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Original Article

Prognostic significance of renal arterial resistance index in living related kidney transplant recipients from elderly donors

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Abstract: The aim of this study was to evaluate the clinical correlation of the renal arterial resistive index (RRI) in living related kidney transplantation (LRKT) recipients from elderly donors as well as its role in predicting outcome of patients and grafts. 136 LRKT recipients from elderly donor with blood pressure monitoring and renal color doppler ultrasonography as well as laboratory tests. We analyzed the association between RRI value and its baseline characteristics. Next, univariate survival analysis was performed using Kaplan-Meier method and the Log-rank test. Finally, a Cox multivariate analysis model was performed to investigate the predictor role of RRI in recipient's survival. We found that RRI was related to recipient age, serum creatinine and eGFR measured at day 7 after LRKT. However, there was no difference observed in gender, BMI, immunosuppressive regimen, blood pressure and proteinuria. Kaplan-Meier analysis with the log-rank test revealed that high RRI (>0.7) had a significant impact on recipient overall survival. Finally, in a multivariate Cox model, we found that high RRI value was an independent poor prognostic factor for overall survival rate. Our results indicated that RRI was an important indicator in LRKT recipients from elderly donor.

Keywords: Living related kidney transplantation, elderly donor, renal arterial resistance index, prognostic analysis, overall survival

Introduction

Kidney transplantation (KTx) is the most effective treatment of choice for end-stage renal disease [1, 2]. Living related donors have become one of the major sources of renal transplantation. Yet, the increasing number of potential candidates for kidney transplantation has led to a greater acceptance of living donation from older individuals [3]. However, the safety of aged graft was controversial from the start. This situation suggests the need to expand our control efforts by exploring specific markers for predicting outcome of living related kidney transplantation from elderly donors.

Doppler ultrasonography is an important method for analyzing gross structural pathology of the kidney. An elevated renal arterial resistive index (RRI) has been reported to be closely related to renal allograft function and death from cardiovascular disease in transplant recipients [4]. However, the relationship between RRI and survival of kidney transplant recipients from elderly donors has not yet been reported.

The aim of this study was to evaluate the clinical correlation of the RRI in living related kidney transplant recipients from elderly donors as well as its role in predicting outcome of patients and grafts. We firstly analyzed the association between RRI value and its baseline characteristics. Next, univariate survival analysis was performed using Kaplan-Meier method and the Log-rank test. Finally, a Cox multivariate analysis model was performed to investigate the predictor role of RRI in recipients survival.

Materials and methods

Patients

A total of 136 living related kidney transplantation (LRKT) recipients with end-stage renal disease on regular follow-up at our center from

Table 1. Patient characteristics

	RRI < 0.7 n=101	RRI ≥ 0.7 n=35	*P* value
Donor age (y)	58.55±3.20	58.97±3.37	0.513
Recipient age (y)	31.95±5.14	35.03±4.43	0.08*
Gender			0.295
Female	28 (27.72%)	13 (37.14%)	
Male	73 (72.28%)	22 (62.86%)	
BMI	20.76±3.42	21.49±3.01	0.264
Immunosuppressive regimen			0.239
CSA+MMF+PRED	37	9	
TAC+MMF+PRED	64	26	
Systolic blood pressure (mm Hg)	127.1±15.02	129.00±16.09	0.528
Diastolic blood pressure (mm Hg)	83.33±8.09	85.00±9.67	0.318
Serumcreatinine (mg/dL)			0.028*
< 1.5	82 (81.2%)	29 (18.8%)	
≥ 1.5	22 (62.9%)	13 (37.1%)	
Proteinuria	20 (19.8%)	14 (40.0%)	0.017*
eGFR day 7 (mL/min)	49.13±12.15	44.19±12.24	0.04*

*: P < 0.05.

May 2004 to July 2014 were prospectively enrolled.

Exclusion criteria were according to previous living related renal transplantation. Other exclusion criterias were donor age < 60 years old, pretransplantation hemodialysis for >1 year, prior diagnosis of graft vascular problems (thrombosis, stenosis, etc), or less than 6 months follow-up.

At the time of donation, imaging and laboratory tests were extensively used to assess donor kidney, and the results were satisfactory. For comparison, kidney allograft function post-transplant was assessed by serum creatinine, eGFR (estimated GFR) using modification of diet in renal disease (MDRD) formula: eGFR (mL/min/1.73 m^2)=186* serum creatinine (mg/dl)-1.154 *age*0.203-0.742 (female). Proteinuria was defined as urine protein ≥ (+) or 24 hours urinary protein quantitation >150 mg.

