

Comparative Ultrasound Evaluation of Renal Resistive Index in Hypertensive and Normotensive Adults in Ibadan, SouthWestern, Nigeria

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ABSTRACT

Background: Renal resistive index is a useful measure for quantifying alterations in renal blood flow. It is considered to be a reflection of renal parenchymal vascular resistance. The aim of this study is to determine the difference in renal resistive index between patients with essential hypertension and non-hypertensive control group.

Patients and Methods: Seventy -two patients with essential hypertension of varying duration and 68 patients without hypertension were evaluated sonographically in this prospective study. The renal resistive index was determined by use of Doppler ultrasound of the interlobar arteries.

Results: Mean renal resistive index in the hypertensive patients was 0.60 ± 0.04 ($\pm$ SD) and in the controls was 0.56 ± 0.04 ($\pm$ SD) ($p = <0.001$). Renal resistive index correlated significantly with systolic blood pressure ($r=0.382$, $p = <0.001$) and diastolic blood pressure ($r= 0.364$, $p = <0.001$). It correlated weakly with body mass index ($r= 0.170$, 0.044). No significant association was found with age, gender, duration of hypertension and creatinine clearance. Multiple regression linear analysis showed systolic blood pressure to be the only independent variable influencing renal resistive index.

Conclusion: The renal resistive index is increased in essential hypertension and correlates with patient's blood pressure and body mass index. Doppler

ultrasound provides a non-invasive parameter for follow up of patients with essential hypertension especially in developing countries.

INTRODUCTION

Hypertension is the second most common cause of end stage renal disease after Diabetes Mellitus according to the United States Renal Data System Report [1]. Rostand *et al* reported that end stage renal failure relating to hypertension was 17.7 times more common in blacks than whites [2].

Various studies in parts of Nigeria show different incident rate of renal disease as a complication of hypertension. In a study carried out in University of Port Harcourt Teaching Hospital (UPTH), South-south Nigeria, 9.4% of their study cases had renal failure as complication of hypertension [3]. Nwankwo *et al* in Maiduguri found that impairment of renal function occurs frequently amongst hospitalized hypertensive patients in the Northeastern Nigeria. 45% of their study population had elevated serum creatinine which is a marker of onset of nephropathy [4]. Akinkugbe also reported that 9.1% of the 210 hypertensive patients screened in Ibadan had renal failure [5].

Early detection of renal damage from hypertension is essential to delay progression to end stage renal failure. Most clinicians currently rely on measurements of blood pressure, proteinuria and glomerular filtration rate (GFR) or creatinine clearance rather than ultrasound studies when evaluating hypertensive patients and predicting future progression of chronic kidney disease. This is probably

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because routine grey scale ultrasound studies only assess renal length, volume, echogenicity, cortical thickness and the pelvicalyceal system. Renal echogenicity and size correlate well with histopathology but are only useful in evaluating disease chronicity [6]. In the early stage of the disease, there may be no significant change in the gross appearance of the kidneys. In a study by Egberongbe *et al* [7] in Ile Ife, Nigeria, sonographically evaluating the renal volume of hypertensive patients with duration of hypertension ranging between six months and forty years, they found no significant difference in the renal volume of hypertensive patients compared to the normotensive group. Soldo *et al* [8] in Zurich found that renal changes in diabetic patients are detectable by conventional ultrasound only in very advanced stages of the disease. The lack of significant morphologic changes in early renal disease limits the use of conventional ultrasound in evaluation of medical renal diseases.

Doppler Ultrasound (DUS) assessment of renal vasculature is a reliable (sensitivity 93%, specificity 92%), non-invasive evaluation technique whose clinical application has steadily increased in recent years [9]. Its usefulness ranges from the diagnosis of renal artery stenosis and renovascular disease to the assessment of intra renal hemodynamics in several different pathological conditions such as essential hypertension, acute and chronic renal failure, pre and post-transplant assessment and graft rejection [9].

Calculating the resistive index (RI) at the level of the interlobar arteries was shown to be a very accurate and reproducible indicator of vascular impedance to downstream blood flow [9]. An increase in the RI has been reported to relate to intra renal arteriolar and glomerular sclerosis [10] as well as to the presence and extent of interstitial damage in renal parenchyma disease [11].

More recently, an increased RI has been reported to be related to macro vascular atherosclerotic damage in hypertensive diabetic patients, increased blood pressure and duration of disease in patients with essential hypertension, suggesting that it could reflect intra parenchymal arteriolar damage and could serve as a prognostic marker of hypertensive renal injury [12].

