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Original Article

Increased renal resistive index in patients with essential hypertension: a marker of target organ damage

Roberto Pontremoli, Francesca Viazzi, Carlo Martinoli, Maura Ravera, Clizia Nicolella, Valeria Berruti, Giovanna Leoncini, Natia Ruello, Paola Zagami, Gian Paolo Bezante, Lorenzo E. Derchi and Giacomo Deferrari

Department of Internal Medicine, Institute of Radiology, and Department of Neuroscience and Neurorehabilitation, University of Genoa, Genoa, Italy

Abstract

Background. Increased renal resistance detected by ultrasound (US) Doppler has been reported in severe essential hypertension (EH) and recently was shown to correlate with the degree of renal impairment in hypertensive patients with chronic renal failure. However, the pathophysiological significance of this finding is still controversial.

Methods. In a group of 211 untreated patients with EH, we evaluated renal resistive index (RI) by US Doppler of interlobar arteries and early signs of target organ damage (TOD). Albuminuria was measured as the albumin to creatinine ratio (ACR) in three non-consecutive first morning urine samples. Left ventricular mass was evaluated by M-B mode echocardiography, and carotid wall thickness (IMT) by high resolution US scan.

Results. RI was positively correlated with age ($r=0.25$, $P=0.003$) and systolic blood pressure (SBP) ($r=0.2$, $P=0.02$) and with signs of early TOD, namely ACR ($r=0.22$, $P=0.01$) and IMT ($r=0.17$, $P<0.05$), and inversely correlated with renal volume ($r=-0.22$, $P=0.01$) and diastolic blood pressure ($r=-0.23$, $P=0.006$). Multiple linear regression analysis demonstrated that age, gender, ACR and SBP independently influence RI and together account for $\sim$20% of its variations ($F=8.153$, $P<0.0001$). When clinical data were analysed according to the degree of RI, the patients in the top quartile were found to be older ($P<0.05$) and with higher SBP ($P<0.05$) as well as early signs of TOD, namely increased ACR ($P<0.002$) and IMT ($P<0.005$ by ANOVA), despite similar body mass index, uric acid, fasting blood glucose, lipid profile and duration of hypertension. Furthermore, patients with higher RI showed a significantly higher prevalence of microalbuminuria (13 *vs* 12 *vs* 3 *vs* 33% $\chi^2=11.72$, $P=0.008$) and left ventricular hypertrophy (40 *vs* 43 *vs* 32 *vs* 60%, $\chi^2=9.25$, $P<0.05$).

Conclusions. Increased RI is associated with early signs of TOD in EH and could be a marker of intrarenal atherosclerosis.

Key words: atherosclerosis; essential hypertension; microalbuminuria; renal vascular resistance; target organ damage

Correspondence and offprint requests to: Giacomo Deferrari, MD, Department of Internal Medicine, University of Genoa, Viale Benedetto XV, 6, I-16132 Genova, Italy.

Introduction

Ultrasound (US) Doppler of renal vasculature is a reliable, non-invasive evaluation technique whose clinical application has increased steadily in recent years. In fact its usefulness varies from the diagnosis of renal artery stenosis and renovascular disease [1,2] to the assessment of intrarenal haemodynamics in several different pathological conditions such as essential hypertension [3], acute [4] and chronic renal failure [5,6], and graft rejection [7–9].

Several parameters can be calculated during the cardiac cycle on the basis of the shape of Doppler waves at various sites of the renal vasculature both extra- and intra-parenchymally. These parameters are independent of the angle and the position of the exploring probe, allowing for accurate and reproducible measurements of downstream vascular impedance. In particular, increased resistive (RI) and pulsatility (PI) indexes measured at the level of the interlobar arteries recently have been associated with the severity and duration of essential hypertension [10] and with worse renal function in renal parenchymal disease [5], although the pathophysiological significance of these findings deserves further investigation.

The present study was initiated to investigate the relationship between US Doppler RI of the intrarenal vasculature and early target organ damage such as left ventricular hypertrophy (LVH), microalbuminuria and extracardiac vascular changes in patients with essential hypertension.

