Diagnostic Value of Simultaneous Brachial and Ankle Blood Pressure Measurements for the Extent and Severity of Coronary Artery Disease as Assessed by Myocardial Perfusion Imaging

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Background  Although the simultaneous measurement of brachial and ankle blood pressure is a simple method of evaluating atherosclerosis, its diagnostic value for coronary artery disease (CAD) is undetermined.

Methods and Results  To evaluate the diagnostic value of ankle–brachial pressure index (ABI) and brachial-to-ankle pulse wave velocity (baPWV), 334 consecutive patients with suspected CAD were evaluated. Patients with a previous myocardial infarction or coronary intervention were not included. The magnitude of myocardial ischemia was evaluated by myocardial perfusion imaging. Using a 20-segment model, the percent of ischemic segments to total segments was expressed as %myocardium ischemic. In patients with ≤1, 2 and ≥3 coronary risk factors, %myocardium ischemic was 2.7±0.4, 4.0±0.5, 7.9±0.8%, respectively (p<0.0001 for trend). Performing ABI with a cutoff of 1, the %myocardium ischemic was similar in patients with ≤1 or 2 risk factors. In patients with ≥3 coronary risk factors, however, an ABI <1 reflected greater %myocardium ischemic than an ABI ≥1 (10.1±1.3, 6.6±1.0%; p=0.03). No such additional value was observed with baPWV.

Conclusions  The addition of simultaneous brachial and ankle blood pressure measurements will help further stratify patients with multiple risk factors. Although this approach is simple, it facilitates the identification of high-risk patients who require aggressive treatment because >10% myocardium ischemic is regarded as a scintigraphic indicator for coronary revascularization.  

Key Words:  Ankle–brachial pressure index; Coronary artery disease; Coronary risk factors; Myocardial perfusion imaging; Pulse wave velocity

Simultaneous measurement of brachial and ankle blood pressures enables evaluation not only of blood pressure but also pulse wave analysis.1,2 The 2 most important indexes, ankle–brachial pressure index (ABI) and pulse wave velocity (PWV), are easily derived and are reported to be diagnostic and prognostic markers of atherosclerosis.3–6 Of the diseases related to atherosclerosis, the diagnosis and treatment of coronary artery disease (CAD) is very important in clinical practice because of its high prevalence and mortality.7 Although noninvasive markers of atherosclerosis are considered to have a significant role in screening large populations in order to identify the high-risk group, the diagnostic role of simultaneous brachial and ankle blood pressure measurements for CAD is unclear.6,8 Accordingly, in the present study we used myocardial perfusion imaging to evaluate the diagnostic value of ABI and brachial-ankle PWV (baPWV) for the extent and severity of CAD.

Methods

Study Patients  Three hundred thirty-four consecutive patients with suspected CAD, who underwent both simultaneous brachial and ankle blood pressure measurements and myocardial perfusion imaging, were evaluated retrospectively. They were aged 65±11 years; 242 were men and 92 women. No patient with previous myocardial infarction, unstable angina, or a history of coronary revascularization was included. Of the 334 patients, 253 underwent coronary angiography (CAG) because of clinical symptoms, electrocardiographic abnormalities or scintigraphic findings. Written informed consent was obtained from the participants.

Assessment of Coronary Risk Factors  Risk factors included in the assessment were clinically documented hypertension, hypercholesterolemia, diabetes mellitus, cigarette smoking, and family history of CAD. Hypertension was defined as a history of systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or documented hypertension on at least 2 occasions at an outpatient clinic. Hypercholesterolemia was defined as fasting serum total cholesterol of ≥220 mg/dl.9 Diabetes mellitus was diagnosed using the criteria proposed by the Japanese Diabetic Society.10 Based on the number of risk factors (≤1, 2, and ≥3), patients were classified into low-,
sine triphosphate disodium (0.16 mg·kg–1·min–1) was administered when submaximal heart rate, chest pain, and the exercise was then continued for 1 min at the same intensity. Image acquisition was commenced 30 min after the administration of the radiotracer. In the remaining 56 patients, adenosine triphosphate-loading myocardial SPECT was performed; in 103 patients, SPECT was performed during exercise, and the remaining 131 patients underwent adenosine triphosphate-loading myocardial SPECT. The protocols to stress these patients were similar to previous methods. Using an ECG-gated program, delayed images were acquired 4 h later.

