Pulsating Renal Blood Flow Distribution Measured Using Power Doppler Ultrasound: Correlation with Hypertension

Michinobu NAGAO, Kenya MURASE*, Hideyuki SAEKI**, Teruhito MOCHIZUKI***, Shigenori SUGATA***, and Junpei IKEZOE***

Arterial compliance is associated with the first stage of hypertension and atherosclerosis. We propose here a compliance index, which measures pulsating renal blood flow distribution using a power Doppler ultrasound (US). We assessed the relationship between the compliance index and blood pressure and between the compliance index and risk factors of atherosclerosis. The subjects consisted of 136 consecutive patients (96 males, 40 females) who underwent a physical checkup. Ages ranged from 40 to 60 years with a mean of 50.1 years. Patients with past renal disease and/or renal dysfunction were excluded. Using a power Doppler US combined with an ECG-gated and echo-tracking system, we recorded the vascular distribution of the renal parenchyma at 8 to 10 time points during an interval of the R wave of the ECG. Using a color pixel counting technique, we calculated the area (A) corresponding to the colored vascular distribution at power Doppler US. The relationships between A and the time points (t) were fitted to a quadratic equation. The compliance index of renal parenchymal vessels was obtained by twice differentiating the quadratic equation obtained above (d²A/dt²), and taking the result as a new hemodynamic index. In the univariate correlation analysis, the compliance index was correlated with age (r = - 0.26, p = 0.002), systolic blood pressure (r = - 0.33, p = 0.0001), diastolic blood pressure (r = - 0.45, p < 0.0001), serum uric acid (r = - 0.28, p = 0.001), and body mass index (r = - 0.32, p = 0.0002). On the multivariate stepwise regression analysis, the compliance index was significantly correlated with diastolic blood pressure (r = - 0.36, p < 0.0001) and body mass index (r = - 0.18, p < 0.0001). In conclusion, the compliance index is a candidate for a new hemodynamic marker of renal blood flow abnormality caused by hypertension. (Hypertens Res 2002; 25: 697–702)

Key Words: power Doppler US, renal vessels, hypertension

Introduction

Increasing arterial stiffness and decreasing arterial compliance are now thought to be the first step of the hypertension and atherosclerosis process (1–4). Decreased arterial compliance is associated with the elevation of blood pressure. Hypertensive arteriopathy in the kidneys is known to modulate hemodynamically as a result of arteriolar contraction (5, 6).

Recent improvements in imaging technology have identified early vascular changes that can be assessed noninvasively using ultrasound (US) (4–8). The resistive index measured by Doppler ultrasound has become integral to echographic assessment of renal blood flow, and provides a simple and useful index of renovascular resistance and a sensitive indicator of renovascular hypertension (8, 9). But waveform
Doppler analyses such as the resistive index have a disadvantage in that they cannot readily visualize renal blood flow in the low-velocity and low-amplitude flow state. Power Doppler imaging is generally more sensitive to low-velocity flow states and more amenable to normalization (10, 11). Power Doppler is appropriate for quantifying the distribution of small vessels in the renal parenchyma.

We conjectured that the compliance or the construction of renovascular distribution might be associated with vascular damage caused by hypertension and atherosclerosis. We therefore hypothesized that the measurement of pulsating renal blood flow distribution on power Doppler might be useful for assessing vascular damages caused by hypertension and atherosclerosis. In this study, we describe a new method for measuring pulsating renal vascular distribution using power Doppler US, and use this method to assess the relationship between pulsating renal vascular distribution and blood pressure or atherosclerosis risk factors.