Subjects and methods

Patients

From January 1996 to January 1997, all patients with essential hypertension attending the outpatient clinic of our department were asked to take part in this clinical study which had been approved by the Ethical Committee of our Institution. Patients with neoplastic, hepatic and/or renal disease, chronic heart failure (NYHA class III and IV), diabetes mellitus, renal failure (defined as serum creatinine $\geqslant 124$ μmol/l males, $\geqslant 106$ μmol/l females), severe obesity (defined as body weight $>150\%$ of ideal body weight according to the 1983 Metropolitan Life Insurance Company tables), disabling diseases such as dementia or inability to cooperate were excluded from the study. Altogether 350 hypertensive patients were seen at our clinic within that period of time; 258 (74%) were eligible to participate in the study on the basis of available clinical and laboratory data. Twenty seven of these patients did not meet study criteria based on the results of additional tests prescribed for clinical reasons during their first visit to our clinic. Of the remaining 231 patients, 20 refused or were unable to complete the washout period, and 211 (91%) form the basis of the present report. Of the participating patients, 44 (21%) had received antihypertensive treatment in the past, albeit intermittently, while 82 (39%) had never been treated for hypertension, and the remaining 85 (40%) agreed to discontinue treatment temporarily. Written informed consent was obtained from each participant. All patients underwent complete physical examination and routine biochemical analyses of blood and urine as well as evaluation of the presence and extent of target organ damage. Diagnosis of essential hypertension was made in all cases by the attending physician, and additional testing was performed only when signs or symptoms suggesting secondary hypertension were present. Hypertension was defined according to JNC V criteria as an average blood pressure $\geqslant 140/90$ mmHg on at least three different occasions or by the presence of antihypertensive treatment. A 24-h urine sample was obtained from each subject on the day prior to the study to assess dietary sodium intake. All patients were on a free, salt-unrestricted diet at the time of the study. They had either never been treated for hypertension or had been taken off therapy at least 4 weeks prior to the study. On the study day, blood pressure (BP) was measured on the right arm by a trained nurse, with the patient in the sitting position after a 5 min rest, with a mercury sphygmomanometer (cuff size 12.5×40 cm). The systolic and diastolic BPs were read to the nearest 2 mmHg. Disappearance of Korotkoff's sounds (phase V) was the criterion for diastolic BP. The lowest of three consecutive readings was recorded. Body mass index (BMI) was calculated using the formula: BMI = weight (kg)/height $(m)^2$. Creatinine, blood urea nitrogen, electrolytes, uric acid, triglycerides, total and high density lipoprotein (HDL)-cholesterol and other standard biochemical evaluations were performed on serum according to routine methods. Low density lipoprotein (LDL)-cholesterol was calculated using Friedewald's formula [11], and creatinine clearance using Cockroft's formula [12]. Family history of hypertension was ascertained by means of a standardized questionnaire and was defined as a diastolic BP >90 mmHg or BP elevation requiring antihypertensive therapy occurring in a parent or sibling. Smoking was graded on a five-point scale: non-smoker, ex-smoker, smoking 1–14 g/day, smoking 15–25 g/day or smoking >25 g/day (1 cigarette = 1 g).

Albuminuria

Urinary albumin excretion was evaluated at the end of the washout period, if any, as the albumin to creatinine ratio (ACR) on three non-consecutive first morning samples in the presence of a negative urine culture. Whenever a positive urine culture was found, urine samples were discarded, appropriate antibacterial treatment instituted and collections for albuminuria repeated only after a second culture tested negative. The ACR was calculated as urine albumin concentration (mg/l)/urine creatinine concentration (mmol/l). Creatinine levels were determined by the routine Jaffe reaction and albumin concentration by a commercially available radioimmunoassay kit (Sclavo, Cinisello). The median of three urine collections was taken as the ACR for each patient. Normal values of albumin excretion as previously defined in our laboratory were obtained by simultaneously measuring both albumin excretion rate in timed overnight urine collections and ACR in first morning urine samples within the same group of 63 normal subjects recruited from among the staff of our hospital. To account for differences in basal creatinine excretion rates and BMI, different criteria were used to define microalbuminuria in men (ACR between 2.38 and 19) and women (ACR between 2.96 and 20). These criteria proved to have good sensitivity and specificity for the detection of an albumin excretion rate between 20 and 200 μg/min [13]. The intra- and interassay variabilities of the method in our laboratory were 4.5 and 6.1%, respectively.

