.03 ± 19.03	
<10% (n = 25; 17.1%)	53.82 ± 10.1		57.16 ± 10.37	
≥10% (n = 27; 18.5%)	54.37 ± 17.16		54.90 ± 20.40	
Tubular atrophy		.044		.006
0 (n = 93; 63.7%)	62.39 ± 19.03		65.52 ± 17.97	
1 (n = 53; 36.3%)	56.26 ± 14.04		56.61 ± 18.75	
Interstitial fibrosis		.995		.63
0 (n = 116; 79.5%)	60.19 ± 18.42		62.69 ± 18.71	
1 (n = 30; 20.5%)	60.17 ± 14.33		60.84 ± 18.83	
Arteriolar hyaline thickening		.676		.681
0 (n = 125; 85.6%)	60.44 ± 18.06		62.57 ± 18.78	
1 (n = 21; 14.1%)	58.70 ± 14.95		60.75 ± 18.5	
Vascular fibrous intimal thickening		.295		.081
0 (n = 140; 95.9%)	60.51 ± 17.75		62.87 ± 18.70	
1 (n = 6; 4.1%)	52.79 ± 12.81		49.26 ± 13.75	
Interstitial inflammation		.799		.451
0 (n = 141; 96.6%)	60.13 ± 17.67		62.09 ± 18.86	
1 (n = 5; 3.4%)	62.41 ± 17.18		69.84 ± 9.57	

eGFR, estimated glomerular filtration rate.
Univariate analysis was conducted using the independent *t*-test and analysis of variance.