Renal arterial resistive index

Renal arterial resistive index was performed at day 7 after kTx and measured as described previously [5]. Colour Doppler examination was performed byechograph (Vividsystem 7, GE Vingmed Ultrasound, General Electric) after echocardiographic examination. The RRI was calculated according to the following formula:

RRI = (1 - maximum enddiastolic velocity/maximum systolic velocity) * 100

According to the RRI (0.7) [6], patients were divided into 2 groups, above and below the value, respectively.

Statistical analysis

Statistical analysis was carried out using SPSS 18.0 software (SPSS, Inc., Chicago, IL, USA) and GraphPad Prism 5 (GraphPad Software Inc., CA, USA). $P < 0.05$ was considered significant. Count data were analyzed by the χ^2 or Fishers exact tests. Continuous variables were compared using Student *t*-test. Survivals were examined using Kaplan-Meier analysis and compared using the log-rank test. Multivariate survival analysis was performed using the Cox multivariate analysis model.

Results

Association between RRI and baseline characteristics

A total of 136 patients participated in this study. Among the 136 patients, 101 (74.26%) had high RRI value (≥ 0.7), 35 (25.74%) had low RRI value (< 0.7). The clinical characteristics of the recipients are summarized in **Table 1**. The groups of patients with different RRI value showed similar distributions of donor and precipitant factors, including elderly donor age, gender, BMI, immunosuppressive regimen, systolic blood pressure and diastolic blood pressure, and proteinuria. Recipients with a high RRI were older, had higher serum creatinine level and incidence of proteinuria, and a lower eGFR measured at day 7 after KTx compared with recipients with a lower RRI.

Because the RRI was linked closely to baseline characteristics of recipients, we postulated that RRI may play an important role in kidney transplant recipients. To test this hypothesis

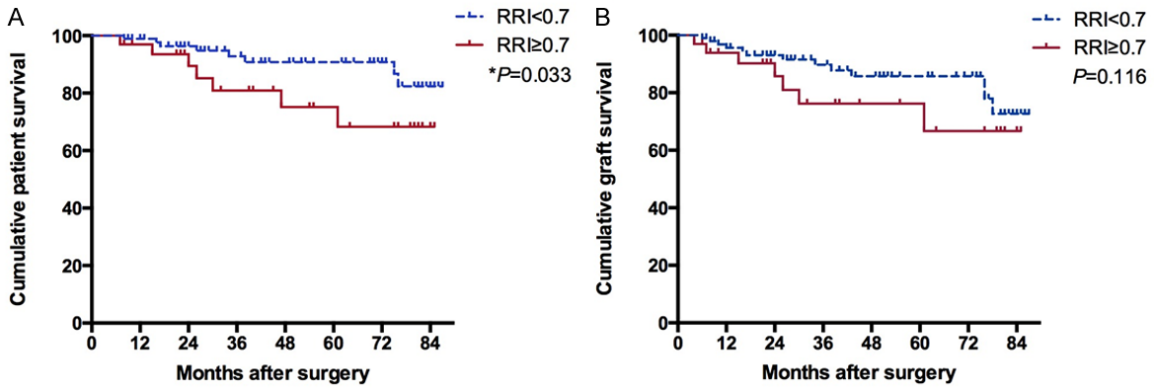

Figure 1. Long-term patient and graft survival were examined for the recipients after LRKT. A. High RRI (>0.7) had a significant impact on recipient overall survival. B. There was no significant difference on graft survival was observed between the two groups.

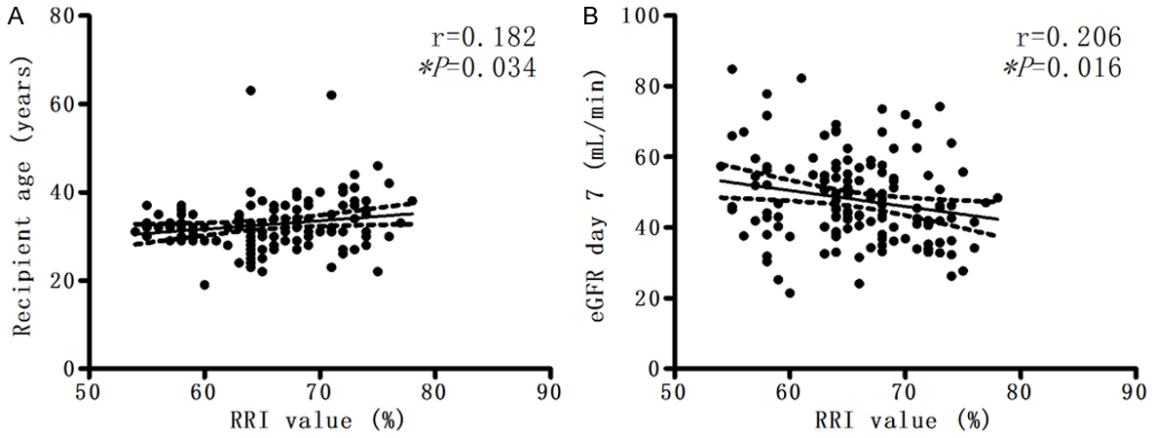

Figure 2. A. Correlation of recipient age with renal resistive index (RRI). B. The correlation of eGFR and RRI value was analyzed.