Renal US and Doppler studies

Renal parenchymal echogenicity, renal volume and mean RI were evaluated in a total of 422 kidneys at the end of the washout period. Renal parenchymal echogenicity was classified on the basis of Hricak's grading system [14]. Renal volume was measured by use of the ellipsoid formula and corrected for BMI [15]. Doppler signals were obtained from the interlobar arteries by placing the sample at the edge of the medullary pyramids. The mean RI [(peak systolic velocity − end diastolic velocity)/peak systolic velocity] was calculated by using six measurements (three from each of the two kidneys) taken for each patient. US examination of the kidneys and pulsed Doppler analysis of the intrarenal arteries were performed using a Hitachi AU 450 machine with a 3.5 MHz transducer working at 2.5 MHz for Doppler analysis.

Echocardiography

Left ventricular mass index (LVMI) was evaluated by standard echocardiography. All echocardiographic studies were performed using an Acuson XP-128 ultrasound machine. Echocardiograms were obtained with the patient at rest and supine in the left lateral position, using standard parasternal and apical views. The overall monodimensional left ventricular (LV) measurements and the bidimensional (apical four and two chamber) views were obtained according to the recommendations of the American Society of Echocardiography [16,17]. All tracings were obtained and read by a single observer blinded to the clinical characteristics of the patients under observation. LV mass was derived from the formula described by Devereux and associates [18] corrected for surface area (LVMI), and expressed in units of g/m^2. LVH was defined for LVMI $\geqslant 134$ g/m^2 (men) or $\geqslant 110$ g/m^2 (women) [19]. None of the patients showed

dissynergic areas that would invalidate the theoretical assumptions behind the cardiac mass calculations.

Common carotid US scan

The intima plus media thickness (IMT) of both carotid arteries was evaluated by high-resolution US scan as described by Kawagishi [20]. Carotid arteries were investigated in the longitudinal and the transverse projections by high resolution real-time ultrasonography using a 10 MHz in-line duplex Diasonic Spectra System. The carotid artery was scanned at the bifurcation and at the common carotid artery (CCA). At each longitudinal projection, the far-wall IMT, as defined by Weldelhag [21], was measured at the distal end of the CCA, where the near and far walls lose their parallel configuration. Each measurement was calculated taking the averages of three readings.

Statistical analysis

All data are expressed as mean $\pm$ SEM. Differences between variables were assessed using the appropriate statistical tests based on the underlying distribution of the variables. To study the linear relationship between RI and other variables, Pearson's correlation test was used. Multiple regression analysis was performed to assess the independent contribution of several variables on RI. One-way analysis of variance (ANOVA) with multiple comparison post-test was used to analyse data from patients with different degrees of RI. Differences between prevalences were assessed by χ^2 test or Fisher's exact test as appropriate [22]. All statistical analyses were performed using SAS (SAS Institute, Carey, NC) software.

Results

Clinical characteristics of study patients are reported in Table 1. The overall prevalence of microalbuminuria and LVH was 14 and 45%, respectively. These values are similar to those previously reported in the literature in untreated hypertensive patients [12,23–26]. On average, women had a somewhat better biochemical risk profile (i.e. lower uric acid and triglycerides, higher HDL-cholesterol) and lower serum creatinine, higher RI and prevalence of LVH as compared with men though with similar ACR and prevalence of microalbuminuria (Table 1). Significant univariate correlations between RI and selected clinical variables in the entire study group are shown in Table 2. The RI showed a positive correlation with systolic BP and age as well as with signs of early end-organ damage, namely ACR and carotid IMT. A negative correlation was present between RI, renal volume and diastolic BP.

The relationship between RI and several variables including albuminuria, was investigated further by the use of multiple regression analysis (Table 3). Renal vascular resistance is significantly and independently influenced by age, gender, urinary albumin excretion and systolic BP. Altogether these factors explain $\sim$20% of variations in the renal vascular impedance.

