

Relation of Resistive and Pulsatility Indices With Graft Function After Renal Transplant

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Abstract

Objectives: There are conflicting data regarding the use of some measured indices by Doppler ultrasound such as the resistive index and the pulsatility index in predicting renal allograft dysfunction. This study sought to evaluate the association of early postoperative Doppler indices and 3-month serum creatinine levels in renal transplant recipients.

Materials and Methods: During a 1-year period, all patients who underwent renal transplant at our hospital were recruited into a prospective study. Doppler ultrasound was performed on all patients 6 days and 3 months after the transplant and the resistive index and the pulsatility index were calculated for each patient. Then, the association between these indices and 3-month outcomes of patients were investigated.

Results: Thirty-eight patients including 21 men (mean age, 36.6 ± 13.1 y) were evaluated. There was a positive correlation between the resistive index and the pulsatility index at 6 days after transplant and the serum creatinine measured at the same day ($P < .001$ and $r=0.570$ for resistive index; $P < .001$ and $r=0.547$ for pulsatility index). There was also a positive correlation between the pulsatility index and the resistive index at 6 days after transplant and 3-month serum creatinine

level ($P = .009$ and $r=0.420$ for resistive index; $P = .009$ and $r=0.417$ for pulsatility index). There were negative correlations between the resistive index and the pulsatility index on the sixth day after surgery and creatinine clearance measured at 6 days and 3 months after transplant.

Conclusions: This study reveals a strong-to-medium correlation between the resistive index and the pulsatility index, serum creatinine level, measured 6 days after transplant.

Key words: Creatinine, Doppler ultrasound, Kidney, Transplantation

Introduction

Advantages in renal transplant compared with dialysis include a lower cost, higher long-term survival, and improved quality of life for patients with end-stage renal disease make it the treatment of choice for these patients.¹ However, renal transplant half-life is still poor in spite of significant advances in immunosuppression therapy that have resulted in improved short-term (1 y) renal allograft survival.^{2,3} Although allograft rejection during the first year after transplant infrequently causes immediate loss of the graft, it can cause constant allograft dysfunction in a considerable percentage of cases.² Moreover, it has been shown that acute rejection and delayed graft dysfunction adversely affect long-term survival of the graft after renal transplant.⁴⁻⁶ Early diagnosis of acute allograft rejection is important for long-term renal allograft survival.²

Histologic examination of the percutaneous needle transplant biopsy is still the criterion standard for diagnosing acute rejection; however, it is an invasive procedure and has some limitations.⁶ Thus, a noninvasive technique to detect acute rejection in the renal allograft has been sought.⁷

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Duplex Doppler ultrasonography is suggested as a noninvasive way of assessing the hemodynamics of renal blood flow in renal and intrarenal arteries in patients with various renal diseases and patients undergoing renal transplant.^{8,9} However, there are conflicting data regarding the reliability of some indices, such as the resistive and the pulsatility indices in renal transplant recipients by this technique.⁹⁻¹³ The present study was designed and conducted to evaluate the association between the value of these indices during the first week after transplant and 3-month outcomes in renal transplant recipients.

Materials and Methods

After approval of the ethical committee of human research of the Ahvaz Jundishapur University of Medical Sciences, this study was carried out at the Golestan Hospital, Iran, between October 2009 and October 2010. All patients with end-stage renal disease who underwent a living-donor renal transplant during this time were recruited in this prospective study after informed consent was obtained. All protocols conformed with the ethical guidelines of the 1975 Helsinki Declaration. Patients who had a serum creatinine (Cr) level > 265.2 $\mu\text{mol/L}$ (3 mg/dL) during the 6 days after transplant (because these patients were considered as having delayed graft function that could interfere with the follow-up after 3 month), those with hydronephrosis of grade 2 or higher, renal artery stenosis of 50% and more, compressing mass (eg, hematoma or seroma around the grafted kidney), severe hypotension (systolic blood pressure of < 70 mm Hg), acute pyelonephritis, and a diagnosis of acute tubular necrosis after transplant were excluded. Those patients who did not reach to an acceptable creatinine level were not suitable cases to follow-up, and we preferred to have a more homogenous population of renal function and so, patients with Cr > 3 $\mu\text{mol/L}$ were excluded. For each patient, in addition to the demographics, age of the donor and the recipient, systolic and diastolic blood pressures, heart rate of recipient before and after transplant, serum level of cyclosporine, history of cigarette smoking, and duration of dialysis before transplant were recorded.

