Brachial-Ankle Pulse Wave Velocity for Predicting Functional Outcome in Acute Stroke

Jinkwon Kim, MD; Tae-Jin Song, MD; Eun Hye Kim, MD; Ki Jeong Lee, MD; Hye Sun Lee, MS; Chung Mo Nam, PhD; Dongbeom Song, MD; Hyo Suk Nam, MD, PhD; Young Dae Kim, MD, PhD; Ji Hoe Heo, MD, PhD

Background and Purpose—We investigated whether the brachial-ankle pulse wave velocity (baPWV) has prognostic value for predicting functional outcome after acute cerebral infarction and whether the prognostic value differs between stroke subtypes.

Methods—We included 1091 consecutive patients with first-ever acute cerebral infarction who underwent baPWV measurements. Stroke subtypes were classified using the Trial of Org 10172 in Acute Stroke Treatment classification. Poor functional outcomes were defined as modified Rankin Scale score ≥2 at 3 months after stroke onset.

Results—We noted that 181 (16.59%) patients had a poor functional outcome. In multivariate logistic regression, patients in the highest tertile of baPWV (>22.25 m/s) were found to be at increased risk for poor functional outcome (adjusted odds ratio, 1.88; 95% confidence interval, 1.06–3.40) compared with those in the lowest tertile (<17.55 m/s). No significant interaction between baPWV and stroke subtype was noted. Receiver operating characteristic curve analysis indicated that the addition of baPWV to the prediction model significantly improved the discrimination ability for poor functional outcome.

Conclusions—baPWV has an independent prognostic value for predicting functional outcome after acute cerebral infarction. The prognostic value did not differ according to the stroke subtype. (Stroke. 2014;45:00-00.)

Key Words: prognosis ■ pulse wave analysis ■ stroke

During an individual’s lifetime, the elastic component of the artery decreases because of the aging process, hypertension, atherosclerosis, or other mechanisms that are not completely understood.1 Because a loss of arterial elastic properties results in structural and functional changes within circulation, the measurement of arterial stiffness has been proposed for the early detection of vascular damage and for cardiovascular risk evaluation. The carotid-femoral pulse wave velocity (cfPWV) is currently the gold standard tool to measure central arterial stiffening noninvasively.3 The brachial-ankle PWV (baPWV) is a recently developed, alternative method for the measurement of arterial stiffness.4 In clinical practice, measurement of baPWV is simpler than that of the cfPWV, because it involves the use of an automated device and does not require exposure of the femoral site. The baPWV value is highly reproducible, and the cfPWV and baPWV are closely related.5,6

Patients with acute stroke with a higher cfPWV were found to be at increased risk for poor long-term functional outcome and early neurological outcome.7,8 However, it remains unknown whether the baPWV also has a prognostic value for functional outcome in acute stroke. Furthermore, cerebral infarction is a heterogeneous disease; the mechanism underlying the development of stroke is variable, which includes small-vessel occlusion, large artery atherosclerosis, and cardioembolism.9,10 Considering that arterial stiffness reflects vascular damage and systemic atherosclerosis, the prognostic effect of baPWV may differ according to the subtypes of cerebral infarction. In the present study, we aimed to evaluate whether baPWV, measured in cases of acute cerebral infarction, has prognostic value for predicting long-term functional outcome and whether this prognostic value differs between stroke subtypes.

Methods

Participants

This study was a hospital-based, retrospective observational study. There were 2194 candidates who admitted to the neurology
department because of first-ever acute cerebral infarction, <3 days of symptom onset, between November 2008 and May 2013, and who were prospectively registered in the Yonsei Stroke Registry. Of them, we excluded 775 patients according to the exclusion criteria (see the online-only Data Supplement; Figure 1). Of the remaining 1419 candidates, 1134 patients completed baPWV measurement <7 days after admission. We noted that patients with older age and higher initial stroke severity were more frequently excluded for the lack of baPWV measurements (Table I in the online-only Data Supplement). Current smoking and coronary artery disease were more frequent in patients who underwent baPWV. The modified Rankin Scale scores at 3 months after stroke onset were available in 1091 patients (96.21%) who were finally included. The Institutional Review Board of Severance Hospital, Yonsei University Health System, approved this study and waived the need for informed consent because of the retrospective and observational nature of the study.

Measurement of baPWV

The baPWV was measured in a supine position at once <7 days from admission using an automated device (VP-1000; Colin Co. Ltd, Komaki, Japan) that has been validated in previous studies. This device simultaneously measures bilateral brachial and posterior tibial arterial pulse waveforms and arterial blood pressures by the oscillometric method. The baPWV is automatically calculated as the transmission distance divided by the transmission time. A more detailed method for the measurement of baPWV has been described previously. The ankle-brachial index is simultaneously calculated by dividing the lower value of systolic arterial pressure in the lower limbs by the higher value of systolic pressure in the upper limbs. We also collected data for systolic, diastolic, and mean pressure ([systolic pressure+2×diastolic pressure]/3) in the brachial artery, which has been reported to be a potential confounder of baPWV. The higher baPWV and blood pressure values between the right and left sides were used for the analyses.

