Original Article

Early Sonographic Evaluation of Intrarenal Arterial Resistive Index and Long-term Renal Function in Renal Transplant Recipients in South Western Nigeria

Ajana George Madubueze*

Department of Radiology, St. Nicholas Hospital, Lagos State, Nigeria

Abstract

Background: Color Doppler ultrasonography of intrarenal arterial Resistive Index (RI), performed early after kidney transplant, has proven to reliably predict short-term allograft function. The aim of this study was to assess whether early Doppler assessment could correlate with long-term renal function. **Methods:** This was a retrospective study of intrarenal RI using ultrasound in 41 stable kidney transplant patients who underwent RI assessment within 1 month after the transplant. Color Doppler ultrasonography was done to calculate the intrarenal RI within the first 4 weeks after transplant. The mean values of the intrarenal RI of the interlobar arteries of the allograft kidneys were measured and recorded. The data were analyzed with the aid of computer-based SPSS 20.0 software for windows (IBM, International Business Machines Corporation, Company, Armonk, New York, USA). **Results:** Older recipient age, active smoking, and proteinuria were associated with a higher intrarenal RI. Multivariate analyses showed that renal RI and donor age were independent predictors of allograft outcome. Kaplan–Meier estimates of cumulative graft survival were significantly worse in patients who had the values of the RI of 0.7 or more than they were in patients who had the values of the RI of <0.7. **Conclusion:** This study reveals that renal RI determined within the 1st month after renal transplant correlates with long-term allograft function in kidney transplant recipients.

Keywords: Doppler ultrasonography, graft survival, renal resistive index

Introduction

Chronic kidney disease (CKD) is a progressive loss of glomerular function caused by a long-standing renal parenchymal disease. It is present when the glomerular filtration rate (GFR) is <60 ml/min/1.73 m^2 for 3 consecutive months.[1] CKD is a prevalent disease, affecting between 10% and 15% of the adult population globally.[2]

Its symptoms start silently, progress through renal dysfunction, and terminate in end-stage renal disease. In addition, CKD is now recognized as an important risk factor for other adverse outcomes, such as acute kidney injury, cardiovascular disease, and premature death.[3] Therefore, appropriate treatment of CKD is of high clinical significance.

The most cost-effective and desirable treatment for CKD is renal transplantation,[4] but the majority of allografts do not function for the remainder of a recipient's lifetime.[5] Grafts fail for a variety of reasons, including acute rejection, glomerular disease, and interstitial fibrosis. Although the acute rejection rate has steadily decreased to <10% in the 1st year after transplant,[6] graft survival has not commensurately improved.[6,7] Death-censored attrition rates after the first posttransplant year remain at approximately 4% annually, and 20%–30% of grafts fail in living recipients by 10 years.[8] These data suggest that modern graft monitoring and management strategies are not working optimally.[5]

The introduction of Doppler ultrasonography to determine the intrarenal arterial resistance index (RI) is a useful, noninvasive

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Address for correspondence: Dr. Ajana George Madubueze, Department of Radiology, St. Nicholas Hospital, 57 Campbell Street, Lagos Island, Lagos State, Nigeria.
E-mail: madubuezeajana@gmail.com

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diagnostic tool for early diagnosis of acute allograft rejection and following up patients with transplanted kidneys.[9] The RI is significantly affected by the vascular compliance of the recipient. In addition, intrarenal and extrarenal hemodynamic factors have a major impact on the RI of the allograft. The RI may be a surrogate measure of both arterioscleroses.[10] Correlations have been reported between RI and recipient age, allograft histology, presence of acute rejection, and acute tubular necrosis.[9] Assessment of the RI in the early period after a renal transplant has proven to reliably predict short-term allograft function.[11] Although Saracino *et al*.[12] suggest that early determination of a RI can help predict long-term graft function, the effect of determining the renal RI on long-term renal functions is not well known. These lacking data led us to examine the predictive value of intrarenal RI on the development of chronic allograft nephropathy and long-term allograft outcome.

Materials and Methods

This retrospective study was carried out over 24 months at the Radiology Department of St. Nicholas Hospital, Lagos, in South western Nigeria. Ethical approval for the study was obtained from the hospital ethical review committee, with the hospital review board approval number of Ref No: SNH/REC/2017/2.8/1, which was approved on 08th February, 2017.

