Relation between resistivity and pulsatility indices of renal and intrarenal arteries and degree of albuminuria in type 2 diabetic patients

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Introduction
Macrovascular complications are well known in diabetes mellitus and diabetic nephropathy. This work aimed to study the relation between resistivity index (RI) and pulsatility index (PI) of the main renal and intrarenal arteries and the degree of albuminuria in diabetic patients.

Patients and methods
The study included 60 type 2 diabetic patients with more than 5-year duration of diabetes. There were 14 male and 46 female patients. They were divided into three groups: group I included patients with no albuminuria [albumin/creatinine ratio (ACR) in first voiding morning urine sample <30 mg/g creatinine]; group II included patients with microalbuminuria (ACR: 30–300 mg/g creatinine), and group III included patients with macroalbuminuria (ACR: ≥300 mg/g creatinine). Patients with fever, urinary tract infection, uncontrolled blood pressure, congestive heart failure, critically ill patients, or patients having other renal disease were excluded. All patients were subjected to measurement of ACR in the first voiding morning urine sample, serum creatinine, estimated glomerular filtration rate using Cockroft–Gault formula, and HbA1C. RI and PI of main renal and intrarenal arteries were measured on both sides using duplex Doppler ultrasonography

Results
RI and PI of renal and intrarenal arteries were found to be significantly higher in group III than in group II and group I, with group II patients having higher values compared with group I ($P < 0.001$ for all). ACR was found to be positively correlated with RI and PI of all studied renal and intrarenal arteries ($P < 0.001$ for all).

Conclusion
In type 2 diabetes mellitus, RI and PI of renal arteries on duplex Doppler ultrasonography examination are related directly to the degree of albuminuria, which could serve as an indicator to the degree of resistance in renal arteries.

Keywords:
albuminuria, diabetes, Doppler, pulsatility, resistivity

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Introduction

Diabetic nephropathy is responsible for 15–40% of end-stage renal diseases (ESRD) [1]. Patients with diabetic kidney disease have a high rate of cardiovascular morbidity and mortality [2]. In addition to typical changes of diabetic nephropathy, renal biopsy lesions in type 2 diabetes showed arteriosclerotic glomerulosclerosis [3]. Hemodynamic alterations, including intraglomerular hypertension, raised renal vascular resistance, and the so-called ischemic nephropathy are responsible for the discrepancy of various stages of diabetic nephropathy [4]. Pulsatility index (PI) and resistivity index (RI) of renal arteries were found to correlate significantly with effective renal plasma flow, renal vascular resistance, and the filtration fraction in patients with chronic renal failure [5]. In patients with ESRD, it was found that a PI higher than 1.55 or RI higher than 0.75 was associated with a faster decline in renal functions evaluated by reciprocal serum creatinine [6]. In patients with renal dysfunction secondary to type 2 diabetes mellitus, PI and RI were significantly increased compared with patients with nondiabetic renal disease [7]. Intrarenal arterial resistance was found to play a nontrivial role in deteriorating renal function in type 2 diabetic patients. RI was found to be a noninvasive diagnostic procedure, which strongly predicted the outcome of renal function in type 2 diabetic patients, even when glomerular filtration rate patterns were still normal [8]. RI was significantly higher in patients with type 2 diabetes and albuminuria than in patients without albuminuria [9].

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Both RI and PI could be used as sensitive indicators of changes in intrarenal vascular flow, although RI may have a small coefficient of variance and may be more reproducible compared with PI [6]. The aim of this work was to study the relation between RI and PI of the main renal and intrarenal arteries and the degree of albuminuria in type 2 diabetic patients.

Patients and methods

A total of 60 type 2 diabetic patients with a duration of diabetes more than 5 years were included in the study. They were randomly selected from Nephrology Clinic and from Diabetes and Endocrinology Clinic, Kasralainy Hospital, Faculty of Medicine, Cairo University, Egypt. The study was started after the approval of local ethical committee of Faculty of Medicine, Cairo University. Informed consent was obtained from each patient before enrollment in the study. Patients were divided according to urine albumin excretion rate presented by albumin/creatinine ratio (ACR) in the first morning voiding urine sample into three groups of 20 patients each as follows: group I included patients with normal ACR (<30 mg/g creatinine); group II included patients with microalbuminuria (ACR: 30–300 mg/g creatinine); and group III included patients with macroalbuminuria (ACR: >300 mg/g creatinine). The following patients were excluded by history and examination: patients with uncontrolled hypertension, those with cardiac failure, smokers, patients receiving NSAID, patients suffering from acute or chronic urinary tract infections, patients suffering any febrile illness, critically ill patients, and patients with nondiabetic renal disease. All patients were subjected to measurement of serum creatinine and estimated glomerular filtration rate (eGFR) evaluation using Cockroft–Gault formula [10]:

$$\text{eGFR}\left(\text{ml}/\text{min}\right) = \frac{\left(140 - \text{age}\right) \times \text{lean body weight}\left(\text{kg}\right)}{\text{Creatinine}\left(\text{mg}/\text{dl}\right) \times 72}$$