Data Collection for Analysis

We collected data on sex, age, National Institute of Health Stroke Scale at admission, presence of risk factors, and premorbid use of medications in each patient (Table 1). Hypertension was diagnosed in cases when a patient was on antihypertensive medication at admission. All the cerebral angiographic findings were obtained from digital subtraction angiography, MR angiography, or computed tomographic angiography, which were performed at admission. All the cerebral angiographic findings or had systolic arterial pressures ≥140 mmHg or diastolic arterial pressures ≥90 mmHg on repeated measurements during admission. Peripheral artery disease was determined when the patient had an ankle-brachial index <0.9.

Classification of Stroke Subtype

We subdivided patients into 4 groups, including those with small-vessel occlusion, large artery atherosclerosis, cardioembolism, and undetermined cause, based on the Trial of Org 10172 in the Acute Stroke Treatment classification. Cerebral angiographic findings for classification were obtained from digital subtraction angiography. MR angiography, or computed tomographic angiography, which were performed at admission. All the cerebral angiographic findings

Table 1. Clinical Characteristics of Included Patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Study Patients (n=1091)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>693 (63.52)</td>
</tr>
<tr>
<td>Age, y</td>
<td>64.99±12.29</td>
</tr>
<tr>
<td>NIHSS score at admission</td>
<td>3 (1–5)</td>
</tr>
<tr>
<td>Use of thrombolysis treatment</td>
<td>113 (10.36)</td>
</tr>
<tr>
<td>Stroke subtype</td>
<td></td>
</tr>
<tr>
<td>Small-vessel occlusion</td>
<td>98 (8.98)</td>
</tr>
<tr>
<td>Large artery atherosclerosis</td>
<td>201 (18.42)</td>
</tr>
<tr>
<td>Cardioembolism</td>
<td>308 (28.23)</td>
</tr>
<tr>
<td>Undetermined cause</td>
<td>484 (44.36)</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>789 (72.32)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>323 (29.61)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>278 (25.48)</td>
</tr>
<tr>
<td>Current smoking</td>
<td>302 (27.68)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>271 (24.84)</td>
</tr>
<tr>
<td>Peripheral artery disease</td>
<td>96 (8.80)</td>
</tr>
<tr>
<td>Premorbid medication</td>
<td></td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>327 (29.97)</td>
</tr>
<tr>
<td>Anticoagulant</td>
<td>67 (6.14)</td>
</tr>
<tr>
<td>Statin</td>
<td>180 (16.50)</td>
</tr>
<tr>
<td>Antihypertensive</td>
<td>382 (35.01)</td>
</tr>
<tr>
<td>Laboratory findings</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>14.21±1.66</td>
</tr>
<tr>
<td>hs-CRP, nmol/L</td>
<td>6.25±15.14</td>
</tr>
<tr>
<td>Cholesterol, mmol/L</td>
<td>4.93±1.08</td>
</tr>
<tr>
<td>Triglyceride, mmol/L</td>
<td>1.41±1.02</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>4.27±0.40</td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
<td>8.00±3.45</td>
</tr>
<tr>
<td>Blood urea nitrogen, mmol/L</td>
<td>5.96±2.72</td>
</tr>
<tr>
<td>Creatinine, μmol/L</td>
<td>87.29±59.08</td>
</tr>
<tr>
<td>baPWV, m/s</td>
<td>20.82±6.29</td>
</tr>
<tr>
<td>Blood pressure at the baPWV measurement, mmHg</td>
<td></td>
</tr>
<tr>
<td>Systolic arterial pressure</td>
<td>152.46±23.79</td>
</tr>
<tr>
<td>Diastolic arterial pressure</td>
<td>86.95±14.08</td>
</tr>
<tr>
<td>Mean arterial pressure</td>
<td>108.78±16.41</td>
</tr>
</tbody>
</table>

Values were presented as mean±SD, median (interquartile range), or number (%). baPWV indicates brachial-ankle pulse wave velocity; hs-CRP, high-sensitivity C-reactive protein; and NIHSS, National Institute of Health Stroke Scale.

Figure 1. Flow chart of inclusion and exclusion criteria. baPWV indicates brachial-ankle pulse wave velocity; and mRS, modified Rankin Scale.
and the stroke subtypes were evaluated and determined during the weekly stroke conference, after a consensus by stroke specialists; the patients were then prospectively registered in the Yonsei Stroke Registry.11

**Determination of Functional Outcome**

Long-term functional outcome was assessed using the modified Rankin Scale via a direct interview performed by a clinician or through a telephone interview conducted by a well-trained research nurse after 3 months from stroke onset. Poor functional outcome was defined as a modified Rankin Scale score ≥2.