When the data were analysed on the basis of different degrees of RI, patients in the top quartile showed significantly higher age (45.8 ± 1.6 *vs* 48.3 ± 1.1 *vs* 46.4 ± 1.5 *vs* 52.4 ± 1.2, $P = 0.005$), systolic BP (157.4 ± 2.3 *vs* 158.1 ± 2.4 *vs* 161.3 ± 2.1 *vs* 165.2 ± 2.7, $P = 0.002$), level of albuminuria (0.94 ± 0.2 *vs* 1.3 ± 0.4 *vs* 0.8 ± 0.1 *vs* 3.5 ± 1.0, $P = 0.002$) and increased carotid IMT (0.65 ± 0.03 *vs* 0.69 ± 0.03 *vs* 0.63 ± 0.03 *vs* 0.79 ± 0.04 $P = 0.005$) despite a similar lipid profile, renal function and smoking habits (data not shown). Furthermore, patients with the highest degree of RI also showed a significantly higher prevalence of microalbuminuria (Figure 1a), LVH (Figure 1b) and IMT values above the median for the entire study group (Figure 1c).

Discussion

US Doppler has proved to be a useful non-invasive tool for evaluating renal vasculature in several different pathological conditions such as acute renal failure [4], acute and chronic renal graft rejection [7–9,27], urinary tract obstruction [28] and chronic glomerular and interstitial diseases [29,30]. In particular, calculating the RI at the level of the interlobar arteries was shown to be a very accurate and reproducible indicator of vascular impedance to downstream blood flow [31]. An increase in the RI has been reported to relate to intrarenal arteriolar and glomerular sclerosis [29] as well as to the presence and extent of interstitial damage in renal parenchymal disease [30]. More recently, an increased RI has been reported to be related to macrovascular atherosclerotic damage in hypertensive diabetic patients [32], to increased BP and to duration of disease in patients with essential hypertension [10], suggesting that it could reflect intraparenchymal arteriolar damage and could serve as a prognostic marker of hypertensive renal injury.

The present study shows that increased Doppler renal RI is associated with early hypertensive end-organ damage, namely microalbuminuria, increased carotid IMT and LVH in patients with essential hypertension. Furthermore, the degree of renal vascular impedance correlates with other cardiovascular risk factors such as BP levels and age. Although the pathogenesis of increased renal vascular impedance is still unknown, these associations suggest that it could be due either to functional vasoconstriction secondary to the severity of the hypertensive state, to the presence of structural intrarenal atherosclerotic lesions or also to the combination of both factors. Smoking habits might have an impact on renovascular resistance. However, while acute nicotine consumption induces renal vasoconstriction in healthy non-smokers, tolerance to its renal haemodynamic effects has been reported in chronic smokers [33]. Accordingly, we could not demonstrate any association between chronic cigarette consumption and renal RI in our patient population.

The higher RI observed in women, despite a similar age and a somewhat better biochemical risk profile, is rather difficult to explain. However, the study design