Six days after transplant, Doppler ultrasound was performed on all patients by an ultra-

sonographer who was blind to the Cr level of the patients. The ultrasonographer used a convex probe of MHz (ProSound 3500Plus, Aloka, Japan) that was repeated 3 months after transplant under the same conditions. Resistive index (RI) was calculated using following equation: $\text{RI} = \frac{\text{peak systolic velocity (PSV)} - \text{end-diastolic velocity (EDV)}}{\text{PSV}}$. Pulsatility index (PI) also was calculated using following ratio; $\text{PI} = (\text{PSV} - \text{EDV}) / \text{mean velocity}$.

Serum Cr level was measured at 6 days and 3 months after renal transplant and clearance of Cr was estimated using the Cockcroft-Gault equation as below:¹⁴

$\text{Clearance of Cr} = \frac{[140 - \text{age (y)}] \times \text{weight (kg)}}{[72 \times \text{plasma Cr } (\mu\text{mol/L}) \times 88.4]} \times (0.85 \text{ if female})$.

Statistical analyses

Statistical analyses were performed with SPSS software (SPSS: An IBM Company, version 17.0, IBM Corporation, Armonk, New York, USA). Continuous data are expressed as means $\pm$ standard deviation and were compared using paired samples *t* test and Wilcoxon signed rank test (for variables without normal distribution). Pearson product moment correlation analysis also was performed to evaluate the correlation between RI and PI with other variables. We considered $r \geq 0.50$ as strong and $0.30 \leq r < 0.50$ as medium correlations. Finally, linear regression analysis was done to find some models to predict the relation between serum Cr and clearance of Cr and RI and PI measured at 6 days after transplant.

Results

During the study, 43 patients underwent renal transplant. Five cases were excluded owing to renal artery stenosis of 70% ($n=1$), death ($n=1$), segmental artery stenosis ($n=1$), and acute tubular necrosis ($n=2$). Four out of the remaining 38 patients, did not present for a 3-month sonographic evaluation and these patients were only included in the analysis of PI and RI measured 6 days after transplant.

Thirty-eight patients (21 men; mean age, 36.6 ± 13.1 y) were included in the final analysis. At 6 days after transplant, systolic blood pressure in recipients was significantly higher compared to pretransplant systolic blood pressure (153.4 ± 12.2 vs 142.6 ± 11.9 mm Hg; $P < .001$). However, there was

no significant difference between the transplant (89.1 ± 10.5) and posttransplant (92.07 ± 10.8) diastolic blood pressure of recipients ($P = .12$). Mean SCr level was $112.26 \pm 47.73 \mu\text{mol/L}$ and $99.89 \pm 32.70 \mu\text{mol/L}$ at 6 days and 3 months after transplant ($P = .17$). Mean Cr clearance was 77.8 ± 22.4 at 6 days after transplant while it increased to 82.08 ± 21.9 three months after renal transplant ($P = .36$). There was a medium negative correlation between serum cyclosporine level and serum Cr level, while there was a positive medium correlation between serum cyclosporine level and Cr clearance. In this study, we did not find an association between the recipient and donor age, the duration of dialysis before transplant, history of cigarette smoking, heart rate, and pretransplant blood pressure with RI and PI ($P > .05$).

Mean PSV was 34.2 ± 10 and 34.3 ± 7.9 at 6 days and 3 months after transplant which was not statistically significant ($P = .96$). Similarly, there was no significant difference between mean EDV values at 6 days and 3 months after renal transplant (10.9 ± 3.6 vs 11.4 ± 1.3 ; $P = .40$). Mean RI at 6 days and 3 months after the operation was 0.68 ± 0.08 and 0.66 ± 0.08 ($P = .26$). However, there was significant difference between mean PI values at 6 days and 3 months after renal transplant (1.37 ± 0.31 vs 1.21 ± 0.29 ; $P = .02$).