**Statistical Analyses**

The patients were subdivided into tertile groups (T1–T3) according to the baPWV value. We compared the clinical characteristics of patients across the tertile groups. To identify the potential factors associated with functional outcome, the clinical characteristics were compared between patients with good and poor functional outcomes. Then, we performed multivariate logistic regression with adjustments for sex, age, and variables that exhibited a P value <0.10 in the univariate analyses. To better understand the effect of baPWV on functional outcome, we established a smoothing spline plot for the estimated probability according to baPWV, based on the generalized additive regression model. For evaluating the discriminatory ability of baPWV in predicting functional outcomes, receiver operating characteristic curve analysis was used. The area under the curve (AUC) was calculated and the optimal cut-off value of baPWV was determined at the level with the highest Youden index (sensitivity + specificity − 1). To measure improvement in prediction performance by addition of baPWV, we computed change of AUC, continuous net reclassification improvement, and integrated discrimination improvement between the multivariate models with and without baPWV. All statistical analyses were performed using the R package for Windows (version 3.0.2; R Foundation for Statistical Computing, Vienna, Austria). A 2-sided P value <0.05 was considered statistically significant. Additional information for inclusion/exclusion criteria, definition of risk factor, cerebral angiography, management of stroke, and statistical method is provided in the online-only Data Supplement.

**Results**

In a total of 1091 patients, mean age was 64.99±12.29 years, and men were 63.52% (Table 1). The mean baPWV value was 20.82±6.29 m/s, and median (interquartile range) was 19.83 (16.39–24.03). Across the baPWV tertile groups (Table II in the online-only Data Supplement), a higher baPWV value was associated with female sex, older age, higher National Institute of Health Stroke Scale score at admission, stroke subtype, presence of hypertension, diabetes mellitus, or peripheral artery disease, premorbid use of antiplatelet or antihypertensive agents, a higher level of high-sensitivity C-reactive protein, glucose, blood urea nitrogen, or creatinine, and higher blood pressures at the baPWV measurement. Current smoking and hemoglobin level were negatively associated with baPWV.

At 3 months after stroke onset, 181 (16.59%) patients had poor functional outcome (modified Rankin Scale score ≥2). The higher baPWV was associated with poor functional outcome; this association was found to be significant in all stroke subtypes (Table 2). The presence of cardiac arrhythmia or ankle-brachial index <0.95 could interfere with accurate measurement of baPWV.12,13 When we performed subgroup analyses for the presence of cardiac arrhythmia or ankle-brachial index <0.95, the significance of baPWV was present in both subgroups. In the univariate analysis (Table III in the online-only Data Supplement), the other factors associated with poor functional outcome (P<0.05) were female sex, older age, use of thrombolysis treatment, hypertension, peripheral artery disease, nonsmoking status, higher National Institute of Health Stroke Scale score at admission, higher high-sensitivity C-reactive protein levels, and lower levels of hemoglobin, triglycerides, or albumin. There was no significant association between functional outcome and blood pressures simultaneously obtained at baPWV measurement. In the multivariate analysis, baPWV remained an independent predictor of poor functional outcome (Table 3). The patients in the higher baPWV tertile (T3; >22.25 m/s) more frequently had poor functional outcome (adjusted odds ratio, 1.88; 95% confidence interval [CI], 1.06–3.40) compared with those in the lower baPWV tertile (T1; <17.55 m/s). When baPWV was considered as a continuous variable, the adjusted odds ratio (95% CI) was 1.30 (1.07–1.59) for 1 SD increase in baPWV.

No significant interaction was noted between baPWV and stroke subtype in the models, which suggested that the

<table>
<thead>
<tr>
<th>Table 2. Subgroup Analysis for Functional Outcomes and baPWV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>baPWV, m/s</strong></td>
</tr>
<tr>
<td><strong>Patient Group</strong></td>
</tr>
<tr>
<td>All patients</td>
</tr>
<tr>
<td>Stroke subtype</td>
</tr>
<tr>
<td>Small-vessel occlusion</td>
</tr>
<tr>
<td>Large artery atherosclerosis</td>
</tr>
<tr>
<td>Cardioembolism</td>
</tr>
<tr>
<td>Undetermined cause</td>
</tr>
<tr>
<td>Presence of cardiac arrhythmia or ABI &lt;0.95</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
</tbody>
</table>

Values were presented as mean±standard deviation. ABI indicates ankle-brachial index; baPWV, brachial-ankle pulse wave velocity; and mRS, modified Rankin Scale.

*Derived from the independent t-test.
discrimination improvement values for baPWV were 0.217 continuous net reclassification improvement and integrated to 85.29% (95% CI, 82.18–88.40; \( P =0.044 \)). In addition, the significantly increased from 84.73% (95% CI, 81.52–87.95) when the continuous value of baPWV only was considered as a predictor of poor functional outcome, the AUC was 67.21% (95% CI, 62.78–71.65). The optimal cut-off point of baPWV is limited from the 5th to the 95th percentile of baPWV.

In receiver operating characteristic curve analysis (Figure 3), when the continuous value of baPWV was considered as a predictor of poor functional outcome, the AUC was 67.21% (95% CI, 62.78–71.65). The optimal cut-off point of baPWV was \( >21.33 \) m/s (at this point, sensitivity was 62.43% and specificity was 66.48%). When we compared the AUC of multivariate models with and without baPWV, the AUC was significantly increased from 84.73% (95% CI, 81.52–87.95) to 85.29% (95% CI, 82.18–88.40; \( P=0.044 \)). In addition, the continuous net reclassification improvement and integrated discrimination improvement values for baPWV were 0.217 (95% CI, 0.058−0.376; \( P=0.008 \)) and 0.006 (95% CI, −0.001 to 0.014; \( P=0.097 \)), respectively. These findings suggest that baPWV could provide additional prognostic information for functional outcome after acute cerebral infarction.