Evaluation of resistive index (RI) in hypertensive patients might be an important method

of detecting early renal disease before the morphological changes occur on ultrasound. This study was therefore designed to compare the renal resistive index in the hypertensive and normotensive in Nigeria and find its clinical and laboratory correlates.

MATERIALS AND METHODS

Seventy-two hypertensive patients as defined by the Joint National Committee (JNC VI) classification [13] who consented were recruited for the study. This included patients with Systolic Blood Pressure of 140mmHg and above and Diastolic Blood Pressure of 90mmHg and above on at least two occasions. Patients with known renal disease, diabetes mellitus, liver disease, haemoglobinopathies, and other significant medical conditions apart from hypertension as well as pregnant women were excluded from the study. Patients with obvious sonographic renal anomalies e.g polycystic kidney disease, renal tumor, hydronephrosis and those whose renal vessels could not be assessed due to excessive bowel gas shadows were also excluded. A control group comprising of 68 healthy adults of similar age and gender distribution were also studied.

The socio-demographic parameters were obtained from the patients. Clinical history was obtained and physical examination was carried out on all the patients. Height and weight were measured and body mass index (BMI) was calculated.

Ultrasound examination of the kidneys including pulsed Doppler analysis of the intra-renal arteries was performed using a General Electric Logiq P5 ultrasound machine with a 2.5-5.0 MHz curvilinear transducer. Patients were scanned after an overnight or about eight [8] hours fast to minimize bowel gas shadows which can obscure the kidneys. Patients were made comfortable on the examination couch and procedure was explained including the need for occasional breath holding when indicated. The grey scale imaging of the kidneys was done with patient in supine, decubitus or prone positions as appropriate. Coupling gel was applied to the lumbar regions and the kidneys scanned in longitudinal and transverse planes using the liver and the spleen as acoustic windows. Measurement of the longitudinal (LS), transverse (TS) and antero posterior (AP) diameter of the kidneys was taken and the volume calculated using the formula: $LS \times TS \times AP \times 0.52$ [14]. The

LS span is bipolar length, TS and AP diameters were taken in transverse scan at the level of the renal hilum.

Renal echogenicity was graded into 4 categories: grade 0 (normal), where renal cortex was less echogenic than the liver, grade I (mild), where renal cortex and liver were equally echogenic, grade II (moderate), where renal cortex was more echogenic than the liver and grade III (severe), where the renal cortex and sinus were equally echogenic [15].

The cortical thickness was measured in the sagittal plane at the level of the mid kidney as described by Moghazi *et al* [16]. The cortical thickness measurement was taken over a medullary pyramid, perpendicular to the capsule, as the shortest distance from the base of the medullary pyramid to the renal capsule.

Evaluation of the intra-renal arteries was done through a flank approach with the patient in the decubitus position. The transducer was placed along a lateral or slightly posterior approach and a plane obtained in which no spleen or liver is visible. This ensured that the distance to the intra-renal vessels is minimized. Color Doppler interrogation is essential to map the vascular anatomy. The intra-renal Doppler waveform was obtained at angles less than 30 degrees so that the early systolic peak could be visualized. The transducer was rotated more posteriorly to improve the Doppler angle for the upper pole intra-renal arteries. For the mid kidney, the probe was centered in a coronal plane. The best Doppler angle for the lower pole intra-renal arteries was obtained by rotating the probe slightly anterior to the mid coronal line. Waveforms were optimized for measurement using the lowest pulse repetition frequency without aliasing (to maximize waveform size), the highest gain without obscuring background noise, and the lowest wall filter. Three to five reproducible waveforms from each kidney were obtained and RIs from these waveforms were averaged to arrive at mean RI values for each kidney. This is obtained by adding the RI from upper, mid and lower pole intrarenal arteries and dividing by 3.

Venous blood samples were collected for fasting blood sugar, fasting blood lipid and serum creatinine after an 8-12 hour fast. Creatinine clearance was calculated from the serum creatinine using Cockcroft-Gault formula [17] which approximates the kidney glomerular filtration rate:

$$(GFR): \frac{(140 - \text{Age}) \times \text{weight (kg)} \times (0.85 \text{ for women})}{72 \times \text{serum creatinine (mg/dl)}}$$

The study was approved by the Joint University of Ibadan/University College Hospital Institutional Review Board (IRB).

The data obtained was analyzed using the statistical package for social sciences (SPSS 16) Inc. Chicago, Illinois. The data was standardized and appropriate tests of significance like the student's t-test was applied. All values in the text and tables are expressed as means ($\pm$ SD). Categorical variables were analyzed using chi square. Bivariate analysis using Pearson's correlation was performed to determine the significance of association between renal resistive index (RRI) and the following independent variables: age, body mass index (BMI), systolic blood pressure (SDP), diastolic blood pressure (DBP), duration of hypertension, total cholesterol, triglyceride, HDL cholesterol, LDL cholesterol, serum creatinine and creatinine clearance.