Methodology

All the individuals' hospital case files were cross-checked to ascertain their renal biochemistry status. The biochemical data, especially the serum creatinine and proteinuria, were obtained at 6 weeks, 1 month, and 24 months after the transplantation.

Serum creatinine concentration was determined using a kinetic enzymatic ultraviolet assay method. Urinary protein excretion was measured by standard automated clinical chemistry analyzers. Creatinine was assayed on blood samples taken on the day of the color Doppler examination, whereas proteinuria was determined on a sample from the urine collected during the 24 h preceding the ultrasonographic examination.

Each of the individuals was psychologically reassured, and the procedure was comprehensively explained to them. Individuals were scanned using a real-time/color-coded scanner (Mindray DC-6 Shenzhen, China) coupled with a 3.5MHz transducer. The individual lay down supine on the examining couch. Scanning was done in supine position after the application of adequate amount of coupling gel on the area of interest to permit sound conduction, with subsequent placement of the transducer. A global examination of the transplanted kidney was performed [Figure 1].

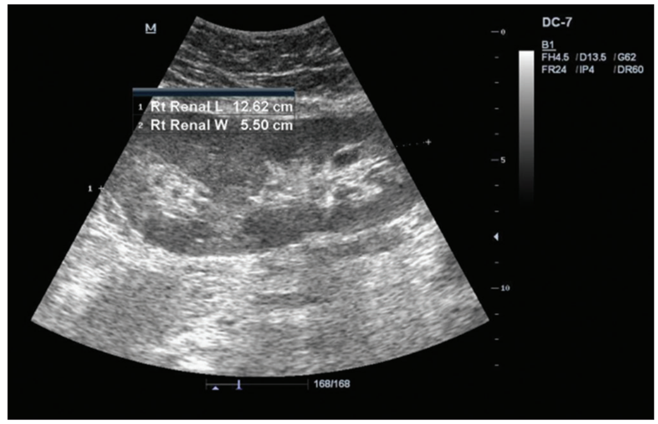

Figure 1: Renal ultrasonogram

Color mapping was performed to image blood flow in the transplanted kidney [Figure 2]. First of all, the main renal artery was assessed for exclusion of atherosclerosis before proceeding to the area of interest (interlobar arteries). Three Doppler waveforms were obtained from each kidney by sampling the interlobar artery (along the border of medullary pyramids) of the superior, middle, and inferior portions of the graft and average value calculated manually, since intraobserver variability is a potential limitation in the measurement of renal resistive index. This variability was reduced to the minimum by taking the average of three measurements.

The flow velocity waveform was obtained at an optimal insonating angle of <30° so that the early systolic peak could be visualized. The Doppler tracing was also obtained by placing a gate of 2-4mm on the pulsating intrarenal artery (Interlobar artery). The height of the Doppler waveforms was maximized to facilitate measurement. A trend of 3–5 similar sequential Doppler waveforms was obtained during suspended respiration. Then, the measurement of resistive index (RI) was determined using the internal calipers and analytical software of the sonography unit. RIs from these waveforms were averaged to arrive at mean RI values for the transplanted kidney [Figure 3]. This was obtained by adding the RI from upper, mid, and lower pole intrarenal arteries and dividing by three. The resistance parameter, RI, could also be manually calculated as follows:

RI = PSV– EDV/PSV.[13]

RI = Resistive index.

PSV = Peak systolic flow velocity.

EDV = End diastolic flow velocity.

Results

A total of 41 individuals who fulfilled the inclusion criteria were recruited in this study [Table 1]. The age range of the renal transplanted recipients in this study was between 22 and 67 years. The group was made up of 28 males and 13 females.