Discussion

Previous clinical studies on baPWV and cfPWV primarily assessed their prognostic value in patients in a stable condition, for predicting the new development of cardiovascular events or mortality. Few recent reports have examined the prognostic value of arterial stiffness in the acute phase of vascular events. In patients with acute stroke, a higher cfPWV was found to be associated with decreased early improvement in stroke severity and worse long-term functional outcomes. A higher baPWV was associated with progressive neurological deficit in acute deep subcortical infarction. We observed that baPWV has an independent prognostic value for predicting long-term functional outcome after acute stroke regardless of stroke subtype. This finding suggests that the measurement of baPWV, a simple and alternative method for determining arterial stiffness, during acute cerebral infarction may be useful for identifying individuals at increased risk of poor outcomes.

The cfPWV has been established as the gold standard method for assessing the stiffness of the central artery and an independent predictor of cardiovascular mortality and morbidity. Unlike the cfPWV, the baPWV reflects the stiffness of both the central and peripheral arteries. Peripheral arteries do not significantly change according to the aging process and disease states. The baPWV has been also criticized that the pulse wave does not propagate directly from the brachial arteries to the posterior tibial arteries in the same arterial tree and that the nomenclature of baPWV is inappropriate. Therefore, the application of baPWV as a clinical tool for cardiovascular risk assessment is concerning. Nevertheless, comparison studies indicated that baPWV shows a good correlation with cfPWV. Similar to cfPWV, baPWV was also associated with the presence of cardiovascular risk factor and atherosclerotic disease. Furthermore, studies indicated that left ventricular mass, diastolic dysfunction, and presence of coronary artery calcification were more strongly related

Table 3. Predictive Value of baPWV for Poor Functional Outcomes

<table>
<thead>
<tr>
<th>baPWV tertiles</th>
<th>Unadjusted OR (95% CI)</th>
<th>( P ) Value</th>
<th>Adjusted OR (95% CI)*</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1: &lt;17.55 m/s</td>
<td>Ref.</td>
<td>0.045</td>
<td>1.02 (0.56–1.85)</td>
<td>0.958</td>
</tr>
<tr>
<td>T2: 17.55–22.25 m/s</td>
<td>1.62 (1.02–2.61)</td>
<td>0.045</td>
<td>1.02 (0.56–1.85)</td>
<td>0.958</td>
</tr>
<tr>
<td>T3: &gt;22.25 m/s</td>
<td>&lt;0.001</td>
<td>3.93 (2.58–6.12)</td>
<td>&lt;0.001</td>
<td>2.28 (1.48–3.54)</td>
</tr>
</tbody>
</table>

At optimal cut-point

baPWV >21.33 m/s

baPWV, per SD (6.29 m/s)

Data were derived from logistic regression analysis. baPWV indicates brachial-ankle pulse wave velocity; CI, confidence interval; OR, odds ratio; and T, tertile.

*Adjusted for sex, age, National Institute of Health Stroke Scale score at admission, use of thrombolysis treatment, stroke subtype, hypertension, current smoking, peripheral artery disease, hemoglobin, high-sensitivity C-reactive protein, triglyceride, albumin, and blood urea nitrogen.

Figure 2. Relationships between brachial-ankle pulse wave velocity (baPWV) level and functional outcome by stroke subtypes. A to D, Black lines and gray shadows represent the estimated probability and the 95% confidence intervals for poor functional outcome (modified Rankin Scale [mRS] \( \geq2 \)) at the baPWV level based on the generalized additive model with splines. The x axis is limited from the 5th to the 95th percentile of baPWV.

Figure 3. Probability of mRS \( \geq2 \) to 0.0.2 for various stroke subtypes. Small vessel occlusion, Large artery atherosclerosis, Cardioembolism, Undetermined etiology.
with baPWV than with cfPWV. Clinical reports and meta-analysis indicate that the prognostic value of baPWV is as significant as that of cfPWV.

There are some possible mechanisms to explain the association between a higher baPWV and poor clinical outcomes after acute stroke. Similar to cfPWV, baPWV was increased in patients with vascular risk factors and atherosclerosis on multiple vascular beds. These coexisting conditions could lead to worse clinical outcomes after acute stroke. However, in the present study, we noted that the predictive value of baPWV remained significant, even after adjustment for multiple risk factors. Furthermore, the addition of baPWV significantly improved the predictive ability of a model for functional outcome. The predictive value of baPWV did not change, irrespective of the stroke subtype. These findings suggest that arterial stiffness may play a significant role in stroke outcome, independent of the stroke mechanism and known vascular risk factors.