we further analyzed the correlation of recipient age and eGFR with RRI. There was a significant correlation between recipient age and RRI (b=0.192, *P*=0.034). The results show recipient age is higher, while RRI has a lower value (**Figure 1A**). The eGFR level was also significantly negatively correlated with RRI in LRKT recipients (shown in **Figure 1B**, b=-0.451, *P*=0.016). These results further confirmed that RRI played an important role in LRKT recipients.

High resistive index predicts poor prognosis of elderly LRKT recipients

Considering that the RRI value was remarkably correlated with recipients age, serum creatinine and eGFR, we hypothesized that RRI might affect the prognosis of grafts and recipients after KTx.

Kaplan-Meier plots of survival among LRKT recipients revealed that recipients with low RRI (≤0.7) survived longer than recipients with high RRI (>0.7) ($P < 0.05$ by log-rank test; **Figure 2A**).However, there was no significantly difference on graft survival (**Figure 2B**).

To verify whether the RRI and other variables are independent prognostic factors for recipients, the multivariate Cox regression model was used. Multivariate analysis revealed that the independent predictors of events were RRI value, BMI, immunosuppressive regimen and serum creatinine. And high RRI value was significantly associated with poor prognosis (shown in **Table 2**).

Table 2. Multivariate analyses for overall survival by Cox regression model

	Wald	*P* value	RR	RR 95.0% CI	
				Lower	Upper
Recipient age	2.283	0.131	0.914	0.814	1.027
Gender	0.172	0.678	0.782	0.244	2.502
BMI	3.997	0.046*	1.257	1.004	1.574
Immunosuppressive regimen	6.754	0.009*	24.093	2.186	265.502
Proteinuria	0.004	0.948	1.043	0.299	3.634
eGFR	0.352	0.553	1.016	0.963	1.072
Systolic blood pressure	0.04	0.841	0.996	0.957	1.036
Diastolic blood pressure	0.001	0.983	0.999	0.929	1.075
Serumcreatinine	9.886	0.002*	19.469	3.059	123.908
RRI	4.362	0.037*	1.122	1.007	1.249

*: P < 0.05.

Discussion

Living kidney donation has shown superior outcomes for the recipient, prolonged the survival time of patient and graft [7]. Nevertheless, the demand continues to exceed the supply. To meet the demand, use of kidneys from elderly donors selected using expanded criteria has become increasingly common [8].

In this study, 136 LRKT recipients from elderly donor were analyzed retrospectively. We found that RRI was related to recipient age, serum creatinine, incidence of proteinuria and eGFR measured at day 7 after LRKT. However, there was no difference observed in gender, BMI, immunosuppressive regimen, blood pressure and proteinuria. These results are concordant with a majority of previous studies [6, 9, 10]. We further analyzed the correlation of recipient age and eGFR with RRI. There was a significant correlation between recipient age and RRI. The results show that recipient age and eGFR level was significantly correlated with RRI in LRKT recipients. Considering that the RRI value play an important role in recipient outcome of clinical parameters, we hypothesized that RRI might affect the prognosis of grafts and recipients after LRKT. In order to verify this guess, Kaplan-Meier analysis with the log-rank test was performed to analyze overall survival of the grafts and recipients. The results revealed that high RRI (>0.7) had a significant impact on recipient overall survival, however, there was no significantly difference on graft survival. Seiler S [8] et al reported that RRI is not an organ-specific predictor of allograft outcome in stable KTx recipients. Finally, multivariate Cox regression analysis was performed to further investigate the predictor role of RRI in recipient's survival. In a multivariate Cox model, we found that high RRI value was an independent poor prognostic factor for overall survival rate, indicating that high RRI value was significantly associated with poor OS in LRKT recipients from elderly donor.

In conclusion, our results demonstrated that RRI offers insights about the function of the kidney allograft and predicts recipient long-term outcome. This data indicated that RRI was an important indicator in LRKT recipients from elderly donor.

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Disclosure of conflict of interest

None.

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