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Value of renal resistance index in detection of diabetes mellitus complications in Egyptian elderly

KEYWORDS: Renal resistance index, diabetic nephropathy, proteinuria.

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ABSTRACT *Aim: determination of the value of renal resistance index in detection of diabetic nephropathy in elderly Egyptian.*

Methods: This study was a case-control comparative study between non nephropathic patients, nonproteinuric nephropathics and proteinuric nephropathic diabetic patients. 130 elderly diabetic patients were serially selected from Ain Shams University hospital inpatient's wards of geriatric and internal medicine departments; males/ females, 60 - 75 years old, with primary diabetes mellitus, diagnosed within the last 10 years. Any patient with known kidney disease, urinary tract infection, hepatitis C using drugs affecting kidney functions were excluded. All patients were subjected to clinical assessment and laboratory investigation, Estimation of glomerular filtration rate by Cockroft-Gault equation , Framingham 10 year coronary risk prediction by LDL tool, Renal duplex to estimate renal resistance index.

Results: Results revealed that patients with nonproteinuric diabetic nephropathy were significantly younger than patients with proteinuria.

After adjusting weight, age, SABP, type of antihypertensive used (ACEi/ARB) and comparing to participants with eGFR>60, there was a statistically significant inverse relationship between RRI and weight adjusted eGFR with p value <0.001. Conclusion: Renal resistance index was inversely correlated with glomerular filtration rate after adjusting ideal body weight.

Introduction:
Elderly individuals are a fast growing subgroup of the general population, and diabetes mellitus is now a major health issue affecting them. The reported incidence of diagnosed diabetes in an elderly cohort is 10% to 18%, compared with roughly 8% of the general American population [(1)].

The prevalence of diabetes has reached new levels, with total crude prevalence (diagnosed and undiagnosed cases) reported as 30% for those older than 60 years. This growing epidemic has been linked to obesity, tobacco use, urbanization, physical inactivity, poor nutrition, and improved survival of diabetic patients, and aging [(2)].

Chronic kidney disease (CKD) complicates diabetes and also has an increased prevalence in elderly individuals. Particularly in those older than 60 years, the most common cause of CKD and end-stage renal disease (ESRD) in the United States is diabetic kidney disease. A third of new ESRD cases in people older than 75 years are caused by diabetic nephropathy (DN) [(3)].

The time of onset of DM2 (Type II Diabetes Mellitus) is rarely known accurately, and cardiovascular events in a patient with DM2 can censor the natural history of DN. A feature of the natural history of DN that is gaining renewed investigation is the progression from normoalbuminuria to proteinuria and then to renal failure. In the classical paradigm, overt proteinuria precedes the decline in renal function. Recently, there have been several reports describing patients with primarily DM2 and presumed DN who have declining renal function with normoalbuminuria or MA (microalbuminuria) and not the previously well-described proteinuria [(4)].

Diabetic nephropathy is a frequent microvascular complication of Diabetes mellitus. Early functional and structural abnormalities may be present a few years after the onset of the disease. In these last decades, Doppler ultrasonography has provided an easily applicable and noninvasive method for investigating renal hemodynamics. Color and power Doppler can provide an accurate morphological and functional evaluation of the intraparenchymal vascularity and detect reduced or no blood flow in the kidney or in a

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portion of the kidney. In this case, there will be color signals from the undamaged part of the kidney but not from the ischemic part. The use of contrast agent increases diagnostic confidence in this type of lesions [5].

The renal resistive index reflects intrarenal vascular resistance. The mechanisams for increased RI values in patients with decreased glomerular function is unknown. In advanced DN, glomeruli become sclerotic, tubuli become atrophic, and interstitial fibrosis is increased. Sclerotic glomeruli may cause increased blood flow resistance measurable at an upstream interlobar artery. Increased interstitial fibrosis may cause elevated RI values [6].

The RI of interlobar arteries seems to be a dependable marker of intrarenal changes. Activation of the renin-angiotensin system is reported to contribute to inrarenal haemodynamic abnormality in diabetic patients. ACE inhibitors have been shown to delay the progression of DN by decreasing the intraglomerular capillary pressure [7].

Intrarenal resistive index (RI) is a more sensitive parameter measured on the renal interlobar arteries, which provides physiopathological information about medical RI is commonly used for evaluating renal arterial resistance, and a significant correlation between RI and renal vascular resistance is repeatedly reported in the literature [8].

However, it should be pointed out that RI is only a marker of renal vascular resistance and not an indicator of renal function. In some diseases, elevated renal arterial resistance is associated with impaired renal function, while other renal pathologies can cause significantly impaired renal function despite little or no changes in renal vascular resistance.