Arterial stiffness is not only considered as a marker of atherosclerosis, but also has a pathophysiologic role, which could promote the development of hypertension, brain structural injury, macro/microvascular damage, and functional impairment. Increased arterial stiffness is responsible for a disproportionate increase in systolic arterial pressure and a relative decrease in diastolic pressure, which leads to the transmission of higher pulse pressure to distal organs, including the brain. The brain is an organ with a large amount of blood flow, and it is particularly susceptible to the excessive pulsatile stress because of low cerebral vascular resistance. High pulsatile stress results in circumferential stretching of the arterial wall, leading to intimal fibrosis, necrosis, remodeling, and atherosclerosis of the vessels. Patients with higher arterial stiffness showed blunted microvascular reactivity to ischemic stress. Structural injury or functional impairment of the cerebral artery, associated with arterial stiffness, may inhibit the formation of collateral blood flow during the acute phase of stroke. Arterial stiffness was also increased in patients with endothelial dysfunction, oxidative stress, and inflammatory conditions. These factors could increase ischemic cerebral injury during the acute phase of stroke.

In previous studies, increased baPWV and cfPWV were found to be independent predictors of new vascular events and cardiovascular mortality in the general population and many different patient groups such as hypertension, diabetes mellitus, and myocardial infarction. Central arterial stiffness determines the extent of diastolic flow reversal in the proximal descending aorta, which may contribute to the development of retrograde aortic plaque embolism. Although we did not have sufficient data for the assessment of new vascular events in the present study, a more frequent recurrence of stroke and cardiovascular events could be a cause of poor functional outcomes in patients with stroke and a higher baPWV.

The present study has both strengths and limitations. The strengths include the large sample size (>1000 patients) and the extensive work-up performed for determining cardiovascular risk factors and underlying systemic atherosclerosis. Moreover, the measurement of functional outcomes was performed in almost all study candidates (96.21%). However, the present study was performed retrospectively at a single center and included a population with a single ethnicity (Korean). Some patients who did not undergo baPWV measurement were excluded from the study, which may have caused selection bias. Even if we collected and adjusted multiple risk factors as possible, there was a possibility of residual confounding effect. Early change of stroke severity or occurrence of new vascular events at baPWV examination might act as a confounding factor between higher baPWV and poor functional outcome. In addition, because of the observational study design, we cannot prove a causal relationship between baPWV and functional outcome after acute stroke. Therefore, further study is needed to evaluate the causality and treatment effect of interventions that can reduce arterial stiffness, such as regular physical activity, intensive cholesterol reduction, and certain classes of antihypertensives.

Conclusions
We indicated that baPWV, a simple noninvasive method for measuring arterial stiffness, has an independent prognostic value for predicting long-term functional outcomes in patients with acute cerebral infarction regardless of stroke subtype.

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This work was supported by a grant from the Korea Healthcare Technology Research and Development Project, Ministry for Health and Welfare, Republic of Korea (HI10C2020, HI08C2149).

Disclosures
None.

References
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SUPPLEMENT MATERIAL

Title: Brachial-ankle pulse wave velocity for predicting functional outcome in acute stroke
short-title: baPWV and stroke functional outcome

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Supplemental Method

Supplemental Table I. Comparison of clinical characteristics between patients who underwent baPWV measurement and those who did not

Supplemental Table II. Comparison of clinical characteristics across the baPWV tertile groups

Supplemental Table III. Univariate analyses of the comparison of patients with good and poor functional outcomes after stroke

Supplemental References
Supplemental Method

Acute cerebral infarction was defined as a sudden onset of acute neurological deficits of presumed vascular etiology lasting 24 hours or evidence of acute infarction on brain computed tomography or magnetic resonance imaging.

Inclusion and exclusion criteria
During the study period, there were 2194 candidates who admitted with first-ever acute cerebral infarction within 3 days of symptom onset and registered in the Yonsei Stroke Registry. Of them, we excluded 687 patients due to the following reasons: 1) the presence of a history of previous stroke, 2) the presence of a history of malignancy, 3) the occurrence of in-hospital stroke (patients who developed stroke during admission for other illnesses), and 4) stroke of other determined etiology based on the Trial of Org 10172 in the Acute Stroke Treatment classification, which might act as a confounding factor for functional outcome. Moreover, we excluded 88 patients with an incomplete laboratory study or who did not undergo cerebral angiography, the findings of which were used for analysis in the present study. Of the remaining 1419 patients, 1134 patients completed baPWV measurement within 7 days after admission. Finally, we included 1091 patients who had available the modified Rankin Scale scores at 3 months after stroke onset.

Definition of Risk factor
Diabetes mellitus was diagnosed in cases when the patient had a fasting plasma glucose level of ≥7.0 mmol/L or was being treated with antidiabetic medications or insulin. Hypercholesterolemia was diagnosed in cases when the patient had a low-density lipoprotein cholesterol level of ≥4.1 mmol/L, total cholesterol level of ≥6.2 mmol/L, or was being treated with lipid-lowering agents after a diagnosis of hypercholesterolemia. Current smoking was considered when the patient had smoked within one year prior to admission. Coronary artery disease was determined in cases where a patient had a history of acute myocardial infarction, unstable angina, angiographically confirmed coronary artery occlusive disease, coronary artery bypass graft or percutaneous coronary artery stent/angioplasty. Use of thrombolysis treatment was considered when the patients received intravenous tissue-type plasminogen activator, intra-arterial thrombolysis, or combined intravenous and intra-arterial thrombolysis.