Data was acquired with a 2- or 3-detector gamma camera (Prism 2000XP or Prism 3000XP, Picker, Cleveland, Ohio, USA) for 180- or 360-degree arcs. For both radioisotopes, a low-energy high-resolution parallel multi-hole collimator was used. The ECG-gated SPECT images were reconstructed from the data by a data processor (Odyssey VP, Picker) combined with a Butterworth filter (order 8; cutoff frequency 0.25 for 99mTc-sestamibi and 0.2 for 201Tl) and a ramp filter.

Scintigraphic findings were visually defined as positive if reversible and/or a fixed perfusion abnormality was observed. According to a method reported elsewhere, each SPECT image was divided into 20 segments, with segments 1–3, 7–9, 13–14 and 19–20 corresponding to the area perfused by the left anterior descending coronary artery; segments 4, 10 and 15–16 corresponding to the areas perfused by the right coronary artery; and segments 5–6, 11–12, and 17–18 corresponding to the areas perfused by the left circumflex coronary artery (Fig 1). The accumulation of radioisotope in the myocardium was visually evaluated by 2 cardiologists using a 5-grade scale: 0 (normal), 1 (slight reduction of uptake), 2 (moderate reduction of uptake), 3 (severe reduction of uptake) or 4 (absent of radioactive uptake). Disagreements in image interpretation were resolved by consensus. The total of the scores for all segments during exercise and at rest was designated the summed stress score (SSS) and the summed rest score (SRS), respectively. The summed difference score (SDS) was defined as SSS minus SRS. In addition, these indices were converted to percent of the total myocardium (% myocardium) involved with stress, ischemia, or fixed defects by dividing the summed scores by 80, the maximum potential score (4×20), and multiplying it by 100.

While taking quantitative ECG-gated SPECT images, the R-R interval was divided by the R-wave trigger into 8 equal portions and then end-diastolic and end-systolic images were obtained. Each reconstructed short-axis gated SPECT image was processed by the quantitative gated SPECT program developed by Germano et al to calculate the left ventricular end-diastolic volume, left ventricular end-systolic volume and left ventricular ejection fraction.

Coronary Angiography

Multi-direction CAG was performed according to Judkins’ method. The degree of coronary artery stenosis was measured by calipers according to the American Heart Association criteria. Significant stenosis was deemed present when >50% actual diameter narrowing was noted.

### Table 1  Clinical Characteristics of the 334 Patients With Suspected Coronary Artery Disease

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>65±11</th>
</tr>
</thead>
<tbody>
<tr>
<td>M/F</td>
<td>242/92</td>
</tr>
<tr>
<td>Coronary risk factors</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>173 (52%)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>208 (62%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>114 (34%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>147 (44%)</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>38 (11%)</td>
</tr>
<tr>
<td>No. of coronary risk factors</td>
<td></td>
</tr>
<tr>
<td>0–1 (low)</td>
<td>106 (32%)</td>
</tr>
<tr>
<td>2 (intermediate)</td>
<td>113 (34%)</td>
</tr>
<tr>
<td>3–5 (high)</td>
<td>113 (34%)</td>
</tr>
</tbody>
</table>

Intermediate- and high-risk groups.

### Measurements of the Ankle-Brachial Pressure Indexes

The baPWV was measured using a volume-plethysmographic apparatus (FORM/ABI, Colin Co Ltd, Komaki, Japan) while the patient was supine after resting in the same position for at least 5 min, as described previously. In brief, this instrument simultaneously records the baPWV and the brachial and ankle blood pressures on the left and right sides, as well as recording the electrocardiogram (ECG) and heart sounds. The electrocardiographic electrodes are placed on both wrists, and cuffs are wrapped around both brachia and ankles. Pulse volume waveforms at the brachium and ankle are recorded using a semiconductor pressure sensor. The ABI was defined as the lowest value for both sides and the baPWV as the highest baPWV value for both sides, as described previously. All recordings were performed while the patients were taking their regular medication, but not receiving intravenous drugs.