### Materials and Methods

The subjects consisted of 136 consecutive patients who underwent a physical checkup at Matsuyama Medical Center for cancer and cardiovascular disease between September 2000 and September 2001. There were 96 males and 40 females. Ages ranged from 40 to 60 years (mean ± SD, 50.1 ± 6.8 years). A detailed medical history was recorded for each subject, with particular attention to evidence of hypertension, diabetes mellitus, and renal disease or stones. Blood pressure was measured three times after a 5-min seated rest. All subjects underwent a battery of laboratory tests, including tests for traditional atherosclerotic risk factors. The atherosclerotic risk factors considered in this study were diabetes mellitus, hypercholesterolemia, hyperuricemia, obesity, and smoking history (Table 1). In all subjects, end-organ damage of hypertension and atherosclerosis were assessed by funduscopy and ECG. ECG abnormalities were diagnosed when there was left ventricular hypertrophy (abnormally high QRS complex voltage) and/or ischemic ST-T changes. Hypertensive retinopathy was classified based on hypertensive (H) and arteriosclerotic changes (S) according to Scheie’s classification. Renal function was evaluated by proteinuria, serum creatinine, blood urea nitrogen, and creatinine clearance. Subjects with past renal disease and/or abnormalities of renal function were excluded from this study. Twenty-six patients treated with calcium antagonist and/or angiotensin converting enzyme inhibitor for chronic hypertension and 6 patients treated with medication for diabetes mellitus were included, and the treatment period for these two diseases was longer than 6 months. All patients with hypertension and diabetes mellitus stopped their medications at 3 days before their physical check up.

### US Examination

All subjects were examined in the morning after an overnight fast. All examinations were performed with a commercially available US system equipped with power Doppler imaging (Toshiba Power Vision 6000; Toshiba, Tokyo, Japan). All cases were examined using a convex transducer that automatically shifts from 3.75 MHz to 4.2 MHz when in power Doppler mode. For power Doppler studies, the following imaging parameters were used: color threshold, 100%; wall motion filter, adaptive; reference frequency, 2.5 MHz; line density, high; frame per second, 6; velocity range, 7.75 cm/s; cut-off, 4. Power Doppler gain was set at a level where background color was suppressed just enough to allow detection of small vessels.

Patients were scanned without any special preparation in the spine position, with a lateral or translumbar subcostal approach to the left kidney. The scanning plane was selected for the long axis view of the left kidney. This approach minimized the depth of the target region to provide technically adequate color flow visualization of the intrarenal vascular architecture. A minimum of three similar-looking power Doppler distributions adequate for measurement were recorded within a few seconds while the patient held his or her breath.

### Compliance Index

We drew the rectangular region of the interest (ROI) in the middle parenchyma using a long axis view of the left kidney, since interlobular vessel distributions were the main target in this analysis. The longitudinal length of the ROI was defined as the thickness of a hyperechoic area and less than 15 mm from the outside margin. The width of the ROI was defined to be as large as possible and to include the renal parenchyma. A hyperechoic area corresponding to the medullary region and fatty tissue in the central region of the kidney was

### Table 1. Subjects Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number of subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (M/F)</td>
<td>96/40</td>
</tr>
<tr>
<td>Age (year-old)</td>
<td>50.1 ± 6.8</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>123.6 ± 15.9</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>72.8 ± 12.9</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>211 ± 37</td>
</tr>
<tr>
<td>Serum uric acid (mg/dl)</td>
<td>5.7 ± 1.3</td>
</tr>
<tr>
<td>Fasting blood sugar (mg/dl)</td>
<td>95.8 ± 21.9</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.3 ± 3.5</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>0.9 ± 0.2</td>
</tr>
<tr>
<td>Creatinine clearance (ml/min)</td>
<td>82.4 ± 6.2</td>
</tr>
<tr>
<td>Number of subjects</td>
<td></td>
</tr>
<tr>
<td>Proteinuria</td>
<td>0</td>
</tr>
<tr>
<td>Current and former smokers</td>
<td>54</td>
</tr>
<tr>
<td>Medication for hypertension</td>
<td>26</td>
</tr>
<tr>
<td>Medication for diabetes mellitus</td>
<td>6</td>
</tr>
</tbody>
</table>

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not included in the ROI. Using a power Doppler US combined with an ECG-gated and echo-tracking system, we recorded the vascular distribution inside the ROI at 8 to 10 intermittent imagings during an R–R interval (Fig.1). The obtained images were stored on a 230 MB MO disk and transferred to a computer. The number of pixels inside the ROI and the number of pixels corresponding to the colored vasculatures were measured by a color pixel counting software. The following equation was used to calculate the area (A) of the colored vasculatures:

\[
\text{Colored vascular area (A) (mm}^2) = \frac{\text{ROI area (mm}^2) \times \text{the number of pixels of colored vasculatures}}{\text{the number of pixels in the ROI}}
\]

The relationship between A and the time points (t) was fitted to a quadratic equation. The compliance index of renal parenchymal vessels was obtained by twice differentiating the quadratic equation obtained above (d²A/dt²), and the result was taken as a new hemodynamic index (Fig. 2). The value for each subject was defined as the average value of two compliance indexes.