Cerebral angiography
Cerebral artery atherosclerosis was evaluated in the anterior, middle, posterior cerebral artery, basilar artery, internal carotid artery, and vertebral artery based on at least one of the cerebral angiographic study using digital subtraction angiography (DSA), magnetic resonance angiography (MRA), or computed tomographic angiography (CTA). For those patients who received both DSA and MRA or CTA, the results of the DSA were used for analysis. We defined that cerebral atherosclerosis was occlusion or ≥50% stenosis in any intracranial or extracranial cerebral artery. The degree of stenosis in the extracranial cerebral artery was measured using the method in the North American Symptomatic Carotid Endarterectomy Trial, and that in the intracranial cerebral artery was measured using the method in the Warfarin vs. Aspirin for Symptomatic Intracranial Disease Trial. CTA was performed using the 64-slice CT scanner (Siemens Sensation 64, Siemens Medical Solutions, Forchheim, Germany). MRA was performed using a 3.0-T system (Achieva, Philips, Best, the Netherlands, or Trio, Siemens, Erlangen, Germany).

Management of patients
Patients were treated according to the standard treatment protocols in our hospital that are based on the current guidelines for stroke. Patients admitted within 6 hours of stroke onset were considered for treatment with intravenous tissue-type plasminogen activator, intra-arterial thrombolysis, or combined intravenous and intra-arterial thrombolysis, according to our thrombolysis protocol.
Patients with high-risk for cardiac sources of embolism, such as atrial fibrillation, intracardiac thrombus, and mechanical prosthetic valve placement, received anticoagulation treatment. The other patients received antiplatelet agents, unless a contraindication to antithrombotic medication was present. All the patients, except for those with contraindications, were administered statin. Early rehabilitation was strongly encouraged for patients with neurological deficits.

Statistical method
The intergroup difference was determined using Fisher’s exact test, independent t-test, one-way analysis of variance, Mann–Whitney U test, or Kruskal–Wallis test, according to the type of variables. The NIHSS score was considered as a continuous variable. We computed the difference of area under curve between the models using the DeLong method. Continuous net reclassification improvement and integrated discrimination improvement were accessed using R-package of “PredictABEL”.

2
**Supplemental Table I.** Comparison of clinical characteristics between patients who underwent baPWV measurement and those who did not

<table>
<thead>
<tr>
<th>Variables</th>
<th>Did not undergo baPWV measurement (n = 285)</th>
<th>Underwent baPWV measurement (n = 1134)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, male</td>
<td>161 (56.49)</td>
<td>712 (62.79)</td>
<td>0.056</td>
</tr>
<tr>
<td>Age, year</td>
<td>69.07 ± 13.46</td>
<td>65.13 ± 12.44</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NIHSS score at admission</td>
<td>7 [3–16]</td>
<td>3 [1–6]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stroke subtype</td>
<td></td>
<td></td>
<td>0.031</td>
</tr>
<tr>
<td>Small vessel occlusion</td>
<td>16 (5.61)</td>
<td>99 (8.73)</td>
<td></td>
</tr>
<tr>
<td>Large artery atherosclerosis</td>
<td>66 (23.16)</td>
<td>214 (18.87)</td>
<td></td>
</tr>
<tr>
<td>Cardioembolism</td>
<td>94 (32.98)</td>
<td>317 (27.95)</td>
<td></td>
</tr>
<tr>
<td>Undetermined etiology</td>
<td>109 (38.25)</td>
<td>504 (44.44)</td>
<td></td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>213 (74.74)</td>
<td>815 (71.87)</td>
<td>0.374</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>86 (30.18)</td>
<td>340 (29.98)</td>
<td>0.943</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>58 (20.35)</td>
<td>287 (25.31)</td>
<td>0.089</td>
</tr>
<tr>
<td>Current smoking</td>
<td>56 (19.65)</td>
<td>311 (27.43)</td>
<td>0.008</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>47 (16.49)</td>
<td>281 (24.78)</td>
<td>0.003</td>
</tr>
<tr>
<td>Premorbid medication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>87 (30.53)</td>
<td>338 (29.81)</td>
<td>0.828</td>
</tr>
<tr>
<td>Anticoagulant</td>
<td>15 (5.26)</td>
<td>69 (6.08)</td>
<td>0.675</td>
</tr>
<tr>
<td>Statin</td>
<td>45 (15.79)</td>
<td>187 (16.49)</td>
<td>0.858</td>
</tr>
<tr>
<td>Antihypertensive</td>
<td>108 (37.89)</td>
<td>400 (35.27)</td>
<td>0.408</td>
</tr>
</tbody>
</table>