### Stress Myocardial Perfusion Imaging

In 100 patients, stress myocardial single-photon emission computed tomography (SPECT) with 99mTc-sestamibi was performed using a 1-day protocol. Symptom-limited multistep exercise using a bicycle ergometer was performed by 44 of the patients. The stress dose of 99mTc-sestamibi (259 MBq) was administered when submaximal heart rate, chest pain, ST-segment depression of ≥0.1 mV or leg fatigue developed and the exercise was then continued for 1 min at the same level. Image acquisition was commenced 30 min after the last exercise session. In the remaining 56 patients, adenosine triphosphate disodium (0.16 mg·kg–1·min–1) was administered intravenously for 6 min and 3 min later, 99mTc-sestamibi (259 MBq) was given intravenously with image acquisition beginning 30 min later. On the same day, the patients were given 99mTc-sestamibi (777 MBq) while at rest and 30 min later, quantitative gated myocardial SPECT images were acquired.

In 234 patients, 201Tl (111 MBq) myocardial SPECT was performed; in 103 patients, SPECT was performed during exercise, and the remaining 131 patients underwent adenosine triphosphate-loading myocardial SPECT. The protocols to stress these patients were similar to previous methods. Using an ECG-gated program, delayed images were acquired 4 h later.

Data was acquired with a 2- or 3-detector gamma camera (Prism 2000XP or Prism 3000XP, Picker, Cleveland, Ohio, USA) for 180- or 360-degree arcs. For both radioisotopes, a low-energy high-resolution parallel multi-hole collimator was used. The ECG-gated SPECT images were reconstructed from the data by a data processor (Odyssey VP, Picker) combined with a Butterworth filter (order 8; cutoff frequency 0.25 for 99mTc-sestamibi and 0.2 for 201Tl) and a ramp filter.

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Statistical Analysis

Results are expressed as mean±1SD, except for the %myocardium ischemic or fixed, which is expressed as mean±standard error. The Student’s t-test was used to compare the means of the continuous variables, and contingency tables were analyzed using a chi-square test. Analysis of variance (ANOVA) was performed for comparisons among 3 groups or more, followed by Bonferroni’s post-hoc test. Analysis for linear correlation and trend were performed where appropriate. A p-value of <0.05 was regarded as denoting statistical significance. The computations were performed using the SPSS-PC+ computer program (Version 11.0; SPSS, Chicago, IL, USA).

Results

Clinical Risk Factors

The prevalence of hypertension, hypercholesterolemia, diabetes mellitus, cigarette smoking and family history of CAD was 52%, 62%, 34%, 44% and 11%, respectively (Table 1). Among the 334 patients, 106 were classified as low-risk, 115 as intermediate-risk, and 113 as high-risk. Although the patients in the high-risk group were younger than those in the low-risk group (63±11 vs 67±10 years; p<0.025), no significant difference was observed when compared with those in the intermediate group (65±11 years). In the high-risk group with ≥3 coronary risk factors, the most common risk factor was hypertension (n=101; 89%), followed by hypercholesterolemia (n=91; 81%) and cigarette smoking (n=81; 72%).

Measurement of ABI and baPWV

The average ABI in all patients was 1.09±0.16, and <0.9 in 33 patients (10%). Although the mean baPWV was 1,625 cm/s, the cut-off values for each quartile were 1,344, 1,550 and 1,835 cm/s, respectively. The ABI showed no or mild correlation with age (r=–0.07; p=NS) and systolic blood pressure (r=–0.14; p=0.013), whereas baPWV significantly correlated with both age (r=0.39; p<0.0001) and systolic blood pressure (r=0.27; p=0.0001).

Scintigraphic Findings

Visual analysis of the stress myocardial SPECT images revealed positive findings in 210 patients (63%) and negative findings in 124 patients (37%). Of the 210 positive patients, 134 had a perfusion abnormality in the left anterior descending arterial territory, 51 had the defect in the left circumflex arterial territory, and 118 had it in the right coronary arterial territory. In all 334 patients, the %myocardium ischemic was 4.9±0.4%, and the %myocardium fixed was 4.5±0.4%. Quantitative gated SPECT was performed in 280 patients (84%) with a mean left ventricular ejection fraction of 56%; the analysis could not be performed in the remaining 54 patients (16%) because of cardiac arrhythmias.

CAG Findings

Based on the clinical symptoms, ECG and scintigraphic findings, CAG was performed in 253 of the 334 patients (76%). No significant difference was observed in ABI (1.09±0.15 vs 1.09±0.18; p=NS) or baPWV (1,598±378 vs 1,710±507 cm/s; p=NS) between patients who underwent CAG and those who did not. After excluding 33 patients with an ABI <0.9, baPWV was also similar (1,605±370 vs 1,717±490 cm/s; p=NS). Patients who underwent CAG had greater %myocardium ischemic than those who did not (5.8±0.4 vs 2.2±0.6%; p=0.0001).