The real value of echo color Doppler analysis of RI in native kidneys can be its predictive use in particular clinical situations. In the literature, RI 0.6 ± 0.2 is considered normal, but most studies agree that RI 0.70 should be the upper limit of normal intrarenal vascular resistance. RI values are higher in interstitial pathologies (≥0.70) compared to purely glomerular pathologies in which RI values exceed 0.70 only in the advanced stage of the disease [9]. The literature reports a positive correlation between RI values and vascular-interstitial pathologies, glomerular sclerosis, fluid retention, focal fibrosis, arteriosclerosis and arteriolar sclerosis, whereas correlation with plasma creatinine levels and renal echogenicity is poor [7]. In patients with chronic renal failure, RI > 0.80 predicts progression of nephropathy more accurately than creatinine clearance and proteinuria, showing a sensitivity and specificity of 64% and 98%, respectively [10].

In the initial phase of nephropathy (diabetes mellitus type 1 and 2), glomerular filtration and renal volume are increased, whereas kidney volume is progressively reduced in the chronic phase. In diabetic patients with normal renal function, 65% of those affected by type 1 and 25% of those affected by type 2 have RI values ≥0.70. Mean RI is higher in patients affected by diabetes type 2 (0.71 vs. 0.65; $p < 0.001$) and can to some extent be correlated with the difference in the patients' age [11]. In these patients, RI values correlate with macroangiopathy, more frequent in patients affected by diabetes mellitus type 2 and in patients with nephroangiosclerotic damage, whereas RI does not correlate with microalbuminuria, which is an indicator of glomerular microangiopathy [12]. Diabetic patients with chronic renal failure and RI values ≥ 0.70 are generally older (62 vs. 44 years old), have higher proteinuria (3.3 vs. 1.1 mg/dl), higher serum creatinine level (3.2 vs. 1.1 mg/ dl), longer duration of diabetes (20 vs. 11 years) and higher blood pressure, and present a higher rate of renal failure requiring dialysis (71% con RI =1.0) [13].

Aim of the work:

The aim of the current study is to study the value of renal resistance index by renal Doppler in detection of diabetic complications as nephropathy, cardiovascular risk in elderly Egyptian patients.

Methods:

This study was a case-control comparative study between non nephropathic patients, nonproteinuric nephropathics and proteinuric nephropathic diabetic patients. One hundred and thirty elderly diabetic patients were serially selected from Ain Shams University hospital outpatient's clinics and inpatient's wards of geriatric and internal medicine departments. All the admitted patients whether males or females, and of age between 60 and 75 years, with primary diabetes mellitus, who were diagnosed within the last 10 years, were included. Any patient with known kidney disease, urinary tract infection, hepatitis C using drugs affecting kidney functions were excluded. All patients were subjected to: 1) Comprehensive geriatric assessment (to exclude other causes of kidney disease, urinary tract infections, and to detect symptoms and signs suggestive of diabetes micro and macrovascular complications). 2) Full Clinical examination. 3) Estimation of glomerular filtration rate by Cockroft-Gault equation [14] 4) Framingham 10 year coronary risk prediction by LDL tool [15]. 5) Laboratory investigations. 6) Radiological investigations (Renal duplex to estimate renal resistance index).

Results:

One hundred and thirty consecutive patients fitting these criteria were included in this study and were divided into three groups according to their eGFR and proteinuria into:

Group 1: nonnephropathic patients with eGFR >60 and no proteinuria (n=20).
Group 2: nephropathic patients with eGFR <60 and no proteinuria (n=50).
Group 3: nephropathic patients with eGFR <60 and proteinuria (n=61).

This study revealed that:

There was a significant difference between the groups in age especially between nonproteinuric nephropathics and proteinuric nephropathics with mean age in group 1 66± 4.9, group 2 63± 3.4 and group 3 65± 3.9 with P value 0.011.

There wasn't a significant difference between the three groups when we measured the RRI, with mean RRI 0.615 ± 0.07 in group 1, 0.6 ±0.11 in group 2, and 0.58 ±0.1 in group 3, and P value 0.359.

When we studied the relation between renal resistance index and different clinical and laboratory variables within the whole sample: it was negatively correlated with age, protein-creatinine ratio, 24 hours urine protein, serum creatinine, systolic arterial blood pressure but this correlation didn't reach statistical significance. It was positively correlated with diastolic arterial blood pressure, fasting blood glucose, Framingham 10 year overall cardiovascular risk score and weight but it was only significantly correlated with weight with P value 0.027. This was similar when we

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tried to find relations within each group.

