Intrarenal Hemodynamic Changes In Type 2 Diabetic Patients

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Abstract

Back ground: A frequent and early manifestation of diabetic nephropathy is hyaline arteriolosclerosis, characterized by hyaline deposition in the arterioles. Measurement of the resistive index (RI) by Doppler sonography may be used as a noninvasive method for estimating the severity of arteriolosclerosis instead of invasive renal biopsy

Objectives: To study the effect of type 2 DM on intrarenal hemodynamics.

Methods: Nineteen patients with type 2 diabetes were included in this study (10 males, 9 females) aged 44±10 years, mean duration of DM was 7±5 years. The resistive index (RI) of interlobular renal arteries was used to assess the intrarenal hemodynamic changes in diabetic patients and compared to that of the normal subjects

Results: Statistically there was significant intrarenal hemodynamic changes in type 2 diabetic patients compared to normal subjects as reflected by higher values of RI in the former. Also there was significant effect of the duration of DM on intrarenal hemodynamics.

Conclusions: Type 2 diabetic patients have higher values of RI compared to non-diabetics, and this increment is proportional to the duration of DM.

Key words: Type 2 diabetic mellitus, intrarenal hemodynamic, resistive index.

Introduction:

Anatomy of renal artery:

The renal artery, a large vessel, arises at right angles from the aorta opposite the body of L2 vertebra. In the region of the hilum renal artery typically gives rise to an anterior and a posterior division. The posterior division supplies the posterior segment, while the anterior division supplies the apical, upper, middle and lower segments [fig.1] (1).

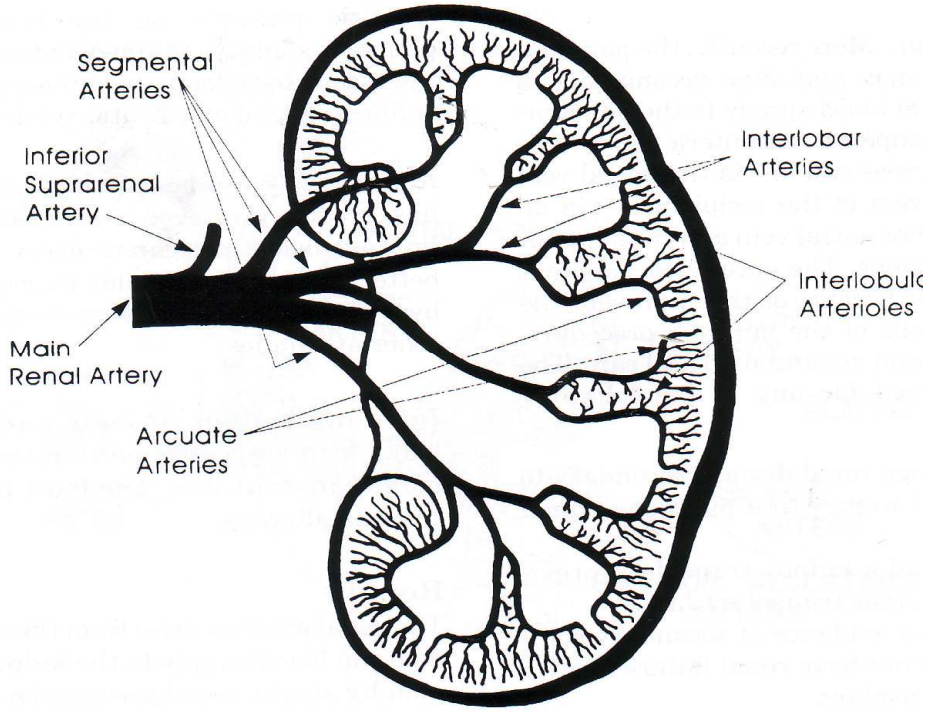

Figure 1: anatomy of renal artery.

The standard pattern is frequently modified by the way the vessels branch,e.g. the vessel to more than one segment may arise from a common stem and several variation are possible but there are five segments with no collateral circulation between them (1).

Patho-physiology of renal blood flow:

In a 70-kg person, renal blood flow (RBF) amounts to a fourth to a fifth of the resting cardiac output, or approximately 1.2 L/min. The renal cortex receives 85 to 90% of this flow as compared with 10% to the outer medulla and 1 to 2% to the inner medulla, including the papilla. With one kidney removed, blood flow to the remaining kidney nearly doubles within a few weeks (2).