The majority of the renal transplanted recipients (31.7%) in this study were within the age of 41–50 years, whereas the majority of the males (35.7%) were within 51–60 years' age group and the majority of the females (34.5%) were within the age of 41–50 years as illustrated in Table 1 and Figure 4. In both the males and females, only 7.7% of the participants were within

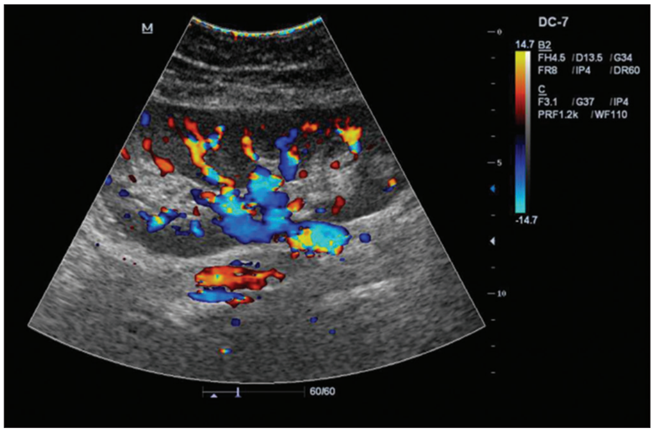

Figure 2: Color Doppler image of the kidney (normal segmental renal arteries and interlobar renal arteries)

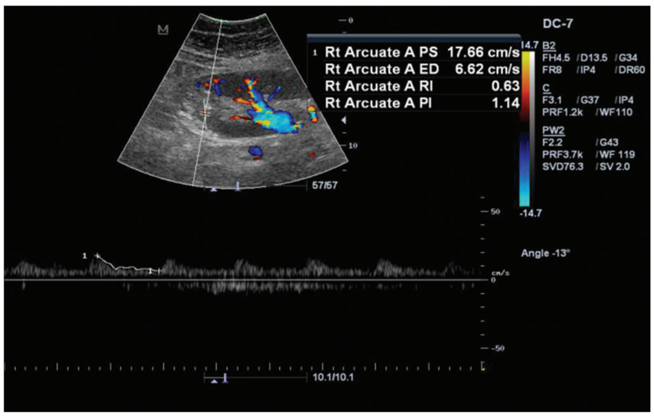

Figure 3: The normal Doppler spectrum of the renal interlobar artery, showing upward systolic upstroke, gradual diastolic decay, and forward flow throughout the cardiac cycle

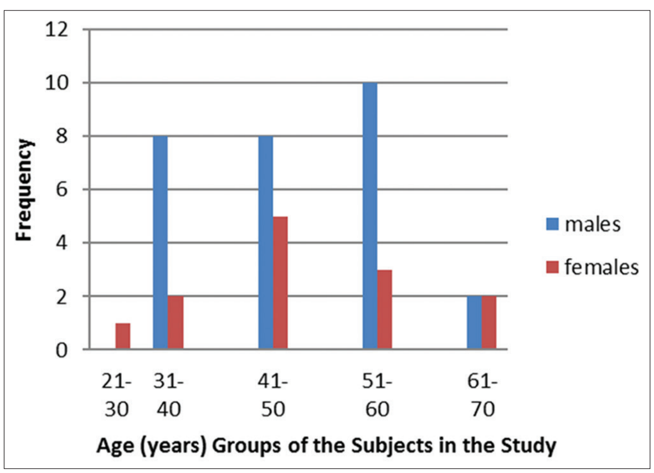

Figure 4: Histogram showing age distribution among male (28) and female (13) participants

the lower limit of 21–30 years. The mean (±standard deviation) ages of both male and female groups were 42.51 ± 6.71 years and 41.35 ± 7.11 years, respectively. This age difference was not statistically significant (*P* = 0.67) [Table 1].

Table 1: Age distribution of participants in the study groups (*n*=41)

Parameters	Frequency (%)		Mean±SD		*P*
Age (years)	Males (*n*=28)	Females (*n*=13)	Males (*n*=28)	Females (*n*=13)	
21-30	0 (0)	1 (7.7)	42.51±6.71	1.35±7.11	0.67
31-40	8 (28.6)	2 (15.4)			
41-50	8 (28.6)	5 (34.5)			
51-60	10 (35.7)	2 (15.4)			
61-70	2 (7.1)	3 (23.1)			
Total	28 (100)	13 (100)			

The *P* value was not statistically significant. SD: Standard deviation

In this study, the recipient age and donor age were higher in those with RI ≥0.7 when compared with those with RI ≤0.7. Those within the range of RI ≥0.7 were more frequently smokers and had higher values of proteinuria (which is defined as a urinary protein excretion of >150 mg/day) than those with RI ≤0.7. In the course of the study, only seven recipients (17.1%), predominantly those with the values of RI ≥0.7, developed graft dysfunction (that is when the GFR is <60 ml/min/1.73 m^2 for 3 consecutive months). They were statistically significant. The rest of the clinical and laboratory parameters were not statistically significant, as shown in Table 2.

