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Renal Vascular Resistance in Glomerular Diseases – Correlation of Resistance Index with Biopsy Findings

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A B S T R A C T

Duplex Doppler sonography has been recognized as a noninvasive method to evaluate hemodynamic features of renal blood in renal and intrarenal arteries in patients with various renal diseases. The significance of duplex Doppler sonography in the evaluation of renal vascular resistance in glomerular diseases has not yet been clearly determined. The aim of the present study was to evaluate renal vascular resistance in patients with glomerular diseases by measuring intrarenal arterial resistance (RI) and to correlate RI with renal functional tests and other clinical and laboratory data. The Doppler parameters were also correlated with histopathological findings in the kidney which underwent the percutaneous biopsy. Duplex Doppler sonography was used to measure RIs in intrarenal arteries in 50 patients with glomerular diseases and 60 age-matched control subjects. The renal vascular resistance index (RI) was determined by the use of Doppler sonography. The mean RI in 50 patients with glomerular diseases was 0.68±0.09, which was statistically significantly higher than in 60 control subjects (the mean RI was 0.596 ±0.035). In a group of patients with membranoproliferative glomerulonephritis the mean RI was 0.817±0.624 which was statistically significantly higher than in other groups of glomerulonephritis. The renal vascular (resistance) RI significantly correlated with serum creatinine, creatinine clearance and β2 microglobulin. Qualitative duplex sonography measure of renal arterial resistance-resistive index does not appear to be reliable in distinguishing different types of glomerulonephritis.

Key words: *Doppler sonography, vascular resistance, glomerulonephritis*

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Introduction

It has been well established that only certain renal diseases produce increased renal vascular resistance. An elevated Doppler sonographic resistance index (RI) reflecting renal vascular resistance (RVR) has been observed in various conditions associated with elevated renal vascular resistance such as kidney obstruction[1], acute tubular necrosis[2], renal vein thrombosis[3], hemolytic-uremic syndrome[4], hepatorenal syndrome[5] and essential hypertension[6,7]. Some reports suggest that renal duplex Doppler sonography has advantages over conventional sonography in noninvasive evaluation of diabetic patients and in follow-up of diabetic nephropathy as well as other parenchymal kidney diseases [8]. It is extensively used for the diagnosis of renal artery stenosis[9]. The significance of duplex Doppler sonography in the evaluation of renal vascular resistance in patients with glomerular disease remains insufficiently illucidated.

There are only few studies in this field to date[10,11]. The purpose of the present study was to evaluate the renal vascular resistance in patients with glomerular diseases and healthy subjects by measuring the intrarenal arterial resistance indexes (RI; Pourcelot[12]) and to correlate RI in patients with glomerular diseases with biopsy data, renal functional tests and other clinical and laboratory data.

Patients and Methods

During a 105-month period from January 1993 to May 1998, 50 consecutive patients with the diagnosis of glomerular diseases verified by renal biopsy were included in this prospective study: 21 were women and 29 men with age ranging from 19 to 71 years (mean 46.5±14.77). Written informed consent was obtained from subjects. Renal disease presented primarily as asymptomatic abnormalities in urine (isolated proteinuria or hematuria, or combination of both), nephrotic syndrome and chronic renal failure. There was no characteristic clinical presentation of specific type of glomerular disease. The clinical presentation was nor specific for each glomerulopathy. Renal, hepatic, cardiac, pulmonary and other diseases were excluded by clinical examination and laboratory studies, including hematologic and blood chemistry status, urine analysis, ECG and chest radiograph. Laboratory and serologic data were available for each patient. These included values for serum creatinine, 24-hour urinary protein, complement fraction for C3 and C4, antinuclear factor, serum antibodies to native DNA and β2-microglobulin.

Sixty healthy, normotensive people constituted the control group: 19 were men and 41 women; with age ranging from 19 to 70 years (mean 44.5±14.9). Criteria for the inclusion in the control group were the absence of a history of any acute or chronic diseases, normal results from blood chemistry tests, normal urinary findings.

Renal biopsies were performed with a Bard biopsy needle using sonographic localisation of the lower pole of the kidney. The parafin embedded sections of the biopsy specimens were reviewed by light microscopy, immunofluorescence and electron microscopy to determine the diagnosis and the primary site of pathologic changes for each biopsy specimen. An attempt was made to determine if the dominant process was within the glomerulus, in the tubulointerstitial compartment, or was vascular. In some biopsy specimens more than one significant process was evident. The pathologist was blinded for renal Doppler data.

