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Arterial Resistive Index (RI) in Type II Diabetic Nephropathy Stages and Healthy Controls

Background/Objective: Doppler ultrasonography can be an effective method to assess the severity of diabetic nephropathy. This study was conducted to investigate the relationship between Doppler ultrasound resistive index (RI) values and the clinical and laboratory findings in patients with diabetic nephropathy.

Patients and Methods: Doppler ultrasound was performed for 45 patients with type II diabetes mellitus and 30 healthy controls. Clinical and laboratory findings of cases and controls were also recorded.

Results: Diabetic patients were categorized into 3 groups according to the severity of their nephropathy, based on the serum creatinine level and 24-hour urine protein. The mean±SD RI was 0.59±0.03 for the control group, 0.67±0.04 for stage I, 0.73±0.02 for stage II, and 0.85±0.07 for stage III diabetic nephropathy ($p<0.001$). RI was significantly associated with the 24-hour urine protein and creatinine ($R^2=0.75$ and $=0.67$, respectively; $p<0.001$) and a suitable regression model was adopted to predict the 24-hour urine protein and serum creatinine level based on RI.

Discussion: RI increases with the progression of diabetic nephropathy. RI can be used for estimation of the 24-hour urine protein and serum creatinine and for determining the stage of nephropathy, especially for patients not cooperating for collection of the 24-hour urine protein.

Keywords: Diabetic Nephropathy, Doppler Ultrasound, Serum Creatinine, 24-Hour Urine Protein

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Introduction

Diabetic nephropathy is an important cause of renal dysfunction and is the most common cause of chronic renal failure.[1] Renal involvement in diabetes has a wide range, from increased glomerular filtration rate (GFR) early in the course of the disease to end-stage nephrosclerosis and azotemia. Conventional ultrasonography (US) has a limited diagnostic value for the condition, since it only detects the increased kidney size early in the disease and the reduced renal parenchyma in late phases.[1,2] Recent studies have shown that Doppler US can be an effective method to assess diabetic nephropathy (in advanced stages) in a non-invasive way.[3,4]

This study was conducted to evaluate the importance of arterial resistive index (RI) for determining the stage of diabetic nephropathy and to investigate the association between RI values and the clinical picture and laboratory findings.

Patients and Methods

We studied 45 patients with type II diabetes mellitus from the Diabetes Clinic of Hashemi-Nejad Hospital. Diabetic patients with a known history

of cardiovascular disease (such as hypertension, coronary artery bypass graft [CABG] and cardiovascular-related drug usage) were excluded from the study. Also, a femoral intima-to-media thickness (IMT) greater than two mm was considered as another exclusion criteria.

Patients with known history of renal disease other than diabetic nephropathy and those with metabolic diseases other than diabetes (e.g., hyperlipidemia and hyperthyroidism) were excluded from the study.

All the above-mentioned exclusion criteria were also considered for the selection of the controls. In addition, all of them were 20 years of age or older.

Thirty healthy individuals who were not taking any medications were also selected based on a negative history of cardiovascular disease, renal disease, hypertension, or other specific clinical problems. Due to the impact of atherosclerosis on RI,[5] those with the femoral artery IMT of more than two mm were excluded.

Laboratory values of serum creatinine and 24-hour urine protein (mg/dL) were measured for all cases. Patients were categorized into three groups according to the severity of their nephropathy. In stage I (n=15), the urine protein was between 30 and 300 mg/dL and serum creatinine was less than 1.4 mg/dL. In stage II (n=20), proteinuria was higher than 300 mg/dL and the serum creatinine was less than 1.4 mg/dL. Patients with creatinine levels higher than 1.4 mg/dL were categorized as stage III.

Renal duplex Doppler US examination was performed with a 3.5 MHz convex transducer with an EUB-515 scanner (Esaote, Italy). First, routine renal B-mode US examinations were performed for each patient. Then, RI values were obtained from intraparenchymal renal arteries (arcuate or interlobar). The RI value for each kidney was then calculated as the mean value of at least three waveforms recorded in three different regions of the kidney. All the Doppler examinations were performed by the same examiner to avoid interobserver variability. An RI value higher than 0.70 was considered abnormal.[1,6]

Interval data were reported as mean±SD. One way ANOVA (and Scheffe *post hoc* test) and Pearson's correlation coefficient and simple linear regression models were used for data analysis.

P values less than 0.05 were considered statistically significant.

Results

Among diabetics, 26 (58%) of the patients were men while they composed 17 (57%) of the control group. The mean±SD age of the patients was 55.9±12.8 and of the controls was 50.1±13.7 years.

Duration of diabetes among the studied cases was between 12 to 300 (mean±SD: 129±64) months. Descriptive characteristics of the 24-hour urine protein, serum creatinine level, renal length and RI are presented in Table 1.

According to the 24-hour urine protein and serum creatinine, patients were categorized into three groups; 15 (33%) were in stage I, 20 (44%) in stage II and 10 (22%) in stage III of diabetic nephropathy.

The mean±SD RI was 0.59±0.03 in the control group, 0.67±0.04 in the stage I diabetic group, 0.73±0.02 in the stage II diabetic group and 0.85±0.07 in the stage III diabetic group (Overall: 0.73±0.07) (p<0.001). The mean RI was significantly different among different stages of diabetic nephropathies (p<0.001) and the mean RI was different between the diabetic and the control group (p<0.001) (Fig. 1).

The mean±SD duration of diabetes was 88.4±64.5 months in stage I, 134±51.4 months in stage II and 180±52.1 months in stage III diabetics.