Table 1. Clinical characteristics of study patients

	Men	Women	All patients	Range	*P*
n	131	80	211		
SBP, mmHg	159 ± 1.5	162 ± 1.7	160 ± 1.1	125–230	NS
DBP, mmHg	104 ± 0.7	103 ± 0.8	103 ± 0.6	80–140	NS
MBP, mmHg	122 ± 0.8	122 ± 1.0	122 ± 0.6	103–163	NS
Age, years	47 ± 0.8	48 ± 0.9	48 ± 0.6	21–65	NS
BMI, kg/m^2	27 ± 0.3	26 ± 0.4	26 ± 0.2	17–38	0.07
Family history of Ht (%)	78	80	79		NS
Duration of disease, months	52 ± 4.7	49 ± 5.1	51 ± 3.5	2–240	NS
Serum glucose, mmol/l	5.1 ± 0.06	4.9 ± 0.07	5.0 ± 0.04	3.5–6.4	NS
Serum uric acid, mmol/l	0.35 ± 0.006	0.3 ± 0.007	0.31 ± 0.006	0.11–0.6	<0.0001
Serum creatinine, μmol/l	86.9 ± 0.9	69.0 ± 1.1	79.8 ± 1.0	44.3–115.3	<0.0001
Creatinine clearance, ml/min[a]	92 ± 2.1	79 ± 2.2	87 ± 1.6	54–167	<0.0001
Triglycerides, mmol/l	1.5 ± 0.07	1.2 ± 0.07	1.42 ± 0.06	0.4–4.2	0.002
Total cholesterol, mmol/l	5.5 ± 0.1	5.7 ± 0.1	5.6 ± 0.1	2.6–8.6	NS
LDL-cholesterol, mmol/l	3.6 ± 0.1	3.5 ± 0.1	3.58 ± 0.08	0.2–4.1	NS
HDL-cholesterol, mmol/l	0.12 ± 0.003	0.14 ± 0.001	0.13 ± 0.002	0.05–0.25	<0.0001
Current smokers (ex-), %	34 (41)	37 (25)	35 (35)		NS
ACR, mg/mmol	1.6 ± 0.3	1.4 ± 0.3	1.53 ± 0.2	0.1–19	NS
Prevalence of Mi (%)	15	12	14		NS
Renal volume (ml)	107.2 ± 1.2	106.3 ± 2.1	106.8 ± 1.1	76–145	NS
RI	0.58 ± 0.01	0.62 ± 0.01	0.60 ± 0.004	0.48–0.75	0.005
LVMI, g/m^2	125.0 ± 2.5	120.3 ± 3.3	123.3 ± 2	48–213	NS
LVH (%)	36	59	45		<0.01
Carotid IMT, mm	0.67 ± 0.02	0.7 ± 0.02	0.68 ± 0.02	0.3–1.25	NS

Data are mean ± SEM. SBP, systolic blood pressure; DBP, diastolic blood pressure; Ht, hypertension. ACR, urinary albumin to creatinine ratio; Mi, microalbuminuria; RI, resistive index; LVMI, left ventricular mass index; LVH, left ventricular hypertrophy, as evaluated by the use of echocardiography; IMT, intima plus media thickness. *P* indicates significant differences between men and women.
[a]Calculated using Cockroft's formula [(140 − age) × lean body mass (kg)/(serum creatinine × 72)], in women the value is × 0.85.

Table 2. Univariate correlation between RI and selected clinical variables

Variable	*r*	*P*	Variable	*r*	*P*
ACR	0.22	0.01	IMT	0.17	0.05
Age	0.25	0.003	SBP	0.2	0.02
Renal volume	−0.22	0.01	DBP	−0.23	0.006

Table 3. Multiple regression linear analysis of RI

Independent variable	β	SEβ	Partial *F*	*P*
SBP	0.000545	0.000288	1.894	0.06
Sex	0.02987	0.00848	3.522	0.0006
Age	0.00124	0.000503	2.462	0.0152
ACR	0.002955	0.001366	2.164	0.0323
Constant	0.4026	0.0508	7.92	0.00001

Dependent variable, RI; independent variable, SBP, sex, age, ACR. Regression degrees of freedom = 4–127, $F = 8.15326$, $P = 0.00001$. $r^2 = 0.20433$.

did not take into consideration several factors which may have a significant impact on renal haemodynamics and RI, such as the activity of the renin–angiotensin system, endothelin and hormonal changes linked to the ovarian cycle.

It is noteworthy that the RI was positively correlated to systolic BP and inversely to diastolic BP, indicating that higher renovascular resistance is associated with higher systemic pulse pressure, a known marker of increased rigidity of the arterial vascular bed [34]. Results of multiple linear regression analysis support this conclusion and show that age, systolic BP and urinary albumin excretion independently influence RI and together account for a significant part of its variation (∼20%). These findings, together with the inverse correlation observed between RI and renal volume ($r = -0.221$, $P = 0.01$, Table 2), provide further evidence that high RI could be the result of hypertensive and atherosclerotic intraparenchymal vascular damage and possibly a marker of unfavourable renal prognosis in essential hypertension. This hypothesis seems to fit with data reported by Veglio *et al.* [10], who described a lack of significant RI variation after acute administration of angiotensin-converting enzyme (ACE) inhibitors in a smaller group of patients with longer duration and more severe degrees of hypertension, and suggested that this phenomenon may reflect an impairment of intrarenal autoregulation due to atherosclerosis.