Renal blood flow and the glomerular filtration rate (GFR) remain relatively constant over a wide range of perfusion pressures, a process that is termed autoregulation. An intrinsic property of smooth muscle cells in the renal vasculature, the myogenic reflex, permits instantaneous alterations in the tone of the vessel wall to maintain RBF and GFR constant over a pressure range of 80 to 180 mm Hg.(2).

Metabolic requirements of the kidney are satisfied with <10% of blood flow. Therefore, decrements of RBF in the presence of anatomic lesions may not be sufficient to explain decrements in renal function (3). Furthermore, during reductions in renal perfusion pressure by up to 40%, RBF and GFR are maintained by autoregulation (4). Greater reductions of renal perfusion pressure are accompanied by steeper declines in GFR than RBF. A 40% decline in renal perfusion pressure occurs when the renal artery is narrowed by 70 to 80%. This degree of obstruction has been termed "critical stenosis" (5).

Doppler sonography and diabetic nephropathy:

Diabetes remains one of the most common causes of renal failure worldwide. Diabetic nephropathy begins with a period of glomerular hyperfiltration and intraglomerular hypertension. Subsequently, glomerular injury develops with the eventual loss of filtration capacity, leading to azotemia, a process that is hastened by frequently coexisting hypertension. Abnormal albumin excretion is an early sign of glomerular disease and may progress slowly from microalbuminuria (30 to 300 mg/d) to macroalbuminuria (more than 300 mg/d) to frank nephrotic syndrome more than 3.5 g/d) (6).

A frequent and early manifestation of diabetic nephropathy is hyaline arteriolosclerosis, characterized by hyaline deposition in the arterioles. Measurement of the resistive index (RI) by Doppler sonography may be used as a noninvasive method for estimating the severity of arteriolosclerosis instead of invasive renal biopsy (7). Also there is evidence that RI correlates with the rate of decline in reciprocal serum creatinine. The index is therefore useful for predicting deterioration in renal function (8).

Duplex Doppler sonography provides a high-quality and noninvasive display of flow in the renal and intrarenal blood vessels and enables measurements of flow parameters that may have importance in several kidney diseases (9).

Intrarenal arterial Doppler parameters are the resistive index (RI), pulsatility index (PI), and acceleration time (AT). RI equals to [peak systolic velocity - minimum diastolic velocity] / peak systolic velocity.

PI equals to [peak systolic velocity - minimum diastolic velocity] / mean flow velocity**.** Acceleration time indicates the elapsed time in milliseconds from the beginning of systole to early systolic peak (10, 11).

Petersen et al. showed that RI and PI correlate significantly with effective renal plasma flow, renal vascular resistance and filtration fraction in patients with chronic renal disease (12).

The RI and PI of patients with diabetic nephropathy were higher than in patients with other types of renal disease and in control subjects. This was equally true for both Doppler indices measured in the interlobar arteries and for Doppler indices measured in the main renal arteries (13, 14).

Some authors related these Doppler indices in diabetic patients to renal vascular resistance and to damage of the renal vascular bed (nephrosclerosis) (15).

However, others relate Doppler indices to alterations of the arterial system. Interestingly, Taniwaki et al. reported that renal resistance indices in patients with diabetic nephropathy were significantly correlated with age, duration of diabetes and systolic and diastolic blood pressure. These data indicate that renal resistance indices reflect systemic vascular damage in diabetic patients (16).

There is growing evidence that renal resistive indices are prognostic markers for patients with renal artery stenosis and chronic renal disease. Their diagnostic value for the management of kidney transplant patients is also well established (17). Patients with chronic renal disease and increased resistance indices of intrarenal arteries displayed a faster deterioration of renal function (18).

Aim of the study:

To study the intrarenal hemodynamic changes in diabetic patients.

Patients and methods:

In this study 19 patients with type 2 diabetes were enrolled, aged 35-60 (44.4±10) years, 10 male and 9 female. The mean duration of diabetes was (7±5) years. Nine patients had hypertension in addition to diabetes. Patients with renal diseases, renal impairment and hyperlipidemia were excluded. This group of patients is compared with apparently healthy subjects aged 30-43 years; 6 male and 4 female.

Patients and control subjects were studied, after a 12-hour fast, in the anterior, lateral decubitus, and, at times, the prone position. Care was taken not to exert much pressure on the kidney when insonating renal arteries as this may hamper the flow and may affect Doppler parameters.