There were strong positive correlations between calculated RI at 6 days and 3 months after transplant ($P < .001$ and correlation coefficient=0.890). Similarly, there were strong positive correlations between calculated PI at 6 days and 3 months after transplant ($P < .001$ and correlation coefficient=0.950). There were medium positive correlations between RI and PI at 3 months after renal transplant with both posttransplant systolic and diastolic blood pressures. Table 1 demonstrates the correlation between PSV, EDV, RI, and PI, with serum Cr and Cr clearance. As the Table shows, there

is a strong positive correlation between both RI and PI at 6 days after transplant and serum Cr measured at the same day. Moreover, there was a medium positive correlation between PI and RI measured on the sixth posttransplant day and 3-month serum Cr level. There were medium negative correlations between sixth day RI and PI and Cr clearance measured at 6 days and 3 months after transplant.

Using linear regression below yielded models for predicting posttransplant levels of serum Cr and Cr clearance:

$$\text{Third month serum Cr} = -0.114 + 1.84 \times \text{RI}_6$$

$$\text{Sixth day serum Cr} = -0.652 + 2.74 \times \text{RI}_6$$

$$\text{Third month Cr clearance} = 145.1 - 90.93 \times \text{RI}_6$$

$$\text{Sixth day Cr clearance} = 163.5 - 123.5 \times \text{RI}_6$$

$$\text{Third month serum Cr} = 0.48 + 0.5 \times \text{PI}_6$$

$$\text{Sixth day serum Cr} = 0.26 + 0.73 \times \text{PI}_6$$

$$\text{Third month Cr clearance} = 115.07 - 24.5 \times \text{PI}_6$$

$$\text{Sixth day Cr clearance} = 124 - 34.7 \times \text{PI}_6$$

Where RI₆ and PI₆ are RI and PI measured 6 days after transplant. Figure 1 demonstrates the correlation between RI and PI of 6 days after renal transplant and latest SCr and Cr clearance.

Discussion

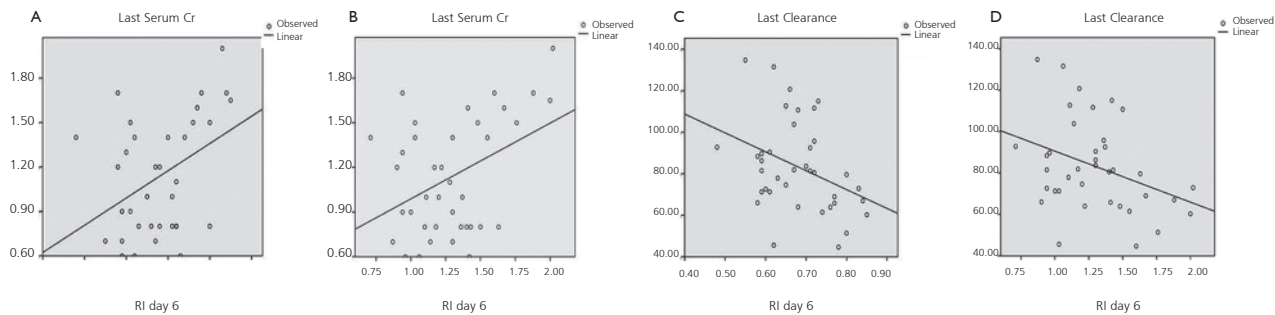
Our findings showed a strong positive correlation between RI and PI 6 days after transplant and serum Cr measured on the same day. Additionally, our results revealed a medium positive correlation between PI and RI calculated at the sixth posttransplant day with a 3-month serum Cr level. Similarly, we found medium negative correlations between the sixth day RI and PI and the CR clearance measured at 6 days and 3 months after transplant. Supporting our results, Ardalan and associates suggested statistically significant correlations between RI or PI with serum Cr level during the first

Table 1. Correlation Between Peak Systolic Volume (PSV), End Diastolic Volume (EDV), Resistive Index (RI), and Pulsatility Index (PI) with Serum Creatinine (SCr) and Clearance of Cr