Multivariate analysis was used to identify predictive factors of RRI using age, BMI, SDP, and DBP as the independent variables. p value of < 0.05 was considered statistically significant.

RESULTS *No tables and figure in the paper* **Clinical characteristics of the Patients**

One hundred and forty patients met the inclusion criteria and were recruited for the study. 72 (51.4%) have hypertension while 68 (49.6%) were normotensive. The age range of the hypertensive patients was 30 – 63 years with mean age of 50.51 ± 8.13 years while the age range of the control group was 30 – 64 years with mean age of 48.87 ± 8.47 years. Table 1 shows the age distribution parameters of the hypertensive and control groups. Majority of the respondents were in the 51- 60 age group comprising of 36 (55.4%) hypertensive and 29 (44.6%) normotensive people. There was no significant statistical difference in the age of the respondents in each group. 71 (50.7%) of the 140 study population were females. 37 (51.4%) of these had hypertension while 34 (50%) had normal blood pressure. Majority of the respondents were married -124 (88.6%) and 48 (34.3%) had secondary level education. 11 (15.3%) and 2(2.9%) of the

hypertensive and control groups respectively had positive family history of hypertension. Only one respondent, a hypertensive patient admitted to positive history of smoking.

The mean height, weight, Body mass index (BMI), systolic blood pressure (SBP) and diastolic blood pressure (DBP) with the standard deviation are shown in Table 2. There is no significant statistical difference in the mean height and weight of the two groups. There is however significant statistical difference in the BMI ($t= 2.366$, $p=0.019$), SBP ($t= 21.911$, $p= <0.001$) and DBP ($t= 13.657$, $p= <0.001$) of the hypertensive group compared with the control group. There was no significant difference in the renal morphology of the two group namely renal volume, cortical thickness and parenchymal echogenicity.

Comparison between the mean RRI values between the right and the left sides within each study group shows slightly higher mean RRI on the right side in both groups but this is not statistically significant. However, there is a statistically significant difference in the Renal Resistive index (RRI) in the hypertensive group compared with the control group on the right and left Table 3.

Figure 1 shows the frequency distribution of the RRI between the two groups. It shows a skew to the right for the hypertensive cases with the greater proportion of the RRI values clustering at about 0.60. However, the control group shows a skew to the left with the greater proportion of RRI values clustered in the region of 0.55.

The serum creatinine, creatinine clearance and lipid profile comprising of High-density lipoprotein (HDL), Low-density lipoprotein (LDL), Triglycerides and total Cholesterol values were generally higher in the hypertensive group than in their normotensive counterparts. However, only Triglyceride and total Cholesterol showed statistically significant difference between both groups and there was no correlation between RRI and serum creatinine, creatinine clearance, total cholesterol, triglyceride, HDL cholesterol and LDL cholesterol as well.

Pearson's correlation was used to analyze the association between RRI, age, systolic blood pressure, diastolic blood pressure and duration of hypertension. There was no statistically significant correlation between RRI, age and duration of hypertension as shown in Table 4. There was also a strong correlation between RRI and systolic and diastolic blood pressure, however, only weak

correlation was seen between RRI and body mass index. Multiple regression linear analysis was conducted to determine the independent predictor of RRI among these variables; age, body mass index, systolic blood pressure and diastolic blood pressure. Only systolic blood pressure significantly and independently influenced RRI Table 5.

DISCUSSION

Renal volume, cortical thickness and cortical echogenicity were evaluated in this study and no significant difference was seen in the renal morphology of the hypertensive and normotensive group. This lack of significant difference explains why grey scale ultrasound imaging is not ideal for detecting early morphological changes in renal disease [16].

This study shows increased RRI in patients with essential hypertension. The mean RRI was 0.60 ± 0.04 in the hypertensive group compared with 0.56 ± 0.04 in the control group ($t = 6.185$, $p= <0.001$). This was similar to the figures recorded by Ozelsancak *et al* [18] in their evaluation of 61 hypertensive patients and 40 healthy controls (0.60 ± 0.04 versus 0.56 ± 0.04) in Turkey. They attributed the difference between the two groups to increased renal vascular impedance that is seen in patients with essential hypertension. Other researchers like Pontremoli *et al* [9] and Miyoshi *et al* [19] did not do a case-control study but reported RRI of 0.60 ± 0.004 and 0.64 ± 0.05 respectively in the hypertensive patients they studied.