Duplex and color-coded Doppler examination of both renal and both intrarenal vessels was performed using an ultrasound machine (HDI 5000, Philips, Philips doppler ultrasound, Netherland, USA). The transducer used is 3.5 MHz. Patients were examined after the routine preparation for abdominal ultrasonography (about 6 h – fasting, enema, and ingestion of charcoal). They were scanned in the supine position, starting with placing the transducer in the middle line at the epigastrium and trying to get the best image of both renal arteries in the sagittal and coronal planes. The simplest way to identify both renal arteries is first to identify the aorta in the epigastrium with the patient supine, and then tilt the probe until the renal artery appears on both sides of the aorta. This is performed to assess the peak systolic velocity, end diastolic velocity, RI, and the PI. The patient is then made to lie on each side to assess the intrarenal vessels by detecting the kidney and the intrarenal vessels to assess the renal vascularity and to assess the peak systolic velocity, end diastolic velocity, RI, and the PI.

Statistical analysis

The statistical analysis system (IBM SPSS version 17, Chicago, Illinos, USA) was used for data management. Data were summarized as mean and SD. Analysis of variance test was used for comparison between groups. Nonparametric tests were used when appropriate. The x^2-test was used for qualitative data. Fisher's exact test and Yates' corrected x^2 were computed for 2 × 2 tables. Pearson's correlation was applied to detect the relations between different parameters. Correlation between different parameters was stratified according to their value as follows: $r \leq 0.25$, weak correlation; $0.25 \leq r \leq 0.5$, mild correlation; $0.5 < r < 0.75$, moderate correlation; and $r \geq 0.75$, strong correlation. All reported P values were two-sided. P less than 0.05 is considered significant.

Results

All three groups were matched as regards age, sex, and BMI. All our patients were mildly obese and showed poor diabetic control (Table 1).

Group III patients showed significantly higher RI and PI of all arteries studied compared with group II and group I, respectively. Moreover, all studied indices were found to be significantly higher in group II than in group I (Table 2).

Urinary albumin/creatinine was found to be positively correlating with RI and PI of all arteries studied in a significant relation (Figs. 1 and 2)

Discussion

Diabetic nephropathy is the most common cause of ESRD in many countries that follows a well-defined clinical course starting with microalbuminuria passing through gross proteinuria and culminating into end-stage renal failure. However, not all patients with diabetic nephropathy progress through these stages. Risk factors such as duration of diabetes mellitus, tightness of glycemic control, and blood pressure are implicated in the pathogenesis of diabetic nephropathy.

Table 1 Demographic and laboratory data of studied groups

	Group I	Group II	Group III	*P*
Age (years)	51.8±4.008	55.65±7.2	54.15±6.8	0.15
Sex (*n* (%))				
Male	6 (30)	4 (20)	4 (20)	0.7
Female	14 (70)	16 (80)	16 (80)	
BMI (kg/m^2)	32.9±5.0	32.3±5.6	32.9±5.6	0.92
Diabetic retinopathy (*n* (%))				
Normal	16 (80.00)	14 (70.00)	5 (25.00)	χ^2=14.126 *P*=0.001
NPDR	4 (20.00)	6 (30.00)	15 (75.00)	
Diabetic neuropathy symptoms (*n* (%))				
Positive	1 (5)	10 (50)	9 (45)	χ^2=10.950 *P*=0.004
Negative	19 (95)	10 (50)	11 (55)	
HbA1C (%)	9.24±1.6	9.6±1.4	9.21±1.2	0.6
Serum creatinine (mg/dl)	0.66±0.14	0.67±0.13	0.77±0.45	0.4
eGFR (ml/min/1.72 m^2)	117.85±34.5	102.76±28.9	75.9±2.0	<0.001
Albumin/creatinine ratio (mg/g)	13.335±5.220	133.970±64.784	775.370±393.174	<0.001