Doppler ultrasound scanner Acuson 128XP (Acuson Corp., Mountain View, CA) with a curve-array multifrequency 2.5–3.5 MHz tranducer was used for all exam-

inations. After the flow in intrarenal vessels was identified with color, a sample volume was positioned in interlobular and arcuate arteries in the typical positions. Spectral analysis was performed and RIs measured at least three times in each kidney, using existing software capabilities of the scanner. Mean RI value for each kidney was calculated from all measurements. The RIs were measured using of the following formula: RI= (peak systolic frequency shift-minimum diastolic frequency shift)/ peak systolic frequency shift[12].

Patients and healthy persons were examined in supine and lateral positions: the average duration of the examination was 30 minutes per person. All sonography examinations were performed immediately before renal biopsy by the same sonographer and the sonographer was blinded to laboratory and biopsy results. The Doppler data was correlated with the laboratory results and the histopathologic results in patients who underwent biopsy.

Renal biopsy findings were analysed and attempt was made to classify the location of the primary abnormality as within the glomerulus, the interstitium or within the vascular compartment.

All patients were divided in 5 groups according to the type of glomerular disease:

Group I: mesangioproliferative glomerulonephritis and IgA nephropathy (10 patients)

Group II: focal segmental glomerulosclerosis (17 patients).

Group III: extracapillary glomerulonephritis (6 patients)

Group IV: membranoproliferative glomerulonephritis (4 patients)

Group V: membranous glomerulonephritis (10 patients)

Three patients were excluded from statistical analysis because endocapillary glomerulonephritis (group VI) was found only in 1 patient and diabetic nephropathy only in 2 patients. Forty seven patients with glomerulonephritis were divided in two groups, those with hypertension (RR ≥140/90 mmHg) and normotension and their RI were analysed.

Statistical analysis. Mean kidney RIs were used for statistical analysis of differences between groups of patients. Mean RIs were compared between the control subjects group and the groups of patients. The statistical significance of the observed differences was calculated with the nonparametric Mann-Whitney U-test. Correlation between variables was evaluated by nonparametric rank correlation using Spearman's test. RI values between types of glomerular diseases were compared using ANOVA. The $p<0.05$ was considered as statistically significant[13].

Results

RI values of 50 patients with glomerular diseases (0.68±0.09 s.d.) were compared to RI values of 60 healthy subjects (0.596±0.035). The mean kidney RI was significantly higher in patients with glomerular diseases compared to normal subjects ($p<0.01$). In 30 of 50 patients (60%) with renal diseases RI value was below 0.70, while in the least 20 patients (40%) RI was higher than 0.70.

No significant differences were observed between RI in the right and left kidney in all examinees.

In group IV (membranoproliferative glomerulonephrtis) mean RI was 0.817± 0.624 (range 0.75–0.90). In this group there were only 4 patients. All these patients had reduced renal function and three of them had hypertension.

Using ANOVA RI values between the types of glomerular diseases were compared and statistically significant differences were obtained (Figure 1, Table 1, $p=0.022$). Among 47 patients with glomerulonep-

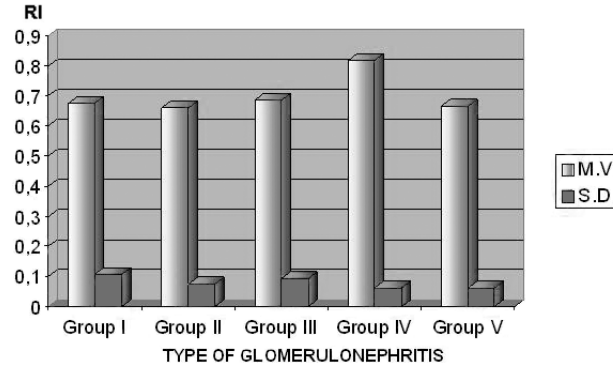

Fig. 1. RI values in different group of patients.

hritis nine patients (22%) were normotensive and 38 (78%) patients had hypertension. Eight (89%) normotensive patients and 20 (53%) hypertensive patients had RI<0.70. The RI[3] 0.70 was present in 1 (11%) normotensive patient and 18 (47%) hypertensive patients. There was no statistically significant correlation between blood pressure and RI (r=0.234, NS).

