Clinical Usefulness of Duplex Ultrasonography for the Assessment of Renal Arteriosclerosis in Essential Hypertensive Patients

Yoshiomi SHIMIZU, Taiji ITOH, Hidetaka HOUUGAKU, Yoji NAGAI, Hiroyuki HASHIMOTO, Manabu SAKAGUCHI, Nobuo HANDA, Kazuo KITAGAWA, Masayasu MATSUMOTO, and Masatsugu HORI

The present study was carried out to investigate whether the renal resistive index (RRI), obtained by ultrasonic duplex scanning, is useful for the evaluation of renal arteriosclerosis in essential hypertensive patients. We also studied the relationships between RRI and other kinds of hypertensive target-organ damage, including carotid atherosclerosis. One hundred and two patients (56.4±9.4 years) with untreated mild or moderate essential hypertension were examined. The normal range of RRI was determined for 12 normal age-matched volunteers (55.0±6.8 years). Hypertensive organ damage was evaluated by funduscopcy, electrocardiograms, and carotid B-mode imaging. Based on the mean and distribution of RRI in normal volunteers (0.60±0.05), the normal upper limit of RRI was found to be 0.7. RRI was correlated with creatinine clearance (CCr) (r=−0.61, p<0.05), and blood urea nitrogen (r=0.46, p<0.05), but not with serum creatinine. In addition, the incidence of abnormal RRI (>0.7) was higher in patients with left ventricular hypertrophy and in those with advanced carotid atherosclerosis (p<0.01, respectively). Thus, RRI appears to be more strongly associated with CCr than with serum creatinine, and it increases in patients with hypertensive end-organ damage. The assessment of RRI may be useful for the evaluation of early renal damage in essential hypertension. (Hypertens Res 2001; 24: 13-17)

Key Words: essential hypertension, ultrasonics, arteriosclerosis, kidney, resistive index

Introduction

Ultrasonic duplex scanning of the renal artery is a noninvasive method for the screening and diagnosis of renovascular hypertension (1-7). This method may also be useful for the evaluation of parenchymal renal damage caused by hypertension, making use of flow velocities, the resistive index, and the pulsatility index (4-8). Previous studies (1-7) have shown that the renal resistive index (RRI) is a reliable marker for moderate and severe renal arteriosclerosis. Because renal hemodynamic changes can occur before the onset of early systems, evaluation of RRI might also be useful for assessment of the early renal arterio-atherosclerosis caused by hypertension.

In the present study, we examined the relationship between RRI and other markers of renal function in patients with WHO/ISH mild-to-moderate hypertension. In addition, we assessed the relationship between RRI and hypertensive end-organ damage, including funduscopcy changes, left ventricular hypertrophy, and carotid atherosclerosis.
Subjects and Methods

One hundred and fourteen subjects were recruited for this study, including 102 untreated essential hypertensive patients (age: 56.4±9.4 years, range: 41-76, 57 men and 45 women) and 12 healthy volunteers of similar age (age: 55.0±6.6 years, range 45-60, 8 men and 4 women). All hypertensive patients met the criteria for WHO/ISH mild- to-moderate hypertension (serum creatinine level <132.6 µmol/l), and had a casual blood pressure ranging from 140 to 200 mmHg for systole and/or 90 to 115 mmHg for diastole on at least three occasions. The healthy volunteers had normal renal function and arterial blood pressure.

The existence of traditional atherosclerotic risk factors was examined in all patients. The risk factors considered in this study were diabetes mellitus (fasting blood glucose >6.11 mmol/l and/or on medication) and hypercholesterolemia (serum total cholesterol level >6.20 mmol/l and/or on medication). In hypertensive patients, end-organ damages was assessed by fundoscopy, electrocardiogram (ECG), and urinalysis. Hypertensive retinopathy was classified based on hypertensive (H) and arteriosclerotic changes (S) according to Scheie's classification. ECG abnormalities were diagnosed when there was left ventricular hypertrophy (abnormally high QRS complex voltage) and/or ischemic ST-T changes. Renal function was evaluated by proteinuria, serum creatinine, blood urea nitrogen (BUN), and creatinine clearance (CrCl). Proteinuria (>30 mg/dl) was diagnosed by a paper test with Urotron RL9 (Boehringer Mannheim Co.). CrCl data were corrected by a surface area of 1.48 m², the mean for Japanese adults. Carotid B-mode imaging was performed with a 7.5-MHz transducer (EUB-555, Hitachi, Inc., Tokyo, Japan). In accordance with our previous studies (9-11), atherosclerotic plaques were defined as local increases (1.1 mm) in the vascular intima-media complex. The plaque score (PS) was calculated by summing up the height of all such plaques (in mm) on the near and far walls at each of four divisions of both sides of the carotid arteries (9). Based on the PS, the severity of carotid atherosclerosis was classified as one of four stages; [none: 0, mild: 1.1-5.0, moderate: 5.1-10.0, severe: >10.0].