The intrarenal hemodynamics was studied using color Doppler sonography Siemens equipment with 2.5 MHz phased array probe. Segmental interlobular renal arteries were studied first by color flow assignment, then by pulse wave Doppler technique by placing the Doppler sample volume cursor at 0^0-35^0 angle, and the sample volume used is adjusted at 3 mm.

Doppler parameter used to assess intrarenal hemodynamic changes ,in this study, was the resistive index (RI). The resistive index was calculated by the formula of peak systolic velocity (PSV) minus end diastolic velocity (EDV) divided by peak systolic velocity. The peak systolic velocity is a measure of maximum velocity of blood flow during systole; end diastolic velocity is a measure of the velocity of blood flow at the end of diastole (10). Both peak systolic velocity and end diastolic velocity were measured in the upper, middle and lower pole of each kidney. Figure 2 and Figure 3.

For evaluation of the effect of DM on intrarenal hemodynamics; M±SD of RI in the three poles of each kidney of the diabetic patients was compared to that of the control subjects. Then the effect of duration of DM and hypertension on intrarenal blood flow was evaluated in the same manner.

For statistical analysis, T-test was used and p- value of less than 0.05 is considered significant.

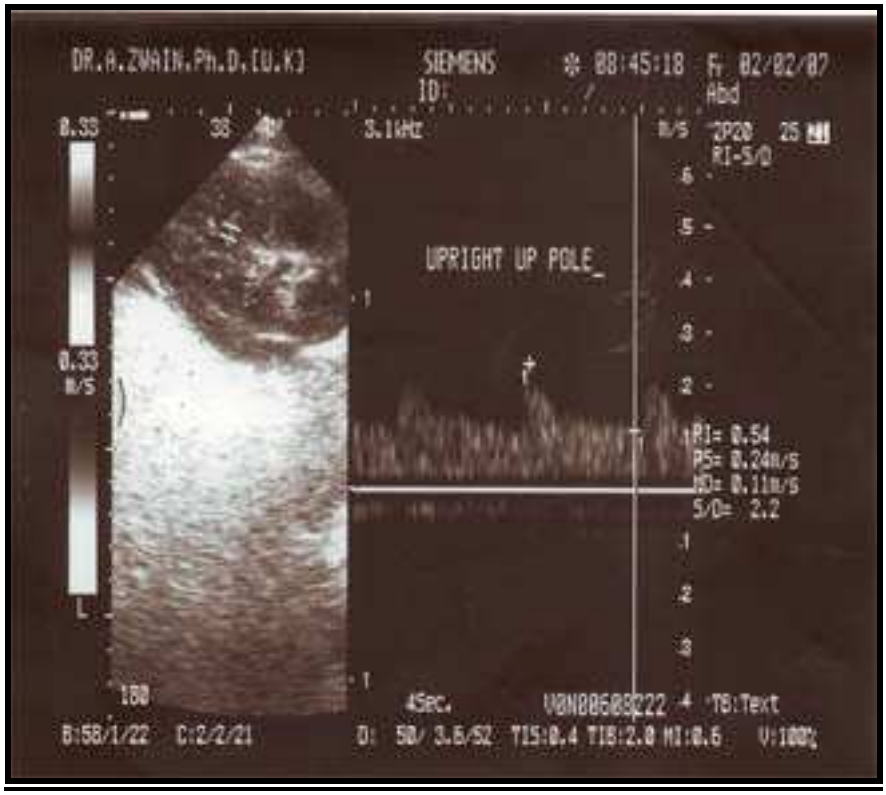

Figure 2: Doppler waves in normal subject.

Figure 3: Doppler waves in diabetic patient

Results:

Statistically there was significant intrarenal hemodynamic changes in the type 2 diabetic patients (10 males. 9 females, 35-60 years old) compared to normal subjects (6 males. 4 females, 30-43 years old) as reflected by higher values of RI in the diabetics (tables 1, 2). Also there was significant effect of the duration of DM on RI (tables 3, 4). However there was no significant effect of hypertension on RI in diabetic patients (tables 5, 6).

Table 1: Comparison of resistive index (RI) of right kidney between diabetic patients and control subjects.

RI M±SD	Diabetic patients n.19	Control subjects n.10
UP*	0.76± 0.20	0.61± 0.17
MP*	0.75± 0.22	0.57± 0.16
LP*	0.78± 0.19	0.60± 0.09

* UP: upper pole, MP: middle pole, LP: lower pole.

p-value = 0.002

Table 2: Comparison of RI of left kidney between diabetic patients and control subjects.