Multivariate analysis showed that only donor age and renal resistive index maintained their independent correlation values which were statistically significant. Moreover, other variables such as body mass index (BMI), recipient age, proteinuria, and acute rejection showed no statistically significant correlation, as noted in Table 3.

The following variables such as recipient age (*P* = 0.004), active smoking (*P* = 0.03), and proteinuria (*P* = 0.04) showed positive correlations with the renal resistive index values. However, the donor age, BMI, and serum creatinine did not show a statistically significant correlation with the renal resistive index values, as noted in Table 4, using Pearson's correlation coefficient.

The functional status of the grafts was classified based on the values of the renal resistive index. The values were calculated separately according to those recipients with RI <0.7 and those with RI ≥0.7. The graft dysfunction was predominantly worse in those graft recipients with RI ≥0.7 when compared with those that had RI <0.7, using Kaplan–Meier analysis to estimate the cumulative graft survival, as demonstrated in Figure 5. This is statistically significant (*P* = 0.002).

Discussion

The renal arterial resistive index (RI) is a sonographic index to assess for renal arterial disease, which provides significant information about the renal hemodynamic changes.

There is a general agreement that RI <0.70 should be considered as a limit of normality in adults but not in children (especially

Table 2: Demographic and clinical parameters of the subgroups according to resistive index values

Characteristics	Within 1 month after transplantation		*P*	After 24 months		*P*
	RI <0.7 (*n*=34)	RI >0.7 (*n*=9)		RI <0.7 (*n*=33)	RI >0.7 (*n*=9)	
Recipient	51.39±17.01	53.32±4.61	0.001	51.31±3.19	53.32±2.56	0.001
Donor age	32.08±0.33	37.03±31.09	0.03	32.19±1.32	37.019±3.01	0.03
Smoker	29.01±25.44	31.32±39.02	0.04	26.11±5.22	30.10±12.04	0.04
Systolic blood pressure	131.11±7.32	136.46±22.09	NS	128.23±7.1	132.01±51.5	NS
Diastolic blood pressure	87.21±16.10	89.34±9.71	NS	78.43±3.91	87.61±31.74	NS
BMI	19.40±3.53	21.13±12.09	NS	18.83±1.39	20.19±20.12	NS
Serum creatinine	1.02±9.04	1.31±10.13	NS	1.01±9.21	1.24±19.52	NS
Proteinuria	18.27±3.65	19.44±82.74	0.01	19.26±6.43	20.31±5.67	0.02
Graft dysfunction, *n* (%)	11.3 (17)	18 (17)	0.002	16 (21)	13 (10.7)	0.002

NS: Not significant, BMI: Body mass index, RI: Resistive Index

Table 3: Relative risk of graft dysfunction associated with selected variables

Independent variables	Multiple correlation coefficient (*r*)	*P*
Recipient age (years)	0.3312	0.060 (NS)
Donor age (years)	0.893	0.021
Renal RI (≥0.7)	1.272	0.001
BMI	1.440	0.204 (NS)
Proteinuria (g/day)	0.933	0.081 (NS)

NS: Not significant, BMI: Body mass index, RI: Resistive index

Table 4: The strength of association between the variables and intrarenal resistive index

Characteristics	Pearson's correlation coefficient (*r*)	*P*
Recipient age	0.662	0.004
Donor age	0.442	NS
BMI	0.182	NS
Active smoking	0.912	0.030
Proteinuria	1.300	0.040
Serum creatinine	0.115	NS