Veglio *et al* found increased RRI to be associated with increasing level of blood pressure and to duration of disease in patients with essential hypertension [20]. This study also demonstrated similar and significant relationship between systolic blood pressure and RRI but no independent correlation with diastolic blood pressure after multiple regression linear analysis. This is close to the finding of Pontremoli *et al* [9] which showed a positive correlation between systolic blood pressure and negative correlation with diastolic blood pressure. This relationship suggests that higher renovascular resistance is associated with higher systemic pulse pressure, a known marker of increased rigidity of the arterial vascular bed [21].

The association between systolic blood pressure and RRI that was found in this study also

confirms the relationship between increased RRI and renal vascular impedance which occurs with increasing blood pressure levels. Although the pathogenesis of increased renal vascular impedance is still not known, the observed associations with blood pressure levels, age and other cardiovascular risk factors suggest that it could be due either to functional vasoconstriction secondary to the severity of the hypertensive state, or due to the presence of atherosclerotic changes within the intrarenal vessels. It could also be due to combination of both [9].

Results of studies by Mostbeck *et al* [10] in Austria and Ikee *et al* [22] in Japan analyzing the relationship between RRI and histopathological changes estimated by renal biopsies suggested that the RI values in hypertensive patients are strongly affected by the degree of arteriosclerosis. Our study did not explore the relationship between RRI and other signs of atherosclerotic changes such as increased carotid intima media thickness. However, Owolabi *et al* [23] while exploring the racial disparity in stroke risk factors found that atherosclerosis is less common in Nigerians compared with the Berlin patients despite the fact that hypertension was a common modifiable risk factor in both groups. A histopathological correlation might be needed to firmly establish the cause of increased renal vascular impedance in Nigerian patients.

Ozelsancak *et al* [18] however found no correlation between systolic blood pressure or diastolic blood pressure and RRI. They suggested that renal damage can develop even in the absence of severe hypertension if there is an enhanced transmission of systemic blood pressure to the renal microvasculature. They also suggested that genetic and acquired differences in intrinsic structure and function of the autoregulation may explain why blood pressure measurements did not affect RRI in their study.

This study did not demonstrate any relationship between creatinine clearance as a biochemical marker of renal damage and RRI. This is contrary to the finding of Derchi *et al* [24] who found a reduction in creatinine clearance to be associated with increased renal vascular impedance. In their study, RRI was inversely related to creatinine clearance and the patients with the highest renal resistance (upper quartile, e'' 0.63) showed a greater prevalence of renal dysfunction. This study actually showed similar number of patients having abnormal creatinine values of 29.17% and 29.41% in the

hypertensive and control group respectively. This suggests that there might be other causes of decreased creatinine clearance other than hypertensive nephropathy in this study groups and further study might be required to evaluate this.

There was no correlation between age and RRI in this study. This is at variance with most studies [9, 18, 25] which show positive correlation between age and RRI. There is increased tendency to have hypertension and atherosclerosis with increasing age. This might be responsible for the correlation found in most study. However, since Owolabi *et al* [23] found atherosclerosis to be less prevalent in Nigerian patients with essential hypertension, the association between age and atherosclerosis might not be strong. This may partially explain the lack of correlation between age and RRI in this study group. Further research is required to explore these associations.

Body mass index (BMI) was positively correlated with RRI in this study but did not show an independent association after controlling for blood pressure. Okura *et al* [25] and Miyoshi *et al* [19] in Japan also found significant correlation between BMI and RRI. This association is probably due to the relationship between obesity and hypertension. Obesity is a modifiable risk factor for hypertension.

CONCLUSION

This study has shown that there is increased renal vascular impedance as demonstrated by the elevated renal resistive index (RRI) in the hypertensive patients even without overt renal dysfunction. The association of RRI with increasing levels of systolic blood pressure suggests that renal vascular impedance can be reduced with proper control of systolic blood pressure, thus probably preventing progression to renal damage.

This study also shows that even though body mass index is not an independent determinant or predictor of RRI, it is weakly associated with RRI and is a modifiable risk factor which combines with elevated blood pressure to influence RRI, hence renal vascular impedance. Weight reduction is therefore a recommended lifestyle modification that could aid in reducing progression to renal damage in hypertensive patients.

Over all, this study has shown that Ultrasound can serve as a non invasive, readily available and

affordable modality for serial monitoring of renal vascular impedance during the course of management of essential hypertensive patients through the evaluation of RRI. It should therefore be considered as part of routine management of patients with hypertension.

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