RRI examinations were performed with the EUB-555 apparatus with a 3.75-MHz transducer. With the subject in the prone position, the transducer was placed on the lumbar portion, and the kidney was displayed by tomographic echography. Blood flow at the renal hilus was visualized with color Doppler sonography superimposed on the tomographic images. Thereafter, Doppler signals were obtained from the segmental arteries in the renal sinus, the interlobar arteries along the border of the medullary pyramids, and the arcuate arteries at the corticomедullary junction. From the hard copy, RRI was calculated by the following equation: (peak systolic shift – end diastolic shift) / peak systolic shift (Fig. 1). RRI was determined at least three times for one kidney and was averaged. The mean RRI of the right and left kidneys was used for the subsequent analyses.

Statistical Analyses

For the analyses, we used correlation analysis, chi-square test, and unpaired t-test. A two-tailed p-value <0.05 was considered statistically significant. Data are presented as mean±SD.

Results

Baseline characteristics of the normal and hypertensive subjects are shown in Table 1. RRI was 0.60±0.05 in the normal controls and did not differ more than 0.05 between the right and left kidneys in all subjects. Based on the mean and SD, we found the upper normal limit of RRI to be 0.7 (mean±1.96 SD).

In the hypertensive patients, RRI showed positive correlations with age (r=0.64, p<0.05) and BUN (r=0.46, p<0.05), and a negative correlation with CCr (r=-0.61, p<0.05) (Fig. 2). However, RRI did not have significant associations with serum creatinine, proteinuria, or sex.

Figure 3 shows the relationships between RRI and other types of hypertensive target organ damage. The incidence of abnormal RRI was higher in hypertensive patients with abnormal ECG than in those with normal ECG (40.8% vs. 15.9%). Also, the incidence of abnormal RRI increased with the severity of the carotid atherosclerosis as defined by PS categories [none: 11%, mild: 11%, moderate: 45%, severe: 90%]. Moreover, abnormal RRI was more often found in patients with arteriosclerotic funduscopic changes [Stage 0: 220 (10%)*, Stage 1: 10/31 (32%), Stage 2: 7/22 (31%), *p<0.01 vs. Stage 2+3], whereas no significant relationships were found between RRI and hypertensive funduscopic changes. Figure 4 shows the relationships of RRI with diabetes and hypercholesterolemia. The incidence of abnormal RRI was higher in essential hypertensive patients with diabetes than in those without (34.4% vs. 26.6%), although the diabetic patients were older than those without diabetes (59.0±9.6 vs. 55.8±9.4 years, p<0.05). Also, the RRI was similar between patients with hypercholesterolemia and those without.

Discussion

Ultrasonic duplex scanning is an established method for the diagnosis of renovascular hypertension (2,3). For example, Handa et al. have shown that renal artery flow parameters such as the acceleration time and acceleration index are useful indicators for renovascular hypertension,
Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Age (y.o.)</th>
<th>MABP (mmHg)</th>
<th>CCr (ml/min)</th>
<th>RRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal controls</td>
<td>12</td>
<td>55±7</td>
<td>91±9</td>
<td>90±5</td>
<td>0.60±0.05</td>
</tr>
<tr>
<td>EHT</td>
<td>102</td>
<td>56±9</td>
<td>114±9</td>
<td>69±22*</td>
<td>0.65±0.08</td>
</tr>
</tbody>
</table>

EHT: essential hypertension; MABP: mean arterial blood pressure; CCr: creatinine clearance; RRI: renal resistive index. Values are mean±SD. *CCr was obtained in 34 patients randomly selected from 102 hypertensives. No significant difference was detected in RRI between normal controls and EHT.

$$RRI = (S-D)/S$$

S: peak systolic frequency shift, and D: end diastolic frequency shift.

Fig. 1. Schematic diagram for the calculation of the renal resistive index (RRI). RRI measurement does not require angle correction of the Doppler beam against the blood-flow direction.

Fig. 2. Association between the renal resistive index and creatinine clearance in essential hypertensive patients. RRI, renal resistive index; CCr, creatinine clearance, r = −0.61, p < 0.05.