In this regard, the correlation between urinary albumin excretion rate and RI (Table 2) and the higher prevalence of microalbuminuria in patients within the highest quartile of RI reported here (Figure 1a) is of particular interest. Microalbuminuria, in fact, has recently been shown to be a powerful, integrated marker of increased cardiovascular risk and target organ damage in essential hypertension [35,36] and could be a predictor of subsequent clinical renal damage [37]. In the context of long-standing hyperten-

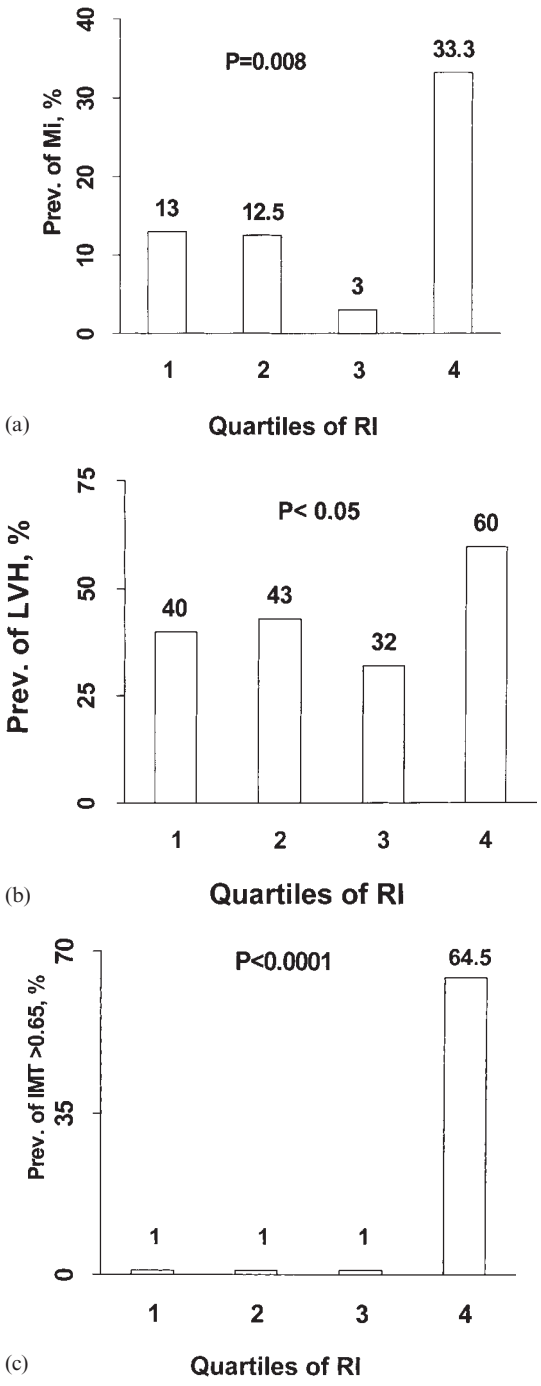

Fig. 1. Prevalence of microalbuminuria (**a**), left ventricular hypertrophy (**b**) and carotid IMT >0.65 mm (**c**) in 211 patients with essential hypertension grouped according to quartiles of renal resistive index (RI).

sion, microalbuminuria and reduction of kidney volume might signal the development of nephroangiosclerosis, which is usually characterized by a reduction of renal blood flow and an increase in renovascular resistance. To investigate further the potential relationship among these factors, we related kidney volume to renal RI and analysed the data on the basis of urinary albumin excretion. Results showed that patients with microalbuminuria would appear to have lower values of kidney volume/RI ratios as compared with normoalbuminuric patients (169 ± 5.4, $n=25$, alb+ *vs* 183 ± 2.8, $n=173$, alb−, $P<0.05$, data not shown). Thus increased renal vascular resistance, lower kidney volume and higher urinary albumin excretion all seem to cluster within the same group of patients.