No statistically significant differences were found in mean RI values between groups with and without proteinuria.Table 2. represents the results of correlation analysis of RI's values with clinical and laboratory findings of 50 patients with renal diseases.

There was a statistically high correlation between RI and value of serum creatinine (r = 0.634, p<0.01), between RI and creatinine clearance (Figure 2, r = –0.585 p<0.01). Twenty two patients had normal renal function and 25 patients had incre-

TABLE 1
RI VALUES IN DIFFERENT GROUPS OF PATIENTS

	Type of glomerulonephritis	N	RI	S.D
Group I	Mesangioproliferative glomerulonephritis	10	0.675	0.107
Group II	Focal segmental glomerulosclerosis	17	0.659	0.075
Group III	Extracapillary glomerulonephritis	6	0.687	0.092
Group IV	Membranoproliferative glomerulonephritis	4	0.818	0.062
Group V	Membranous glomerulonephritis	10	0.665	0.062

TABLE 2
CORRELATION BETWEEN DOPPLER INDEX RI AND LABORATORY AND CLINICAL VARIABLES IN 50 PATIENTS.

Doppler Index	Variables	r	p
RI	Age of patients	0.198	NS
RI	Serum creatinine	0.585	p<0.01
RI	Creatinine clearance	–0.634	p<0.01
RI	24-proteinuria	0.202	NS
RI	β2-microglobulin	0.525	p<0.05

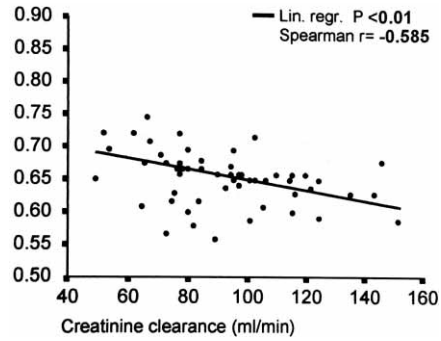

Fig. 2. Correlation of RI and creatinine clearence.

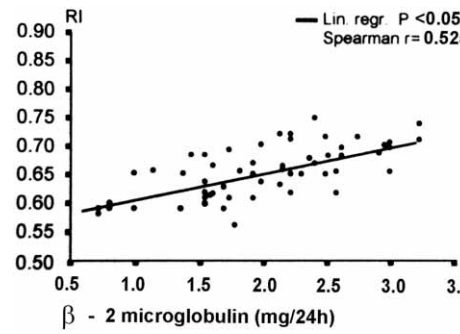

Fig. 3. Correlation of RI and β-2 microglobulin.

sed serum creatinine. Among those patients with reduced renal function all had significant proteinuria, 23 had hypertension and 11 had incresed β2-microglobulin.

There was a statistically significant correlation between RI and value of urine β2-microglobulin (Figure 3, r = 0.525, p<0.05). RI was significantly higher in group IV (membranoproliferative glomerulonephritis) than in other groups (p<0.01), but we had only 4 patients in group IV (Table1, Figure 4 and 5).

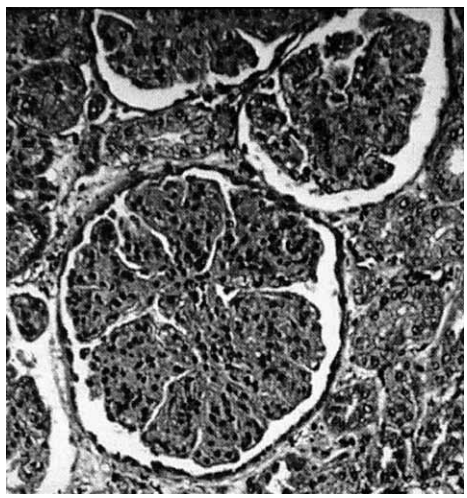

Fig. 4. Membranoproliferative Glomerulonephritis (light microscopy).

Discussion

Duplex Doppler sonography seems to be a very useful method in the evaluation of diverse renal pathological conditions both in native and transplanted kidneys including renal arterial stenosis[10], kidney obstruction[1] and acute transplant rejection[14,15].