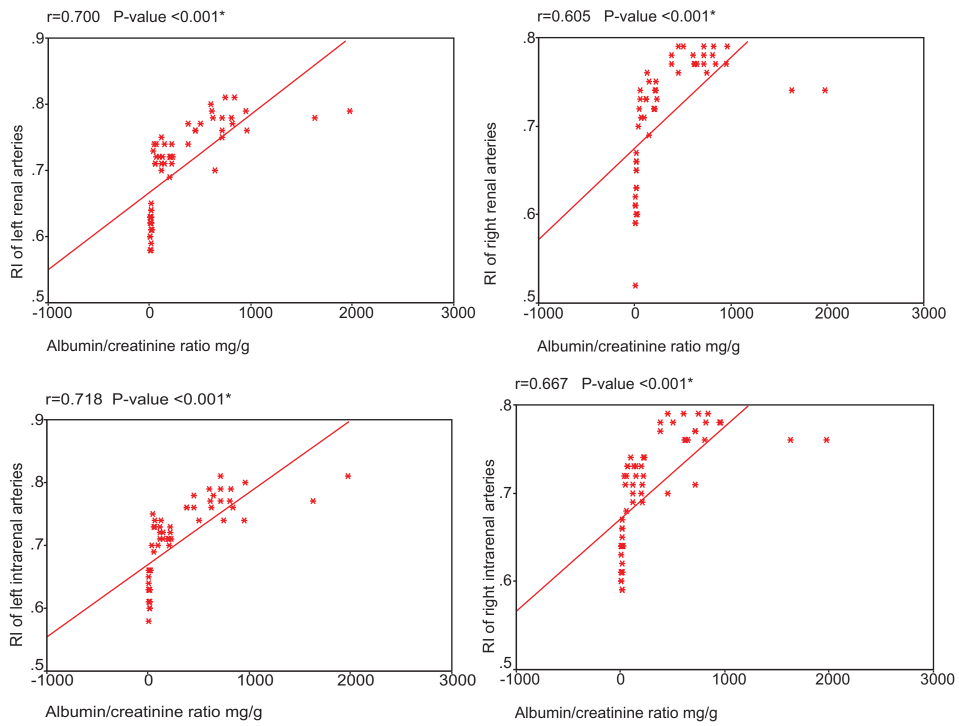
eGFR, estimated glomerular filtration rate; HbA1C, glycated hemoglobin; NPDR, non proliferative diabetic retinopathy.

Table 2 Doppler indices of studied groups

Sites	Doppler indices	Group I	Group II	Group III	*P*
Right main artery	RI	0.62±0.035	0.73±0.018	0.773±0.015	<0.001
	PI	1.16±0.08	1.4±0.05	1.46±0.03	<0.001
Left main artery	RI	0.62±0.02	0.72±0.02	0.77±0.01	<0.001
	PI	1.13±0.10	1.42±0.04	1.49±0.03	<0.001
Right intrarenal arteries	RI	0.625±0.024	0.717±0.018	0.77±0.024	<0.001
	PI	1.12±0.07	1.40±0.05	1.48±0.02	<0.001
Left intrarenal arteries	RI	0.62±0.02	0.72±0.02	0.77±0.2	<0.001
	PI	1.15±0.09	1.41±0.03	1.50±0.04	<0.001