**Statistical Analysis**

Univariate associations between the compliance index and the area and length of ROI were analyzed by calculating Pearson’s correlation coefficients. Univariate associations between the compliance index and the study variables were analyzed by calculating Spearman’s correlation coefficients. Multivariate associations between the compliance index and the study variables were analyzed by the multiple stepwise regression technique. Comparisons of the compliance indices between the subjects with and without ECG abnormality, funduscopic changes, medication for hypertension, and smoking status were analyzed by Mann-Whitney U test.

**Results**

The compliance index for all subjects was 2.49 ± 1.37 (mean ± SD). The area and the length of ROI for all subjects were 882 ± 148 mm² (mean ± SD) and 140 ± 11 mm. The compliance index showed no univariate association with the area (r = -0.004, p = 0.97) or the length (r = -0.13, p = 0.13) of ROI.
In Table 2, the results of Spearman’s correlation coefficients of blood pressure and atherosclerosis risk factors are shown. The compliance index was significantly correlated with age, systolic blood pressure, diastolic blood pressure, serum uric acid and body mass index.

In Table 3, the results of the multiple stepwise regression analysis of blood pressure and atherosclerosis risk factors are shown. The compliance index was significantly correlated with diastolic blood pressure and body mass index.

The compliance indices for 20 subjects with and 110 subjects without ECG abnormalities were 1.58 ± 0.78 and 2.65 ± 1.39, respectively. There was a significant difference between these two groups (p = 0.0013).

The compliance index for 21 subjects with and 115 subjects without hypertensive funduscopic changes were 1.57 ± 0.68 and 2.66 ± 1.39, respectively. There was a significant difference between these two groups (p = 0.0003). The compliance indices for 18 subjects with and 118 subjects without arteriosclerotic funduscopic changes were 1.54 ± 0.66 and 2.64 ± 1.39, respectively. There was a significant difference between these two groups (p = 0.0004).

The compliance indices for 26 subjects with and 110 subjects without medication for hypertension were 1.43 ± 0.63 and 2.68 ± 1.38, respectively. There was a significant difference between these two groups (p < 0.0001).

The compliance index for 82 subjects who had never smoked and 54 current and former smokers were 2.49 ± 1.47 and 2.50 ± 1.20, respectively. There was no significant difference between these two groups.

### Discussion

Doppler US vascularity measurements have been used in several organ systems (12, 13). These measurements are generally used to assess tumor vascularity by the sum of color pixels in standard color Doppler US (13, 14). In this study, we targeted the interlobular vessels throughout the renal parenchyma, since arteriole function is thought to play an important role in the initiation of hypertension and maintenance of blood pressure (15–17). Power Doppler US involves imaging the amplitude of blood flow, rather than the direction or velocity, as in color or pulse Doppler US (10, 11). To measure the distributions of slow velocity vessels such as the interlobular artery, we selected power Doppler mode. The branching pattern of arterioles and small arteries in a living organ describes the arterial tree (15, 18, 19). The cross sectional area, which expands from arteriole to the capillary arteries, increases rapidly and describes a curve similar to that of a quadratic function (19, 20). We hypothesized that the pulsating curve of the colored areas that expressed the interlobular arteries and small arteries on power Doppler US could be fitted to a quadratic equation (Fig. 2). Thus, we produced a compliance index by twice differentiating the quadratic equation obtained above (d²A/dr²).