Cr (6 d)	Clearance of Cr (6 d)	Cr (3 mo)	Clearance of	Cr (3 mo)
EDV (6 d)	$P = .01$ $r = -0.380$	NS	NS	NS
PSV (6 d)	NS	NS	$P = .01$ $r = 0.380$	NS
RI (6 d)	$P < .001$ $r = 0.570$	$P = .002$ $r = -0.488$	$P = .009$ $r = 0.420$	$P = .02$ $r = -0.364$
PI (6 d)	$P < .001$ $r = 0.547$	$P = .002$ $r = -0.493$	$P = .00$ $r = 0.417$	$P = .03$ $r = -0.353$
EDV (3 mo)	$P = .004$ $r = -0.464$	NS	NS	NS
PSV (3 mo)	NS	NS	$P = .02$ $r = 0.376$	NS
RI (3 mo)	NS	$P = .04$ $r = 0.329$	$P = .02$ $r = -0.358$	NS
PI (3 mo)	NS	$P = .03$ $r = -0.358$	$P = .01$ $r = 0.395$	$P = .04$ $r = -0.330$

Abbreviations: NS, nonsignificant

Figure 1. (A). Correlation Between 6-Day RI and Last Measured Serum Cr. (B). Correlation Between 6-Day PI and Last Measured Serum Cr. (C). Correlation Between 6-Day RI and Last Cr Clearance. (D). Correlation Between 6-Day PI and Last Cr Clearance



month after renal transplant.¹⁵ Chudek and colleagues also found significant negative correlations between donor glomerular filtration rate and PI and RI.¹⁶

Renal Doppler ultrasound is the imaging modality of choice for following up of renal transplant recipients. It can diagnose initial graft dysfunction as well as postoperative complications.¹⁷ In addition, Doppler ultrasound can be used to measure some indices. Resistive index is one that is an indirect indicator for degree of resistance of the intrarenal vessels. In other words, it shows the “vascular compliance” of the recipient.¹⁷ However, RI has some limitations such as wide normal range that makes its values limited.¹⁸ Additionally, many conditions such as acute rejection, acute tubular necrosis, venous thrombosis, hydronephrosis, and pyelonephritis can result in elevation of RI immediately after renal transplant,^{17,19} whereas RI changes are not specific for any of these clinical entities.²⁰ Regardless of these limitations, elevation of RI after renal transplant is an indicator of graft dysfunction that may adversely affect long-term graft survival.²¹

There are conflicting results regarding the value of indices such as RI and PI that measure using Doppler ultrasound in predicting graft dysfunction in renal transplant recipients. Many studies support the use of these indices.^{13,21-23} Kahraman and associates showed that and RI > 0.7 and a PI > 1.1 are associated with a decline in allograft function at 1 year compared to 1 month.²² Similarly, Barba and colleagues found a cutoff point of 0.7 for RI in predicting graft dysfunction.¹⁷ On the other hand, many studies failed to show a role for these indices for predicting of allograft rejection.^{7,24,25} However, complicated patients including those with acute

tubular necrosis, acute rejection, delayed function, and cyclosporine toxicity were not excluded from some of these studies, which partly may explain the discrepancy between these studies’ findings and those that support the use of RI and PI for predicting renal graft dysfunction.²² In the present study, we also excluded complicated cases and obtained results supporting the value of these indices for predicting renal allograft function.

Finally, although some authors found an association between recipient age and RI,²⁶ in the present study, we did not find any association between recipient and donor age, duration of dialysis before transplant, history of cigarette smoking, heart rate, and pretransplant blood pressure with RI and PI.

Any of the previous predictors of graft outcome, including early serum Cr level, relative renal size, and also Doppler indices are not definite predictors of further allograft function. So, we tried to find additional indices to predict graft survival, irrespective of etiology. A moderate-to-strong correlation between Doppler indices and early serum Cr could be used as an additional predicting factor for graft outcome. Also, this study could provide a background to compare the sensitivity of Doppler sonography and serum creatinine in graft survival.

In this study, we found a strong-to-medium correlation between RI and PI and serum Cr level measured 6 days after transplant. In addition, a smaller correlation also was found between indices measured by Doppler ultrasound and serum Cr and Cr clearance at 3 month after transplant. Therefore, it seems that RI and PI at 6 days after renal transplant can probably be used to predict serum Cr level as well as Cr clearance in renal transplant recipients.

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