Among the 253 patients who underwent CAG, 1-vessel CAD was found in 51 patients, 2-vessel CAD in 50, and 3-vessel CAD in 47; the remaining 105 patients had insignificant lesions. Mean ages in these 4 groups were similar (64±10, 65±13, 65±9, 63±10 years; respectively). The ABI was decreased in patients with significant CAD compared with those with insignificant lesions (1.07±0.16 vs 1.13±0.13; p=0.002). After excluding patients with ABI <0.9, baPWV was faster in patients with significant CAD than in those with insignificant lesions (1,658±391 vs 1,534±330 cm/s; p=0.012). A significant trend was found between the number of diseased vessels and the magnitude of stress-induced myocardial ischemia, and ABI (p=0.0001 for trend, for both), whereas no such trend was observed for baPWV whether the 33 patients with ABI <0.9 were included or excluded (Fig 2).

Relationship of PWV/ABI to Scintigraphic Findings

A weak but significant inverse correlation was observed.
between ABI and %myocardium ischemic ($r=-0.22$; $p<0.0001$) (Fig 3), and also the %myocardium ischemic in patients with ABI $<1$ was greater than those with ABI $\geq 1$ ($6.6\pm0.8$ vs $4.3\pm0.4$; $p<0.004$). By contrast, no significant correlation was found between baPWV and %myocardium ischemic whether or not the 33 patients with ABI $<0.9$ were included (included: $r=0.013$, $p=NS$; excluded: $r=-0.012$, $p=NS$) (Fig 3). After excluding the 33 patients with ABI $<0.9$, the %myocardium ischemic in each baPWV quartile was $4.0\pm0.7$, $4.8\pm0.8$, $4.3\pm0.7$, $4.3\pm0.7$%, respectively. In the 280 patients who underwent quantitative ECG-gated SPECT, the left ventricular ejection fraction correlated significantly with ABI ($r=0.12$; $p<0.05$), but not with baPWV or %myocardium ischemic ($r=-0.06$, $p=NS$; $r=-0.07$, $p=NS$).

Based on the coronary risk factors, the %myocardium ischemic was $2.7\pm0.4$, $4.0\pm0.5$, and $7.9\pm0.8$% in the low-, intermediate- and high-risk groups, respectively ($p<0.0001$ for trend) (Fig 4). In the low- and intermediate-risk groups, the %myocardium ischemic was similar between patients with ABI $<1$ and those with ABI $\geq 1$ ($3.1\pm1.0$ vs $2.7\pm0.5$%, and $4.3\pm1.4$ vs $3.9\pm0.6$%; $p=NS$ for both). In the high-risk group, however, the %myocardium ischemic was greater in patients with ABI $<1$ than in those with ABI $\geq 1$ ($10.1\pm1.3$ vs $6.6\pm1.0$%; $p=0.03$) (Fig 5). Furthermore, in 32 of the 42
high-risk patients whose ABI was <1, CAG revealed significant CAD in 28 patients (88%): 1-vessel CAD in 6, 2-vessel CAD in 10, and 3-vessel CAD in 12. No such additional value was observed when using baPWV with a cut-off point of 1,600 cm/s (Fig 6).

**Discussion**

The present study has demonstrated that the addition of simultaneous brachial and ankle blood pressure measurements to coronary risk assessment helps to better stratify patients suspected of having CAD. Of the 2 most important indexes derived from simultaneous brachial and ankle blood pressure measurements, ABI, but not baPWV, correlated with the %myocardium ischemic, a function of the magnitude of stress-induced myocardial ischemia. Furthermore, although patients with multiple risk factors are regarded as having a high likelihood of CAD, those with both ≥3 coronary risk factors and ABI <1 had a mean %myocardium ischemic of 10%, which indicated not only the presence of CAD but also the necessity for coronary revascularization in order to achieve a better prognosis.2,8,21 Thus, for patients suspected of having CAD, the combination of coronary risk factors and ABI indispensable for the initial diagnostic assessment because 12.5% of the present patients (32/260) were identified as extremely high-risk by this simple approach. Although the magnitude of myocardial ischemia was evaluated by either 99mTc-sestamibi or 201TI SPECT in this study, the diagnostic accuracy of both radioisotopes has been reported to be similar.22 More importantly, among the high-risk patients with ABI <1, who also underwent CAG, significant CAD was found in 88% (28/32) of the patients and multivessel CAD in 69% (22/32). The results of this study are consistent with large cohort studies in which decreased ABI is a marker for cardiovascular events.4,8,23 Recently, coronary calcium detected by electron beam computed tomography (EBCT) was proposed as a screening test before stress myocardial imaging to identify intermediate- or high-risk subsets of CAD patients.24 Compared with EBCT, simultaneous brachial and ankle blood pressure measurements are much simpler to perform and provide important information about intermediate- or high-risk populations or for the management of patients suspected of having CAD.