Interestingly, Mimran *et al.* [38] previously demonstrated impairment of renal haemodynamics under acute ACE inhibition in hypertensive microalbuminuric subjects using a radioisotopic technique. This finding relates well to the data reported in the present study and points to an association between increased urinary albumin excretion, high RI and intrarenal atherosclerosis. Data presented here need to be interpreted with some caution due to the selection criteria, which probably explain the relatively high prevalence of positive family history for hypertension and microalbuminuria reported. Nonetheless, the association between increased renal RI and atherosclerotic vascular damage has led us to believe that it may signal the presence of intrarenal atherosclerosis.

These conclusions are corroborated by the fact that higher renovascular impedance is a concomitant factor of early extrarenal hypertensive and atherosclerotic organ damage such as LVH and increased common carotid wall thickness (Figure 1b and c).

While further studies are needed to clarify the exact pathophysiological mechanisms underlying increased RI and its prognostic value for the development of more severe renal damage, this abnormality should be regarded as a marker of early renal and systemic vascular damage and could help identify hypertensive patients for whom more aggressive preventive and therapeutic measures are advisable.

References

1. White EM, Choyke PL. Duplex sonography in the abdomen. In: Grant EG, White EM, eds, *Duplex Sonography*. Springer-Verlag, New York, 1987; 129–190
2. Norris CS, Barnes RW. Renal artery flow velocity analysis: a sensitive measure of experimental and clinical renovascular resistance. *J Surg Res* 1984; 36: 230–236
3. Veglio F, Frascisco M, Melchio R *et al.* Assessment of renal resistance index after captopril test by Doppler in essential and renovascular hypertension. *Kidney Int* 1995; 48: 1611–1616
4. Stevens PE, Gwyther SJ, Hanson ME, Boultbee JE, Kox WJ, Phillips ME. Non invasive monitoring of renal blood flow characteristics during acute renal failure in man. *Intensive Care Med* 1990; 16: 153–158
5. Petersen LJ, Petersen JR, Ladefoged SD, Mehlsen J, Jensen HE. The pulsatility index and the resistive index in renal arteries in patients with hypertension and chronic renal failure. *Nephrol Dial Transplant* 1995; 10: 2060–2064
6. Kim SH, Kim WH, Choi BI, Kim CW. Duplex Doppler US in patients with medical renal disease: resistive index vs serum creatinine level. *Clin Radiol* 1992; 45: 85–87
7. Stevens PE, Gwyther SJ, Hanson ME, Woodrow DF, Phillips ME, Boultbee JE. Interpretation of duplex Doppler ultrasound in renal transplants in early postoperative period. *Nephrol Dial Transplant* 1993; 8: 255–258
8. Rasmussen K, Pedersen E. Doppler ultrasound in the diagnosis of renal allograft rejection and in monitoring the effect of treatment. *Scand J Clin Invest* 1990; 50: 56–61