Values were presented as mean ± standard deviation, median [interquartile range], or number (%). *derived from Fisher’s exact test, independent t-test, or Mann-Whitney U test. NIHSS indicates National Institute of Health Stroke Scale; baPWV, brachial-ankle pulse wave velocity.
**Supplemental Table II.** Comparison of clinical characteristics across the baPWV tertile groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>T1; baPWV &lt;17.55 m/sec (n=364)</th>
<th>T2; baPWV 17.55–22.25 m/sec (n=363)</th>
<th>T3; baPWV &gt;22.25 m/sec (n=364)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, male</td>
<td>272 (74.73)</td>
<td>222 (61.16)</td>
<td>199 (54.67)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age, year</td>
<td>56.43 ± 11.89</td>
<td>66.15 ± 10.19</td>
<td>72.40 ± 8.89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NIHSS score at admission</td>
<td>2 [1-5]</td>
<td>3 [1-5]</td>
<td>3 [2-6]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Use of thrombolysis treatment</td>
<td>36 (9.89)</td>
<td>42 (11.57)</td>
<td>35 (9.62)</td>
<td>0.655</td>
</tr>
<tr>
<td>Stroke subtype</td>
<td></td>
<td></td>
<td></td>
<td>0.029</td>
</tr>
<tr>
<td>Small vessel occlusion</td>
<td>28 (7.69)</td>
<td>39 (10.74)</td>
<td>31 (8.52)</td>
<td></td>
</tr>
<tr>
<td>Large artery atherosclerosis</td>
<td>61 (16.76)</td>
<td>70 (19.28)</td>
<td>70 (19.23)</td>
<td></td>
</tr>
<tr>
<td>Cardioembolism</td>
<td>128 (35.16)</td>
<td>86 (23.69)</td>
<td>94 (25.82)</td>
<td></td>
</tr>
<tr>
<td>Undetermined</td>
<td>147 (40.38)</td>
<td>168 (46.28)</td>
<td>169 (46.43)</td>
<td></td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>200 (54.95)</td>
<td>273 (75.21)</td>
<td>316 (86.81)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>69 (18.96)</td>
<td>114 (31.40)</td>
<td>140 (38.46)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>90 (24.73)</td>
<td>95 (26.17)</td>
<td>93 (25.55)</td>
<td>0.905</td>
</tr>
<tr>
<td>Current smoking</td>
<td>137 (37.64)</td>
<td>93 (25.62)</td>
<td>72 (19.78)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>75 (20.60)</td>
<td>100 (27.55)</td>
<td>96 (26.37)</td>
<td>0.063</td>
</tr>
<tr>
<td>Peripheral artery disease</td>
<td>23 (6.32)</td>
<td>25 (6.89)</td>
<td>48 (13.19)</td>
<td>0.002</td>
</tr>
<tr>
<td>Premorbid medication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>87 (23.90)</td>
<td>119 (32.78)</td>
<td>121 (33.24)</td>
<td>0.007</td>
</tr>
<tr>
<td>Anticoagulant</td>
<td>29 (7.97)</td>
<td>15 (4.13)</td>
<td>23 (6.32)</td>
<td>0.093</td>
</tr>
<tr>
<td>Statin</td>
<td>56 (15.38)</td>
<td>62 (17.08)</td>
<td>62 (17.03)</td>
<td>0.786</td>
</tr>
<tr>
<td>Antihypertensive</td>
<td>103 (28.30)</td>
<td>135 (37.19)</td>
<td>144 (39.56)</td>
<td>0.003</td>
</tr>
<tr>
<td>Laboratory findings</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>14.56 ± 1.65</td>
<td>14.17 ± 1.56</td>
<td>13.91 ± 1.70</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>hs-CRP, nmol/L</td>
<td>4.01 ± 9.99</td>
<td>6.30 ± 14.96</td>
<td>8.43 ± 18.85</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cholesterol, mmol/L</td>
<td>4.91 ± 1.05</td>
<td>4.91 ± 1.16</td>
<td>4.97 ± 1.03</td>
<td>0.716</td>
</tr>
<tr>
<td>Triglyceride, mmol/L</td>
<td>1.46 ± 0.98</td>
<td>1.44 ± 1.23</td>
<td>1.34 ± 0.80</td>
<td>0.248</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>4.30 ± 0.38</td>
<td>4.27 ± 0.41</td>
<td>4.23 ± 0.41</td>
<td>0.106</td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
<td>7.40 ± 2.96</td>
<td>8.21 ± 3.49</td>
<td>8.39 ± 3.78</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Blood urea nitrogen, mmol/L</td>
<td>5.48 ± 2.39</td>
<td>5.96 ± 2.66</td>
<td>6.46 ± 3.01</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Creatinine, μmol/L</td>
<td>82.55 ± 51.48</td>
<td>86.17 ± 54.06</td>
<td>93.13 ± 69.69</td>
<td>0.049</td>
</tr>
<tr>
<td>Blood pressure at the baPWV measurement, mmHg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic arterial pressure</td>
<td>138.48 ± 19.21</td>
<td>152.37 ± 20.62</td>
<td>166.52 ± 22.64</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic arterial pressure</td>
<td>81.81 ± 12.01</td>
<td>86.41 ± 13.30</td>
<td>92.62 ± 14.69</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean arterial pressure</td>
<td>100.70 ± 13.55</td>
<td>108.40 ± 14.86</td>
<td>117.25 ± 16.33</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values were presented as mean ± standard deviation, median [interquartile range], or number (%). *derived from Fisher’s exact test, Kruskal-Wallis test, or one-way analysis of variance.
NIHSS indicates National Institute of Health Stroke Scale; hs-CRP, high-sensitivity C-reactive protein; baPWV, brachial-ankle pulse wave velocity.
**Supplemental Table III.** Univariate analyses of the comparison of patients with good and poor functional outcomes after stroke