Some intrinsic renal diseases produce marked alterations in the RI while other renal diseases are characterized by normal RI values. In an attempt to identify specific pathologic features that do or do not affect the RI, two studies compared RI values with kidney biopsy results[10,11]. In a study of Platt et al. carried out on 41 patients, kidneys with active disease in the tubulointerstitial part and/or vasculitis were found to have elevated mean RI values, while kidneys with disease limited essentially to glomerulus normal RIs[10]. This was true no matter how severe or acute the glomerular disease was; without accompanying tubulointerstitial disease or vasculitis RI, all the RIs were normal.

Patients with active tubulointerstitial disease had elevated measurements. The main diseases within this group were acute tubular necrosis and interstitial nephritis (either primary or associated with other renal diseases such as lupus nep-

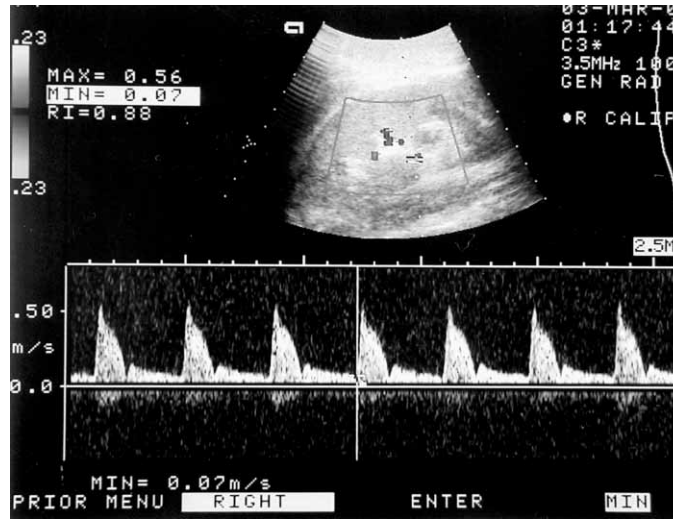

Fig. 5. Renal vascular resistance (RI) in patient with membranoproliferative glomerulonephritis (RI=0.88).

hritis, cryoglobulinaemia or Wegener's granulomathosis).

The observation that glomerulonephritis (GN) generally had a normal RI is consistent with available animal data[16,17]. These data showed that following the first 24–36 hours after onset of experimentally produced GN the renal vascular resistance (RVR) was essentially normal despite often marked disease[16]. The possible explanation for the normal renal vascular resistance in glomerular diseases were findings that vasodilatatory prostaglandins were increased, while the concentration of vasoconstrictory thromboxane A2 was very low.[16]. However, with long-standing chronic GN there was eventually a fall in renal blood flow and an elevation in RVR[17]. Therefore, as in most other causes of end-stage renal disease, severe chronic GN can eventually produce marked RI elevation. In our study all patients with different types of glomerulonephritis had elevated RI in comparison with healthy control subjects. Renal vascular resistance was 0.68+/0.09, which was almost the same as the values of RI of patients with glomerulonephritis described in the study of Platt et al.[15]. The mean RI in our patients was elevated in comparison with healthy control subjects and possible explanation is the presence of pathohistological signs of chronicity in the kidney tissue. As a result of this chronicity the mean serum creatinine value in our patients was 135 ìmol/L. The results of our study are consistent with the results of the above mentioned study[17].

Mostbeck et al[11], published a study correlating renal biopsy findings with RI's in 34 patients. They performed a more detailed study of histopathologic changes affecting RI than had previously been reported. They found that RI correlated with vascular intrarenal disease, glomerular sclerosis, interstitial edema and focal interstitial fibrosis. In agreement with the other biopsy series Mostbeck et al found normal RI values in 67 % of patients with GN[11].

These results are in accordance with those of Platt et al, who found normal values in the kidneys with disease limited to the glomeruli[10] and elevated Ris with tu-

bulointertitial affection. In our study, we used ß2-microglobulin as a marker of tubulointerstial affection and we found statistically significant correlation between value of ß2-microglobulin and RI. These results are consistent with the results of Platt and Mostbeck [10,11].

A positive correlation has been reported between the serum creatinine level and RI[10,18].

Our data comply with these reports. In our patients with membranoproliferative glomerulonephritis there was a statistically significant increase in the serum creatinine level in comparison with serum creatinine level in other types of glomerular diseases. This could be the explanation why RI was statistically significantly higher in membranoproliferative glomerulonephritis in comparison with other types of glomerulonephritis, reflecting a more advanced chronic tubulointerstitial underlying pathology.