After adjusting weight, age, SABP, type of antihypertensive used (ACEi/ARB) and comparing to participants with eGFR>60, there was a statistically significant inverse relationship between RRI and weight adjusted eGFR and also with Framingham 10 year cardiovascular risk score with p value <0.001.

Discussion:

In our study patients with nonproteinuric diabetic nephropathy were significantly younger than patients with proteinuria. This was similar to the results of other studies as that by Mojaheddi and his colleagues where proteinuric patients were significantly older. Similar results can be found in studies by Prasad and his colleagues, by Lou and his colleagues, in the Saudi study by Al-Rubeaan and his colleagues and also in an Egyptian study by Farahat and her colleagues. [16, 17, 18, 19, 20]

When we compared the three groups in RRI we didn't find significant difference between them, with mean RRI 0.615 ± 0.07 in group 1 patients with eGFR > 60, 0.6 ±0.11 in group 2, and 0.58 ±0.1 in group 3, and P value 0.359.

Ishimura and his colleagues also found that patients with diabetic nephropathy with increased values of albuminuria and serum creatinine had increased RRI values although statistical significance was not reached too.[21]

Also in the study by Milovanceva-Popovska and his colleague proteinuria was associated with increased RRI indicating nephropathy though this relation was not statistically significant until follow up after 3 and 6 months and further decline in CrCl [22].

In a study on type 1 diabetic children no correlation between mean RRI and serum creatinine or Albumin Excretion Rate (AER) was found [23].

In the study by Ljubic and his colleagues there was a significant difference in RRI between proteinurics and nonproteinuric diabetic nephropathic patients [24].

After adjusting weight, age, SABP, type of antihypertensive used (ACEi/ARB) and comparing to participants with eGFR>60, there was a statistically significant inverse relationship between RRI and weight adjusted eGFR with p value <0.001. These findings were similar to the results by MacIsaac and Associates where RRI was significantly correlated with eGFR [25].

Disclosure statement:

No potential conflicts of interest were disclosed.

Table 1: comparison between the three groups as regards clinical characteristics:

	Group 1 Nonproteinurics with eGFR >60 N=20		Group 2 (nonproteinuric with eGFR<60) N=50		Group 3 (proteinuric) N= 61		ANOVA
	mean	SD	mean	SD	mean	SD	P value
Age (years)	66.00	4.94	63.52	3.45	65.56	3.97	0.011
SABP (mmHg)	121.05	9.94	125.60	14.87	127.05	20.60	0.186
DABP (mmHg)	78.95	8.75	82.00	10.69	80.98	9.95	0.531
FBS (mg/dl)	128.95	40.09	131.42	34.69	122.25	32.85	0.368
PPBS (mg/dl)	169.32	30.81	181.84	44.08	174.13	44.06	0.469
HbA1c (%)	6.87	1.25	7.30	1.29	7.04	1.33	0.393
HDL-C (mg/dl)	33.16	4.48	35.80	6.01	36.80	7.13	0.032
MMSE	27.58	1.12	26.78	2.44	26.72	1.89	0.260
RI	0.62	0.07	0.60	0.11	0.58	0.10	0.359
risk% Framingham	23.49	8.01	24.86	9.31	28.57	11.55	0.071
uric acid (mg/dl0	6.66	.82	6.39	1.17	6.57	1.18	0.585
Weight (kg)	72.89	14.39	72.14	12.15	69.28	12.72	0.385

Table 2: correlation of renal resistance index with different variables::

	RRI correlation within the whole sample		RRI correlation within the group 1		RRI correlation within the group 2		RRI correlation within the group 3	
	r	P value	r	P value	r	P value	r	P value
age	-0.015	0.868	0.147	0.547	0.018	0.904	-0.061	0.640
DABP	0.041	0.64	-0.190	0.436	0.072	0.618	0.061	0.642
FBS	0.052	0.554	0.136	0.579	0.063	0.663	-0.005	0.972
Protein/creatinine ratio	-0.139	0.116	-0.258	0.286	-0.186	0.195	-0.071	0.589
24 hours protein	-0.143	0.105	-0.253	0.297	-0.068	0.640	-0.103	0.430
Framingham risk	0.059	0.503	0.069	0.327	0.189	0.189	0.057	0.661
s.cr	-0.064	0.467	0.069	0.778	0.043	0.767	-0.014	0.914
SABP	-0.029	0.741	-0.330	0.168	0.056	0.698	-0.036	0.786
weight	0.194	0.027	0.022	0.93	0.092	0.526	0.307	0.016

Table 3: Relation between eGFR with RRI (cutoff 0.7):

	Renal resistance index(>0.7)	
	B	P value
eGFR	-1.720	<0.001
Framingham 10 year risk	5.670	<0.001

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