<table>
<thead>
<tr>
<th>Variable</th>
<th>Good functional outcome (mRS ≤2, n = 910)</th>
<th>Poor functional outcome (mRS &gt;2, n = 181)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, male</td>
<td>602 (66.15)</td>
<td>91 (50.28)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age, year</td>
<td>63.51 ± 12.05</td>
<td>72.44 ± 10.73</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NIHSS score at admission</td>
<td>2 [1–4]</td>
<td>8 [4–14]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Use of thrombolysis treatment</td>
<td>82 (9.01)</td>
<td>31 (17.13)</td>
<td>0.002</td>
</tr>
<tr>
<td>Stroke subtype</td>
<td></td>
<td></td>
<td>0.058</td>
</tr>
<tr>
<td>Small vessel occlusion</td>
<td>87 (9.56)</td>
<td>11 (6.08)</td>
<td></td>
</tr>
<tr>
<td>Large artery atherosclerosis</td>
<td>156 (17.14)</td>
<td>45 (24.86)</td>
<td></td>
</tr>
<tr>
<td>Cardioembolism</td>
<td>256 (28.13)</td>
<td>52 (28.73)</td>
<td></td>
</tr>
<tr>
<td>Undetermined</td>
<td>411 (45.16)</td>
<td>73 (40.33)</td>
<td></td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>646 (70.99)</td>
<td>143 (79.01)</td>
<td>0.029</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>268 (29.45)</td>
<td>55 (30.39)</td>
<td>0.790</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>224 (24.62)</td>
<td>54 (29.83)</td>
<td>0.161</td>
</tr>
<tr>
<td>Current smoking</td>
<td>265 (29.12)</td>
<td>37 (20.44)</td>
<td>0.018</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>220 (24.18)</td>
<td>51 (28.18)</td>
<td>0.259</td>
</tr>
<tr>
<td>Peripheral artery disease</td>
<td>60 (6.59)</td>
<td>36 (19.89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Premorbid medication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>266 (29.23)</td>
<td>61 (33.70)</td>
<td>0.248</td>
</tr>
<tr>
<td>Anticoagulant</td>
<td>55 (6.04)</td>
<td>12 (6.63)</td>
<td>0.738</td>
</tr>
<tr>
<td>Statin</td>
<td>148 (16.26)</td>
<td>32 (17.68)</td>
<td>0.661</td>
</tr>
<tr>
<td>Antihypertensive</td>
<td>314 (34.51)</td>
<td>68 (37.57)</td>
<td>0.443</td>
</tr>
<tr>
<td>Laboratory finding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>14.30 ± 1.62</td>
<td>13.79 ± 1.82</td>
<td>0.001</td>
</tr>
<tr>
<td>hs-CRP, nmol/L</td>
<td>4.96 ± 12.17</td>
<td>12.72 ± 24.27</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cholesterol, mmol/L</td>
<td>4.92 ± 1.07</td>
<td>4.97 ± 1.13</td>
<td>0.611</td>
</tr>
<tr>
<td>Triglyceride, mmol/L</td>
<td>1.45 ± 1.07</td>
<td>1.20 ± 0.63</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>4.30 ± 0.39</td>
<td>4.09 ± 0.40</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
<td>7.96 ± 3.43</td>
<td>8.21 ± 3.54</td>
<td>0.369</td>
</tr>
<tr>
<td>Blood urea nitrogen, mmol/L</td>
<td>5.87 ± 2.47</td>
<td>6.44 ± 3.73</td>
<td>0.050</td>
</tr>
<tr>
<td>Creatinine, μmol/L</td>
<td>87.44 ± 60.92</td>
<td>86.50 ± 48.91</td>
<td>0.844</td>
</tr>
<tr>
<td>baPWV, m/sec</td>
<td>20.17 ± 5.83</td>
<td>24.11 ± 7.39</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Blood pressure at the baPWV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>measurement, mmHg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>151.94 ± 23.28</td>
<td>155.06 ± 26.11</td>
<td>0.107</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>87.25 ± 13.79</td>
<td>85.39 ± 15.42</td>
<td>0.104</td>
</tr>
<tr>
<td>Mean arterial pressure</td>
<td>108.82 ± 16.09</td>
<td>108.62 ± 17.98</td>
<td>0.888</td>
</tr>
</tbody>
</table>
Values were presented as mean ± standard deviation, median [interquartile range] or number (%).
*derived from Fisher’s exact test, independent t-test, or Mann-Whitney U test.
mRS indicates modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; hs-CRP, high-sensitivity C-reactive protein; baPWV, brachial-ankle pulse wave velocity.
**Supplemental References**