Heart (n=93)  

Carotid B-mode (n=76)

Fig. 3. Relationships between the incidence of abnormal RRI and the degree of hypertensive change in each organ. (left panel) Heart, 0: no abnormality, 1: left ventricular hypertrophy and/or ischemic ST-T changes; (right panel) PS, none: 0, mild: 1.1-5.0, moderate: 5.1-10.0, severe: >10.0. PS, plaque score; RRI, renal resistive index. *p < 0.01, **p < 0.01 vs. none or mild group.
with the duplex scanning exhibiting 100% sensitivity, 93% specificity, and 95% overall accuracy with regard to these parameters (2). In addition to such utilities, a moderate inverse correlation was found between RRI and CCR, suggesting a potential utility of RRI as an indicator of earlier renal arteriopathy in essential hypertension.

In essential hypertension, the kidney has long been thought to play a primary role in the initiation and maintenance of the hypertensive process. At the same time, the kidney is one of the major targets of this process. Hypertensive arteriopathy in the kidney is associated with its hemodynamic modulation as a result of arteriolar constriction (8). With arteriolar constriction, renal resistance increases, resulting in an alteration of the renal blood flow patterns. When renal resistance is increased, renal blood flow declines for a given perfusion pressure. Because the decline is more prominent in diastole than in systole, it leads to an increase in RRI. In the present study, we investigated the relationship between RRI and conventional indicators of renal function in hypertensive patients, finding that RRI is most strongly correlated with CCR, followed by BUN, but not with serum creatinine. It is generally known that renal function is more directly reflected in CCR than in BUN or creatinine levels (12). Thus, our findings suggest the potential utility of RRI for the evaluation of renal arteriopathy in essential hypertension. This utility is supported by a study by Mostbeck et al. (4), who have investigated the relationship between renal histology and RRI in patient with parenchymal renal disease. In their study, increased RRI was related with renal arteriosclerosis, glomerular sclerosis, and focal interstitial sclerosis, supporting an association between increased RRI and renal damage.

Terry et al. (6) have reported that CCR levels reach a peak at the age of 30 years in healthy subjects, with a subsequent decline with aging. In addition, Schmieder et al. (13) have reported that patients with established hypertension have an accelerated decline in renal function with aging, reflecting selective functional and/or structural changes in the renovascular bed. However, in older patients, serum creatinine levels don’t necessarily rise until the renal function is moderately impaired (14). Thus, RRI measurement by ultrasonic duplex scanning may be an easy, non-invasive method for the early detection of renal hemodynamic changes caused by hypertension, especially in older hypertensive patients.

It is commonly known that, in hypertensive patients, other target-organ damage progresses in a parallel fashion with renal damage (15, 16). Accordingly, we have previously shown a higher incidence of silent cerebral infarction in hypertensive patients with renal damage (11). In the present study, the normal upper limit of RRI was 0.7 in healthy volunteers, and thus greater or equal values were considered abnormal. Similar values have been reported in the literature (4, 5, 7) and in a recent report from our department (17). In addition, RRI has been shown to be highly reproducible (18) and independent of mean arterial blood pressure (19). These findings support the reliability of our RRI measurements. In the present study, we found a higher incidence of abnormal RRI in patients with moderate or severe carotid atherosclerosis, arteriosclerotic retinopathy, and ECG abnormalities. Moreover, abnormal RRI was more frequently found in patients with diabetes than in those without, in agreement with previous reports (20, 21). However, because the diabetic patients were older than those without diabetes, caution is necessary when concluding that diabetes per se has caused the rise in RRI. On the basis of these findings, abnormal RRI appears to be associated with multiple types of organ damage caused by hypertension, further

---

**Fig. 4.** Incidence of abnormal RRI by the diagnoses of diabetes mellitus and hypercholesterolemia in essential hypertensive patients. RRI, renal resistive index.
supporting the utility of RRI as an indicator of target organ damage in essential hypertension.

In conclusion, compared to conventional measures of renal function, renal RRI appears to be a better indicator of renal function in essential hypertensive patients. In addition, increased RRI may be associated with multiple types of target-organ damage caused by hypertension. Thus, noninvasive evaluation of renal RRI may be useful for the detection of earlier renal arteriosclerosis in patients with essential hypertension.

Limitations

Increased RRI might also be caused by nonspecific vascular and glomerular pathology. As an example, Patrquin et al. (22) have reported increased RRI in the oliguria stage of acute renal failure in hemolytic uremic syndrome. Further study is therefore necessary to determine the relative strength of association between RRI and hypertensive renal damage.

Acknowledgements

We would like to thank Miss Y. Imaeda, Miss Y. Inoue, and Miss R. Morimoto, for their invaluable secretarial assistance.

References