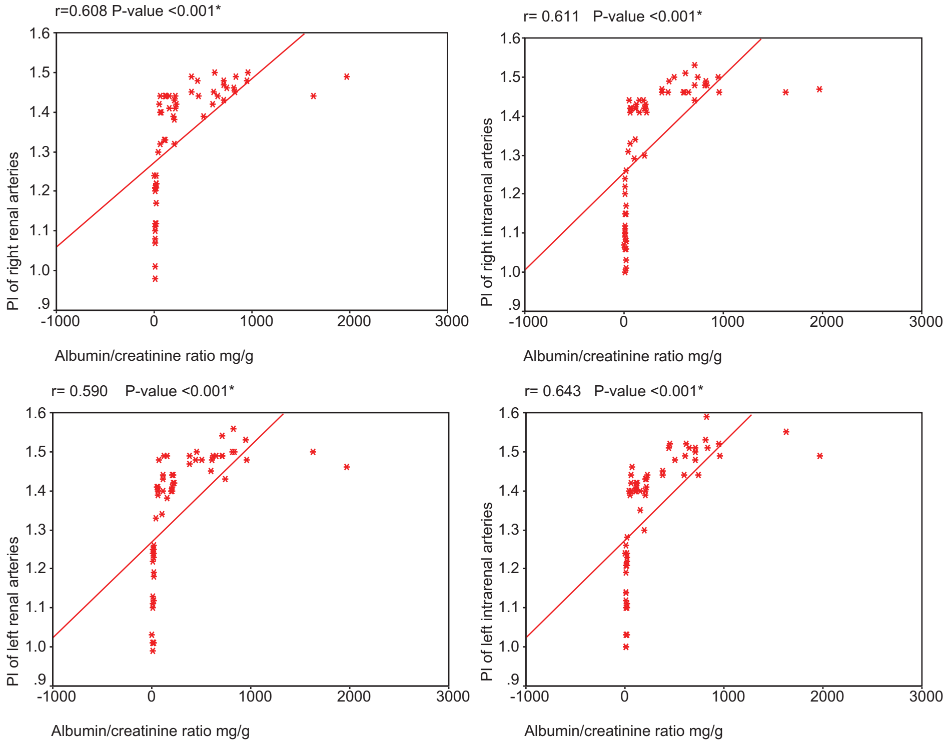
PI, pulsatility index; RI, resistivity index.

Figure 1



Correlation of albumin/creatinine ratio with resistivity indices of the right and left main renal and intrarenal arteries. *(statistically significant)

Figure 2



Correlation of albumin/creatinine ratio with pulsatility indices of the right and left main renal and intrarenal arteries. *(statistically significant)

Other less important risk factors are smoking, dyslipidemia, and dietary factors [11].

This work aimed to study the relation between renal duplex indices in the form of RI and PI of main renal and intrarenal arteries on one side and the severity of diabetic nephropathy presented by the degree of albuminuria on the other.

In this study, our three groups were matched as regards age. This is in agreement with findings of Fallah *et al.* [12], who found no significant difference among their patients as regards their age.

As regards BMI, a high BMI was associated with an increased risk for chronic kidney disease among patients with diabetes [13]. In addition, diet and weight loss may reduce albuminuria and improve kidney function among patients with diabetes [14]. BMI was identified as an independent risk factor for albuminuria [15]. However, the contribution of obesity (or weight loss) to the risk for nephropathy (independent of diabetes and glycemic control) has not been convincingly demonstrated in these studies. This study found that there was no significant difference between the three groups as regards BMI. These results are in agreement with those of Fallah *et al.* [12], who found no significant difference between their three groups as regards BMI. However, other studies found a significant correlation between the progression of diabetic nephropathy and BMI [16,17].

On continuity of describing biochemical profile, assessment of serum creatinine and eGFR using Cockroft–Gault formula was carried out. eGFR values were found to have a significantly negative relationship with ACR. Decreasing glomerular filtration rate occurs with advancing stage of diabetes due to progressive increase in albuminuria [18].

As regards comparison of RI and PI of main renal and intrarenal arteries between studied groups, we found significantly higher values in group III with macroalbuminuria compared with group II patients with microalbuminuria and group I patients without albuminuria, with a significantly higher RI and PI in group II compared with group I ($P < 0.001$). Our results are comparable to a similar study conducted by Mancini *et al.* [19], who found that patients with higher RI values had significantly greater proteinuria. Similar results were also observed by Fallah *et al.* [12] and Hamano *et al.* [9]. Masulli *et al.* [20] found that patients with RI greater than 0.73 had a significantly higher baseline albumin excretion rate and a more frequent progression of the albuminuric state compared with patients with RI less than 0.73. However, Tsai *et al.* [21] failed to find similar differences in three groups of adolescents and young adults with type 1 diabetes divided according to the degree of proteinuria as regards RI of renal arteries.

A strong independent statistically significant correlation was found between renal duplex indices represented by RI on one hand and ACR on the other, both in this study ($P < 0.001$) and in the study by Hamano *et al.* [9]. We also found positive correlations between RI in the intrarenal arteries and the ACR, which was similar to that found by Saif *et al.* [22].

According to these results, the degree of albuminuria in type 2 diabetic patients could be an indicator of resistance in renal arteries, with patients with a higher degree of proteinuria having a higher degree of resistance. This could add to the understanding of the mechanism of hypertension and progression of renal disease in those patients.

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Conflicts of interest
There are no conflicts of interest.

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