NS: Not significant, BMI: Body mass index

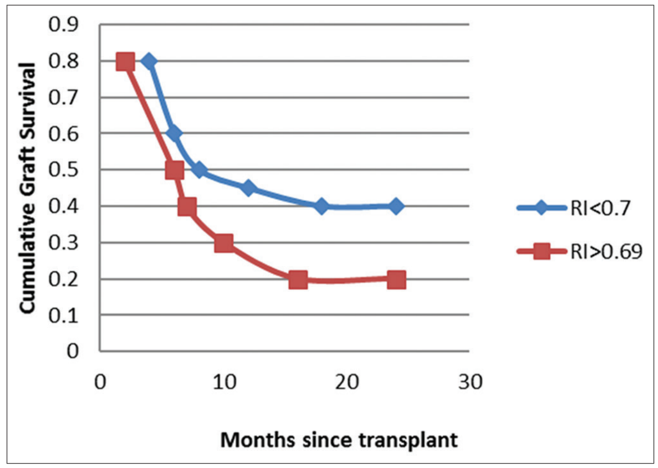

Figure 5: Kaplan–Meier analysis of the graft survival based on the values of RI (RI <0.7 or RI ≥0.7)

within the 1st year of life) and healthy elderly (possibly because of age-related changes in vascular compliance) in whom Renal resistive indices (RRI) typically show higher values.[14,15]

This general agreement is in concordance with the work done by Platt *et al*.[16] who reported that a mean RI <0.70 can be used as an indicator of normal renal vascular resistance in adults, whereas a mean RI >0.70 can be interpreted as a sign of elevated renal vascular resistance, which can be found in several renal parenchymal diseases such as essential hypertension.

As noted in this study, early evaluation of the transplanted kidneys using Doppler ultrasonography has shown to predict long-term renal function. This finding was compatible with that of the study done by Radermacher *et al*.,[10] which suggested that the values of the intrarenal resistive index obtained within 3 months after transplantation can predict long-term allograft outcome.

In contrast to this study, the work done by Trillaud *et al*.[17] did not show a relation between the resistance index measured 6 days after renal transplantation and the level of renal function at 12 months. Hence, the researchers did not use the resistance index to predict allograft survival. It is worthy of noted that the renal resistance index is nonspecific and is influenced by many factors such as the site at which renal resistance is measured[18] and the increased intra-abdominal pressure during forced inspiration (the Valsalva maneuver) influences the index.[19]

This study also showed that the older recipient age and donor age were higher in those with RI ≥0.7 when compared with those with RI ≤0.7, which was in support of the study done by Mastorakou *et al*.[20] which reported that higher values of renal RI ≥0.7 can be seen in elderly people without obvious renal dysfunction. This could be due to the fact that with aging, there is a tendency of vascular compromise that may occur from atherosclerosis that may be responsive for the elevation of the values of the renal RI. In this study, the common iliac arteries (recipient) and the main renal arteries (graft) were first checked before proceeding to the area of interest (intrarenal arteries, especially the interlobar and arcuate arteries) to identify possible plaques and stenosis, but normal findings did not exclude early atherosclerotic changes in the small intraparenchymal renal vessels. Other studies also showed that increasing age is associated with an increased resistance index, particularly in hypertensive patients.[21,22]

The poorer renal function within the first 1 month of transplantation and the presence of proteinuria as shown in this study have been proposed as means for differentiating between patients with a good chance of long-term survival of a renal allograft and those with a poor chance. In concordance with the above findings, the work done by Giral-Classe *et al*.[23] suggested that the delayed graft function of more than 6 days strongly decreases long-term survival of transplanted kidneys. Notwithstanding, none of them, alone or in combination,[24] had a predictive value approaching that of an increased resistance index, although in this study, correlative value was used due to the limited number of participants.

Since the resistance index is significantly correlated with many established cardiovascular risk factors, such as age, increased systolic blood pressure, and decreased renal function, it is not surprising that increased renal vascular resistance predicts not only graft failure but also death due to cardiovascular disease. The resistance index during long-term follow-up has been used to diagnose allograft nephropathy.[25]

Conclusion

This study revealed that renal RI determined within the 1st month after renal transplant correlates with the long-term allograft function in kidney transplant recipients.

Further research is recommended in the black African population to determine the correlation between renal RI and renal biopsy in recipients with graft dysfunction.

Recommendation from the light of this study: Since Doppler ultrasonography is widely available, affordable, and noninvasive, it should be employed fully in evaluating and predicting the long-term renal function in allograft recipients.

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Conflicts of interest

There are no conflicts of interest.

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