RI M±SD	Diabetic patients n.19	Control subjects n.10
UP	0.81± 0.18	0.60± 0.18
MP	0.67± 0.16	0.58± 0.10
LP	0.76± 0.21	0.59± 0.09

p-value = 0.024

Table 3: Comparison of RI of right kidney among diabetic patients according to the duration of DM.

RI M±SD	DM < 10 years n.10	DM > 10 years n.9
UP	0.74± 0.20	0.78± 0.20
MP	0.70± 0.19	0.79± 0.26
LP	0.73± 0.20	0.85± 0.18

p-value = 0.035

Table 4: Comparison of RI of left kidney among diabetic patients according to the duration of DM.

RI M±SD	DM < 10 years n.10	DM > 10 years n.9
UP	0.74± 0.19	0.86± 0.16
MP	0.66± 0.15	0.72± 0.17
LP	0.72± 0.18	0.81± 0.24

p-value = 0.018

Table 5:Comparison of RI of right kidney between diabetic patients with hypertension and those without hypertension.

RI M±SD	Diabetics with HT n.9	Diabetics without HT n.10
UP	0.70± 0.18	0.82± 0.22
MP	0.69± 0.21	0.78± 0.28
LP	0.78± 0.18	0.77± 0.20

p-value = 0.116

Table 6: Comparison of RI of left kidney between diabetic patients with hypertension and those without hypertension.

RI M±SD	Diabetics with HT n.9	Diabetics without HT n.10
UP	0.81± 0.16	0.76± 0.21
MP	0.70± 0.16	0.68± 0.17
LP	0.81± 0.16	0.71± 0.25

p-value = 0.068

Discussion:

Many researchers proved that intrarenal hemodynamic changes are sensitive markers for diagnosis and follow up of many renal diseases particularly diabetic nephropathy; furthermore these changes can reflect the severity of atherosclerotic changes of systemic arteries.

In diabetic patients duplex Doppler sonography can be used as non-invasive tool for early diagnosis of diabetic nephropathy and for follow up of renal function in established diabetic nephropathy.

In the present study, there was significant increase in resistive index of interlobular renal vessels in diabetic patients compared to control healthy subjects. Also there was significant correlation between the duration of diabetes and the severity of intrarenal hemodynamic changes; this observation may be related to the development of diabetic nephropathy.

Dr. Piernicola Pelliccia and colleagues at the University of Chieti, General Hospital in Chieti, Italy, measured the Doppler resistance index in the interlobular renal arteries of 83 study participants and found those with diabetes had significantly higher

values than their age-matched controls, and they suspect that ultrasound is allowing them to diagnose a preclinical stage of diabetic nephropathy (19).

Ishimura E. and colleagues studied intrarenal hemodynamics by duplex Doppler sonography in 112 patients with type II diabetes mellitus (65 males. 47 females, 58 ± 13 years old). Multiple regression analysis revealed that RI values in diabetic patients were significantly affected by creatinine clearance, age, and duration of diabetes (20). Therefore RI can be used as a non-invasive, easily available, parameter for renal evolution in patients with established clinical diabetic nephropathy (21).

Naoki Matsumoto and colleagues found resistive index and pulsatility index significantly increased in the diabetic CRF patients compared to the non-diabetic CRF patients. Multiple regression analysis of all CRF patients revealed that resistive index was independently affected by the presence of type 2 diabetes (22).

In addition to diabetic nephropathy, Ohta Y and colleagues, found increase in RI and PI in chronic glomerulonephritis, and nephrosclerosis. However intrarenal vascular resistance differs depending on the underlying renal disease, and appears to increase to a greater extent in diabetic nephropathy (23).

The increment in renal vascular resistance can be explained by loss of capillaries and glomeruli, and consequent progressive reduction in the number and cross-sectional area of renal vessels (12).

Although some researchers reported significant correlation between systolic and diastolic blood pressure and severity of systemic atherosclerosis (20, 24); our study didn't reveal such relationship probably due to small sample size and short duration of hypertension.

Conclusion:

Type 2 diabetic patients have higher values of RI compared to non-diabetics, and this increment is proportional to the duration of DM.

Recommendation:

Further study is recommended to evaluate the correlation between microalbuminuria and intrarenal hemodynamic changes in diabetic patients.

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