Certainly, neither of these studies suggests that duplex Doppler imaging can replace renal biopsy. It is also likely that studies in which intrarenal Doppler imaging is used as a screening tool for intrinsic renal disease across a heterogenous patient population will yield disappointing results. Therefore, it is not appropriate to conclude that renal Doppler imaging may have tremendous diagnostic potential when used in the clinical setting.

Previously, the major sonographic parameter used to characterize renal parenchymal disease was the change in renal parenchymal echogenicity. In one study, the changes in renal echogenicity were positively correlated with pathologic changes such as global sclerosis, focal tubular atrophy, and focal leukocytic infiltration[18].

Duplex Doppler sonography detects a state of increased arterial vascular resistance (elevated RI) in some forms of renal parenchymal disease but not in others. The primary site of renal disease appears to be the main factor determining whether the RI is elevated. RI as an indicator of renovascular resistance is affected mainly by the changes in vascular system, especially the preglomerular arteries[20]. Therefore, lesions restricted to glomeruli, without significant changes in interlobular and afferent arterioles will not affect the renovascular resistivity. The relatively late stage of disease in our study group may account for the higher RI values obtained in the Doppler studies. In our opinion, the same reason may be responsible for the absence of any statistically significant correlation between Doppler parameters and histopathologic scores findings obtained from specimens in the patients who underwent renal biopsy. Namely, it is well known that the associated chronic tubulointerstitial changes in glomerular diseases often determine the outcome of the disease.

In conclusion, duplex Doppler sonography would seeam to detect a state of incresed vascular resistance (elevated RI) in some forms of renal parenchymal disease but not in others. Literature and our data suggest that active or acute diseases within the tubulointerstial compartment and vasculitis generally elevate RI, whereas disease limited primary to the glomerulus do not. There appears to be a weak relationship between the degree of renal dysfunction and RI, however, this seems to be less important than the primary localisation of renal parenchymal disease present. Our data suggest that certain forms of renal parenchymal disease such as interstitial nephritis and acute tubular necrosis in which the traditional sonogram is generally unremarkable of (except for the changes in echogenicity and size of the kidneys) should generally be expected to have incresed vascular resistance (RI) detected by Doppler study. The precise role of duplex Doppler sonography in the diagnosis, treatment, and follow-up of patients with renal diseases requires further investigation.

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BUBREŽNI VASKULARNI OTPOR U GLOMERULARNIM BOLESTIMA – POVEZANOST INDEKSA OTPORA S NALAZOM BUBREŽNOG BIOPTATA

SAŽETAK

Duplex dopler je neinvazivna metoda kojom se procjenjuju hemodinamske promjene bubrežnog krvotoka u intrarenalnim arterijama u bolesnika s različitim bubrežnim bolestima. Značaj duplex dopler dijagnostike u procjeni bubrežnog vaskularnog otpora u bolestima glomerula nije u potpunosti još određen. Cilj ove studije je određivanje bubrežnog vaskularnog otpora u bolesnika s glomerularnim bolestima pomoću indeksa otpora (RI) te određivanje povezanosti RI s bubrežnim funkcionalnim testovima te ostalim kliničkim i laboratorijskim nalazima. Doplerski indeksi su također korelirani s histološkim nalazom bubrežnog bioptata. RI je određen u 50 bolesnika s bolestima glomerula i 60 kontrolnih ispitanika. Bubrežni vaskularni indeks otpora (RI) određen je koristeći doplersku sondu. Srednja vrijednost RI u 50 bolesnika s bolestima glomerula iznosio je 0.68±0.09, što je statistički značajno više nego kod 60 kontrolnih ispitanika (srednja vrijednost RI je bila u ovoj skupini 0.596±0.035). U skupini bolesnika s membranoproliferativnim glomerulonefristisom srednja vrijednost RI iznosila je 0.817± 0.624 što je statistički značajno više nego u ostalim skupinama glomerulonefritisa. RI je značajno korelirao sa serumskim kreatininom, klirensom kreatinina i β2 mikroglobulinom. U zaključku se može reći da duplex dopler koristeći indeks otpora RI ne može razlikovati pojedine tipove glomerulonefritisa.