The compliance index demonstrates acceleration in which renal blood flow distribution repeatedly extends and contracts during a cardiac cycle. With reduced distensibility at the initiation process of hypertensive arteriopathy (5, 6), renal resistance increases, resulting in an alteration of renal blood flow. When renal resistance is increased, renal blood flow declines for a given perfusion pressure. The process of renal hemodynamic change induces a decrease in acceleration. Consequently, an elevation of blood pressure was strongly correlated with a decrease in the compliance index in the present study. Because the compliance index was obtained from mainly diastolic phase images (Fig. 2), we considered it might be more strongly correlated with diastolic blood pressure than systolic blood pressure. Atherosclerosis involves large arteries such as the main renal arteries, while hypertension involves small arteries such as the interlobular arteries (6, 12, 21). We consider that the compliance index may reflect vascular damages caused by hypertension rather than atherosclerosis.

In the present study, obesity seemed to mitigate hypertension-induced cardiovascular changes in the systemic vascular bed. However, no such mitigation was observed in the renal vasculature, and left ventricular hypertrophy was exacerbated by the presence of obesity. Renal vascular resistance is known to be elevated in obese hypertensive patients (22, 23). As a result, renal vascular compliance decreased with increasing body mass index in this study.

The arterial wall elasticity decreases with increasing age, if atherosclerosis is not present. Creatinine clearance levels...
reach a peak at the age of 30 years in healthy subjects, and decline thereafter (24). In this study, the compliance index gradually decreased with increasing age in subjects over 40 years old. This result indicates that arterial elasticity decreases and renal function declines with aging.

Although hyperuricemia has been shown to be an independent predictor of the development of hypertension (25), hyperuricemia might be the consequence of increased uric acid production and decreased renal capacity to excrete uric acid. In essential hypertension, hyperuricemia is directly related to an increase in renal vascular resistance and inversely corrected with renal plasma flow (26, 27). In this study, the reduced compliance index in hyperuricemia may have been caused by the abnormal renal hemodynamics induced by associated with hyperuricemia.

It is commonly known that in hypertensive patients other target organ damage progresses in parallel with renal damage (28, 29). We found a significantly reduced compliance index in subjects with arteriosclerotic retinopathy and ECG abnormalities. This result supports the reliability of our compliance index and suggests that the compliance index can help estimate other organ damage caused by hypertension and atherosclerosis.

Doppler ultrasound measurement of the resistive index has become integral to ultrasound assessment of the kidneys in many institutions (5, 6, 8, 9). However, the size, numbers, and branching patterns of the arteries that supply the kidneys are extremely variable. Therefore, direct scanning of the renal arteries is time consuming and highly dependent on the skill of the sonographer. Previous reports have suggested that measurement of the resistive index varies according to the influences of the sonographer, individual measurement, and subject (30, 31). In the present study, compliance indexes for two subjects were measured six times by two different operators on two separate days. In a 48-year-old normotensive female, the mean, maximum, and minimum of the six compliance indexes were 4.11, 4.00, and 4.27, and the coefficient of variation was 2.4%. This result indicates that the reproducibility of the measurements was probably satisfactory. However, in a 54-year-old male with hypertension, the mean, maximum, and minimum of the six compliance indexes were 1.58, 1.16, and 2.06, and the coefficient of variation was 23%. Based on these results, we conjecture that blood pressure variability in hypertensive patients is related to the measurement of the compliance index, as previously hypothesized (32, 33). In hypertensive subjects, it may be necessary to maintain the blood pressure when measuring the compliance index in order to improve the reproducibility. The resistive index measures one large artery, such as a main renal artery, while the compliance index measures multiple interlobular vessels. As pointed out in the Results section, the compliance index was not associated with either the size or the length of ROI in the present study. Furthermore, our method, which only requires setting up an ROI, is technically simple. And our method may be more sonographer independent than the resistive index method.

The color pixel counting software used in the present study can calculate the number of color pixels inside a rectangular ROI. If the rectangular ROI is set up in the long axis view of the right kidney, some hepatic vessels may be included within it. Due to this limitation in software, the compliance index for the right kidney was not calculated in this study.

In conclusion, we measured pulsating renal vascular distribution using power Doppler US and color pixel counting software. Noninvasive evaluation of compliance index may be useful for the detection of early renal blood flow abnormality as a predictor of hypertension.

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References


