Relationship between Intra-renal Arterial Resistance Index (RI) and Albuminurin in Diabetic Patients

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ABSTRACT
OBJECTIVE: Diabetic nephropathy is a major diabetes complication. Arterial resistance index (RI) may predict deterioration in kidney function. This study was designed to compare renal arterial RI in different stages of renal function according to glomerular filtration rate (GFR), serum creatinine level and proteinuria.

MATERIALS AND METHODS: In a cross-sectional study on 81 diabetic patients in three groups (Without albuminuria, with microalbuminuria, with macroalbuminuria), pulsatile Doppler ultrasonography was performed to measure intra-renal arterial resistance index and find the association of this parameter with features of diabetic nephropathy. Data was analyzed using SPSS (ver. 16).

RESULTS: Serum creatinine, GFR and proteinuria were significantly different among three groups. RI was highest in the group with macroalbuminuria and the difference among three groups was statistically significant. (P value<0.001) RI was correlated with serum creatinine, GFR and proteinuria.

CONCLUSION: Higher RI correlates with higher proteinuria in diabetic patients.

KEY WORDS: Diabetic Nephropathy, Resistance Index, Creatinine, GFR.

INTRODUCTION
Diabetic nephropathy, a major complication of both types of diabetes, is responsible for 15-40% of end-stage renal diseases (ESRD)(1). The outcome of diabetic nephropathy is various in different patients: some may progress to ESRD and some may come back to a normal state(2,3). It is estimated that diabetes is responsible for 30-40% of all end-stage renal diseases (ESRD) in the US(4).

Many studies have shown that prolonged hyperglycemia leads to chronic complications of diabetes including nephropathy (5). Diabetic nephropathy is characterized by micro-albuminuria (30-300mg/day). Early treatment of diabetes may delay diabetic nephropathy and ESRD and the regular follow-up of the patients is the key for successful treatment(6).

Hypertension is an aggravating factor in diabetic nephropathy(4). It has been shown that treatment of hypertension by angiotensin-converting enzyme inhibitors delays kidney damage in a large number of patients (7, 8).
Renal arterial resistance index of 80 or higher predicts a poor outcome of treatment and also predicts worsening renal function or death in patients with renal diseases (9). According to the annual report of the Japan Dialysis Treatment Society in 2006, the most frequent cause of end-stage renal disease is diabetes (10). Although diabetic nephropathy has been considered to be a microvascular complication, histopathological examination of renal biopsies showed not only typical diffuse or nodular lesions, but also arteriosclerotic glomerulosclerosis (11). RI in diabetic patients with renal dysfunction (chronic renal failure) was significantly increased compared to the patients with non-diabetic chronic renal failure (12).

**MATERIALS AND METHODS**

This was a cross-sectional study conducted on 81 diabetic patients. Patients were randomly selected from those referred to diabetes research center of Shahid Sadoughi University of Medical Sciences for follow-up of diabetes. Twenty seven patients were selected in each of three groups: 1. Without albuminuria; 2. With microalbuminuria; and 3. With macroalbuminuria. All patients underwent pulsatile doppler ultrasonography of renal vessels for measurement of intra-renal arterial resistance index first. The RI ((peak systolic velocity – end-diastolic velocity)/peak systolic velocity) was measured with duplex Doppler ultrasonography (Device: Siemens G40, Germany). The frequency of Doppler was 3.5-5 MHz convex array probe in both real-time/color-coded Doppler and pulse Doppler modes. Assessment was performed; then RI was measured in three parts: lower, middle and upper renal poles. A blood sample was obtained from each subject to measure creatinine level, and urine albumin to creatinine ratio. One time urine specimen (μg/mg) was performed to evaluate albuminuria. GFR was measured by Cockcroft-Gault equation as below (13).

\[
\text{Clr (ml/min)} = \frac{(140 – \text{age}) \times \text{lean body weight(kg)} \times (0.85 \text{ for Female})}{\text{serum Cr (mg/dl)} \times 72}
\]

An informed consent was obtained from all patients. Data was analyzed using SPSS (ver. 16) and level of significance was set at 0.05. Chi square, Pearson's correlation, and ANOVA tests were used for statistical analysis.

**RESULTS**

Eighty one diabetic patients entered the study and were divided into three groups. Fifty six patients (69.13%) were males and 25 subjects (30.87%) were females. Distribution of gender, age, body mass index and duration of diabetes were not significantly different among three groups. Table 1 compares these

<table>
<thead>
<tr>
<th>Group</th>
<th>Age Mean</th>
<th>BMI Mean</th>
<th>Duration of diabetes Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>No albuminuria</td>
<td>57.72</td>
<td>9.63</td>
<td>26.72</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>58.35</td>
<td>11.91</td>
<td>26.24</td>
</tr>
<tr>
<td>Macroalbuminuria</td>
<td>59.44</td>
<td>10.38</td>
<td>27.11</td>
</tr>
</tbody>
</table>

* Body mass index
** Standard deviation

<table>
<thead>
<tr>
<th>Group</th>
<th>Serum creatinine Mean</th>
<th>GFR Mean</th>
<th>Proteinuria Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>No albuminuria</td>
<td>0.98</td>
<td>86.27</td>
<td>133.88</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>1.05</td>
<td>78.66</td>
<td>428.83</td>
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<tr>
<td>Macroalbuminuria</td>
<td>2.72</td>
<td>72.38</td>
<td>665.63</td>
</tr>
</tbody>
</table>

P value <0.001 <0.001 <0.001

** Standard deviation
variables among three groups. Resistance index was highest in the 3rd group (macroalbuminuria) and the difference among 3 groups was statistically significant (p<0.001). Figure 1 shows intra-renal arterial resistance index in the 3 groups.

Pearson’s correlation test showed a direct correlation between serum creatinine and RI (R=0.729, p<0.001) and also between 24-hour urine protein and RI (R = 0.702, p<0.001); but the correlation between GFR and RI was indirect (R= 0.283, p=0.01) (Table 2).

DISCUSSION
This study evaluated the relationship between serum creatinine, GFR, proteinuria, and intra-renal arterial resistance index in three groups of diabetic patients (without albuminuria, with microalbuminuria and with macroalbuminuria). The study showed a statistically significant difference in RI in three groups of patients, so as the patients with macroalbuminuria showed a significantly higher RI. RI was correlated directly with creatinine and GFR and indirectly with proteinuria.

Microalbuminuria is a predictor of diabetic nephropathy and also it is clue for the onset of kidney damage (6). RI≥0.7 can predict kidney function in diabetic patients suffering from micro or macroalbuminuria(14-16). Increased intra-renal artery RI indicates renal impairment which leads to decreased intra-renal vessel area(17).

The relationship between RI and such features of diabetic nephropathy as albominuria, and creatinine level has been assessed in some studies.

Spomenka et al. showed that Doppler ultrasound can help in early diagnosis of diabetic nephropathy by measuring intra-renal artery resistance index and found a direct relationship between intra-renal RI and diabetic nephropathy which was consistent with our study(18).

Another study conducted by Milovanceva et al. showed an association between intra-renal RI and serum creatinine and creatinine clearance consistent with the results of our study(19).

Narooeinejad et al. showed that RI can be used to estimate 24-hour urine protein especially in those patients who are not compliant for 24-hour urine collection(20). Soldo et al. also showed a relationship between RI and serum creatinine(21). Masulli et al. failed to find a relationship between RI and albominuria which was inconsistent with the results of our study.

CONCLUSION
Our study had some limitations. There are some biases in this cross sectional study, so we cannot find the predictive RI in proteinuria. A cohort study is needed for this aim.

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