Previous studies have reported the relationship of ABI with the extent of coronary atherosclerosis as assessed by angiography.4,5 In one study, the Gensini score was calculated to evaluate the extent and severity of coronary atherosclerosis, though this is not commonly used in clinical practice.5 In contrast, scintigraphic scores for myocardial ischemia are widely accepted, well-known markers for prognosis25 and because of its noninvasiveness, this myocardial imaging technique can evaluate the extent and severity of coronary atherosclerosis not only in selected patients who have sufficient risks to warrant CAG, but also in the wider patient population that includes a low-risk subset. Although comorbidity of arteriosclerosis obliterans in any given patient, usually indicated by ABI <0.9, suggests the presence of multivessel CAD, the present study demonstrates that importance of ABI <1 in patients with multiple risk factors.

In contrast to ABI, baPWV was not useful in the diagnosis and risk stratification of patients with suspected CAD. It did not correlate with the extent and severity of myocardial ischemia as assessed by stress myocardial SPECT, and nor did it add any important diagnostic value to the classical coronary risk factors. For a discrete purpose, such as the diagnosis of CAD, baPWV has several limitations. First, it is underestimated in patients with arteriosclerosis obliterans26 although our analyses excluded patients with ABI <0.9, an established indicator for arteriosclerosis obliterans26 this cut-off value may not be sufficient to disregard the confounding effect. Second, baPWV correlates significantly with age27 as was observed in the present study. Because the high-risk patients were younger than the low-risk patients (63 vs 67 years), this difference in age might obscure the diagnostic value of baPWV measurement. Although an age-adjusted nomogram for baPWV derived from healthy middle-aged subjects has been developed, only a dichotomous judgment based on the difference between age-predicted and observed values can be made.28 Thus, it is difficult to quantitatively assess the magnitude of an abnormal value compared with an age-predicted normal value. Third, baPWV also correlates with blood pressure as was found in this study, which may originate from the nature of arterial pulse wave conduction in which arterial media is an important factor and is influenced by blood pressure.2,12 Therefore, ABI rather than PWV is regarded as an important marker of CAD, which is a disease of arterial obstruction and of arterial intima.29 Fourth, antihypertensive medication has a significant effect on the measurement of baPWV, but not for ABI.30 It has not yet been determined how long antihypertensive medication must be withdrawn before the baPWV can be accurately measured. When these limitations of baPWV are taken into account, what is its role in clinical practice? Brachial-ankle PWV may be considered as a dichotomous marker only for the presence or absence of angiographically determined CAD! In a previous study, increased baPWV was regarded as an independent predictor of the presence of CAD.31 However, considering those analyses were based on a heterogeneous patient population including those with valvular heart disease, congenital heart anomaly, and cardiomyopathies, the results may not be readily applied in clinical practice. Alternatively, baPWV may represent the progression of atherosclerosis because previous reports have suggested significant correlations of baPWV with markers for inflammation such as high-sensitive C-reactive protein.31 However, long-term follow-up is necessary before baPWV is established as a comprehensive marker for atherosclerosis.

In conclusion, the addition of simultaneous brachial and ankle blood pressure measurements to evaluation of coronary risk factors helps further stratify patients suspected of having CAD. In particular, those with multiple risk factors and ABI <1 may be grouped as extremely high-risk patients who require aggressive treatment including coronary revascularization. In contrast to ABI, further studies are necessary to establish the clinical role of baPWV, because adjusting for the confounding effects of age, blood pressure and medication on PWV is complicated, despite of the simplicity of its measurement.

**References**