There was a statistically significant difference between stage I and III with respect to the duration of diabetes (Scheffe test, p<0.001). The difference was not significant when comparing stages I and II, nor stages II and III.

Regression analysis of the 24-hour urine protein

Table 1. Measurements Made in the Diabetic Group

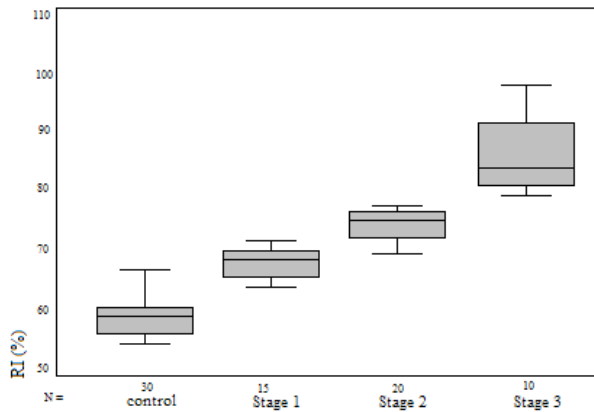| Different Measurements	Mean±SD	Range
Age (yr)	57.2±10.4	32–76
Diabetes Duration (month)	129±64.7	6–300
Renal Length (mm)	90.9±12.4	63–116
Resistive Index	0.73±0.07	0.59–1
Creatinine (mg/dL)	1.2±0.8	0.5–4
24-hour Urine Protein (mg/dL)	483.6±421	30–2000

Fig. 1. Mean RI between the control group and diabetic stages.

and serum creatinine (as dependent variables) and RI (as the independent variable) was carried out separately.

To predict the 24-hour urine protein content and to assess the factors that have an influence on it, variables like gender, age, diabetes duration and renal length were examined. As the p-value was not significant for any of them, they were not taken into account in the regression analysis. The above-mentioned variables did not have a significant effect on serum creatinine (p>0.05) and were excluded from the regression analysis model. Only the RI showed significant good correlation with the 24-hour urine protein and serum creatinine (model R^2=0.75 and =0.67, respectively; both p<0.001) (Fig. 2 A&B).

In total, the above results can be brought into the following equations:

24-hour urine protein = −2941 + 4651×RI
Serum creatinine = −5.4 + 8.9×RI

For all four parameters (both constants and both RI coefficients), the p-value was less than 0.001.

Discussion

In the present study, the mean RIs showed a statistically significant difference between the three nephropathy groups. The mean RIs were higher in stage II patients than in stage I and higher in stage III than in stage II patients.

RI is a useful method for patients who do not have enough cooperation to collect the 24-hour urine sample. In case of an emergent decision for a patient (out-patient or ill patient), US and RI determination is a simpler approach to determine the severity of nephropathy. This finding has not been mentioned in previous studies. Although an R Square Index of 0.75 shows an appropriate regression, it implies that 25% of the 24-hour urine protein changes are associated with other factors than RI. Therefore, further studies are necessary to confirm our findings and to identify other predictors.

Based on the previous studies, the duration of diabetes has an effect on the severity of nephropathy.[7] However, in the present study, the duration of diabetes only had a statistically significant difference between stages I and III, but it failed to show a significant difference between stages I and II or stages II and III. The possible reason for this controversy could be the lack of concurrency between the time of the diagnosis of diabetes and the real time of the development of diabetes. Absence of an appropriate screening program for early detec-
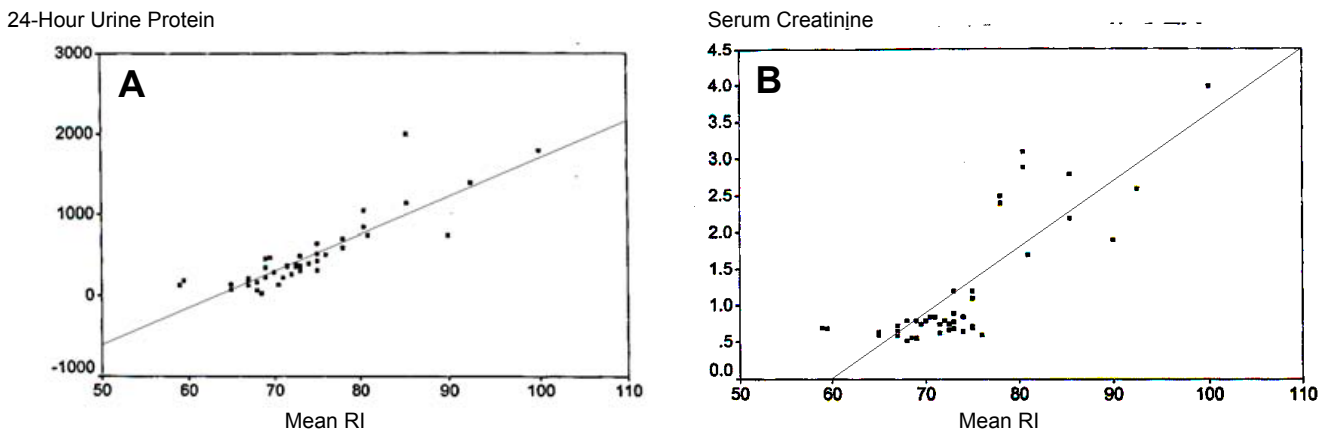

Fig. 2. Linear relationship between
A. RI and 24-hour urine protein
B. RI and serum creatinine

tion of diabetes in our country may be an explanation. Considering the high prevalence of diabetes in our country, it seems necessary to establish screening programs for detection of the disease and to reduce its complications, especially diabetic nephropathy.

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