9. Quarto di Palo F, Rivolta R, Elli A, Castagnone D. Relevance of resistive index ultrasonographic measurement in renal transplantation. *Nephron* 1996; 73: 195–200
10. Veglio F, Provera E, Pinna G *et al.* Renal resistive index after captopril test by Echo-Doppler in essential hypertension. *Am J Hypertension* 1992; 5: 431–436
11. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. *Clin Chem* 1972; 18: 499–502
12. Cockroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976; 16: 31–41
13. Pontremoli R, Sofia A, Ravera M *et al.* Prevalence and clinical correlates of microalbuminuria in essential hypertension: the MAGIC study. *Hypertension* 1997; 30: 1135–1143
14. Hricak H, Cruz C, Romasky R *et al.* Renal parenchymal disease: sonographic–histologic correlation. *Radiology* 1982; 144: 141–147
15. Mittelstaedt CA. *General Ultrasound*. Churchill, London; 1992: 883–1042
16. Sahn DJ, De Maria A, Kisslo J, Weyman A. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements: *Circulation* 1978; 58: 1072–1083
17. Schiller NB, Shah PM, Crawford M *et al.* Recommendations for quantitation of the left ventricle by two dimensional echocardiography: American Society of Echocardiography Committees. *J Am Soc Echo* 1989; 55: 358–367
18. Devereux RB, Reichek N. Echocardiographic determination of left ventricular mass in man. Anatomic validation of the method. *Circulation* 1977; 55: 613–618
19. Devereux RB, Reiche RN. Detection of left ventricular hypertrophy by M-mode echo-cardiography: anatomic validation, standardization and comparison to other methods. *Hypertension* 1987; 9 [Suppl II]: 19–26
20. Kawagishi T, Nishizawa Y, Konishi T *et al.* High-resolution B-mode ultrasonography in evaluation of atherosclerosis in uremia. *Kidney Int* 1995; 48: 820–826
21. Weldelhag I, Wiklund O, Wikstrand J *et al.* Atherosclerotic changes in the femoral and carotid arteries in familial hypercholesterolemia: ultrasonographic assessment of intima–media thickness and plaque occurrence. *Arterioscler Thromb* 1993; 13: 1404–1411
22. Snedecor GW, Cochran WG. *Statistical Methods* Ames Iowa State University Press, Ames, IA: 1967
23. Yudkin JS, Forrest RD, Jackson C. Microalbuminuria as a predictor of vascular disease in non diabetic subjects. *Lancet* 1988; 2: 530–533
24. Palatini P, Graniero GR, Mormino P *et al.* Prevalence and clinical correlates of microalbuminuria in stage I hypertension. Results from The hypertension and ambulatory recording Venezia Study. (Harvest Study). *Am J Hypertension* 1996; 9: 334–341
25. Savage DD, Drayers IM, Henry WL *et al.* Echocardiographic assessment of cardiac anatomy and function in hypertensive subjects. *Circulation* 1979; 59: 623–632
26. Cerasola G, Cottone S, D'Ignoto G *et al.* Microalbuminuria as a predictor of cardiovascular damage in essential hypertension. *J Hypertension* 1989; 7 [Suppl 6]: S332–S333
27. Martinoli C, Bertolotto M, Crespi G, Pretolesi F, Valle M, Derchi LE. Duplex Doppler analysis in interlobular arteries in transplanted kidneys. *Eur Radiol* 1998; in press
28. Deyoe LA, Cronan JJ, Breslaw BH, Ridlen MS. New techniques of ultrasound and color Doppler in the prospective evaluation of acute renal obstruction. Do they replace the intravenous urogram? *Abdom Imaging* 1995; 20: 58–63
29. Mostbeck G, Kain R, Mallek R *et al.* Duplex Doppler sonography in renal parenchymal disease: histopathologic correlation. *J Ultrasound Med* 1991; 10: 189–194
30. Platt JF, Ellis JH, Rubin JM, DiPietro MA, Sedman AB. Intrarenal arterial Doppler sonography in patients with non obstructive renal disease: correlation of resistive index with biopsy findings. *Am J Roentgenol* 1990; 154: 1223–1227
31. Knapp R, Plotzeneder A, Frauscher F *et al.* Variability of Doppler parameters in the healthy kidney: an anatomic–physiologic correlation. *J Ultrasound Med* 1995; 14: 427–429
32. Boeri D, Derchi LE, Martinoli C *et al.* Intrarenal arteriosclerosis and impairment of kidney function in NIDDM subjects. *Diabetologia* 1998; 41: 121–124
33. Halimi JM, Philippon C, Mimram A. Contrasting renal effects of nicotine in smokers and non-smokers. *Nephrol Dial Transplant* 1998; 13: 940–944
34. Bots ML, Witterman JCM, Hofman A, de Jong PTVM, Grobbee DE. Low diastolic blood pressure and atherosclerosis in elderly subjects. *Arch Intern Med* 1996; 156: 843–848
35. Pontremoli R, Viazzi F, Sofia A *et al.* Microalbuminuria: a marker of cardiovascular risk and organ damage in essential hypertension. *Kidney Int* 1997; 63: S163–S165
36. Pontremoli R, Nicolella C, Ravera M *et al.* Microalbuminuria is an early marker of target organ damage in essential hypertension. *Am J Hypertension* 1998; in press
37. Bianchi S, Bigazzi R, Campese VM. Microalbuminuria in essential hypertension. *J Nephrol* 1997; 10: 325–333
38. Mimran A, Ribstein J, DuCailar G. Is microalbuminuria a marker of early intrarenal vascular dysfunction in essential hypertension? *Hypertension* 1994; 23: 1018–1021

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