Ability of the ankle brachial index and brachial-ankle pulse wave velocity to predict the 3-month outcome in non-cardioembolic stroke patients

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Conflict of Interest

Dr. Hosomi reports an honorarium from Mochida Pharmaceutical Co., LTD., which is outside the scope of the submitted work. Prof. Matsumoto reports grants from Takeda Pharmaceutical Co., LTD., Sanofi K.K., Mochida Pharmaceutical Co., LTD., Otsuka Pharmaceutical, and Daiichi Sankyo Co., LTD. and honoraria from Sanofi K.K., Bayer Health Care, and Daiichi Sankyo Co., LTD., which are outside the scope of the submitted work. The other authors declare no conflicts of interest.

Abstract

Aim: Both the ankle brachial index (ABI) and brachial-ankle pulse wave velocity (baPWV) are surrogates for atherosclerosis. The present study aimed to evaluate the ability of the ABI and baPWV to predict stroke outcome in first-ever non-cardioembolic stroke patients. **Methods:** This study included consecutive patients with first-ever non-cardioembolic stroke who were admitted within 1 week after onset to Ota Memorial Hospital between January 2011 and December 2013. Baseline characteristics and NIHSS scores at admission were noted. The ABI and baPWV were evaluated within 5 days after admission. The patients were categorized according to the ABI (cutoff 0.9) and baPWV cutoff 1870 cm/s determined with receiver operation curve for poor outcome. Clinical outcomes were defined based on the modified Rankin Scale (mRS) scores 3 months after stroke onset as good (0 and 1) or poor (2–6). **Results:** A total of 861 patients were available for evaluation. An ABI <0.9 and a baPWV >1870 cm/s were associated with poor outcome in the univariate analysis (p < 0.001 and p < 0.001, respectively). After adjusting for factors that showed differences between groups, an ABI <0.9 was associated with poor outcome. Among patients with an ABI ≥0.9, a higher baPWV showed a slight association with poor outcome after adjustment (odds ratio 1.46 [95%CI 0.95–2.27]).

Conclusion: Our study suggests that the stroke outcome can be predicted with the ABI, and slightly with baPWV when $ABI \ge 0.9$ in non-cardioembolic stroke patients.

Key words: ankle brachial index, brachial-ankle pulse wave velocity, ischemic stroke, non-cardioembolic stroke, outcome, modified Rankin Scale

Running title: ABI and baPWV can predict stroke outcome

Introduction

Atherothrombosis has been proposed as a composite disease that includes myocardial infarction, non-cardioembolic stroke, and peripheral artery disease. This is reasonable because each of the conditions is based on systemic atherosclerosis. Additionally, peripheral artery disease can be highly complicated with stroke. In the REACH Registry, 8.5% of prior stroke and transient ischemic attack patients had peripheral artery disease, and 23.0% of peripheral artery disease patients had stroke and transient ischemic attack¹. Additionally, 2.6% of peripheral artery disease patients developed nonfatal stroke and 8.8% died from stroke or myocardial infarction during a 2-year follow-up period².

Pulse wave velocity (PWV) reflects segmental arterial elasticity. Although carotid-femoral PWV is currently the gold standard measurement method, brachial-ankle PWV (baPWV) is more convenient method and widely available. It is well correlated with carotid-femoral PWV and reflects central arterial stiffness^{3, 4}). BaPWV is associated with subclinical stage of atherosclerosis and is an independent predictor of future cardiovascular events ^{5, 6}). Recently, the ankle brachial index (ABI) and baPWV were reported as predictive factors of stroke outcome⁷⁻¹⁰. Additionally, there is an inter-influence between atherosis and sclerosis, with ABI reflecting arterial atherosis¹¹) and baPWV for the evaluation of pathophysiological conditions related to atherosclerosis diminishes when the ABI is low^{14, 15}). Therefore, with regard to atherosclerosis pathophysiology, the ABI and baPWV are related. Previous studies have not considered the relation of the ABI and baPWV in the evaluation of their influence on stroke outcomes.

Aim

The present study aimed to evaluate the ability of the ABI and baPWV to predict

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stroke outcome in first-ever non-cardioembolic stroke patients. We hypothesized that the ABI and baPWV may be effect modifier of each other with their influence on stroke outcome. Additionally, the influence of the baPWV on stroke outcome may differ between patients with an ABI <0.9 and those with an ABI \geq 0.9.

Methods

Study design and participants

A total of 2413 patients with acute ischemic stroke, without transient ischemic attack, who were admitted to our Brain Attack Center between January 2011 and December 2013, were considered for inclusion in this study. Among these patients, 597 cardioembolic stroke patients, 730 patients with a prior stroke history, 76 patients who were admitted later than 7 days after stroke onset, 92 patients with tissue plasminogen activator treatment, 142 patients who received endovascular therapy, 62 patients who underwent surgical operation, and 546 patients with premorbid mRS \geq 2 were excluded from this study. In addition, there were 105 patients without available ABI and baPWV data, and 53 patients without 3-month modified Rankin Scale (mRS) data. Finally, 861 first-ever acute non-cardioembolic stroke patients (285 female patients; mean age, 70.2 ± 11.6 years) were available for evaluation in this study (Figure 1). This study was approved by the institutional review board of Brain Attack Center Ota Memorial Hospital (No. 133) and was performed according to the Ethical Guidelines for Medical and Health Research Involving Human Subject¹⁶ based on the Helsinki Declaration of 1964. This was a retrospective study, thus we did not obtain the patient's consent.

Diagnosis of stroke and date collection

The final diagnosis of the stroke subtype was made before discharge using echocardiography, brain computed tomography, magnetic resonance imaging, magnetic resonance angiography, or carotid ultrasonography, according to the Trial of Org 10172 in Acute Stroke Treatment classification¹⁷⁾. Physicians collected detailed data from all patients, including baseline characteristics (age, sex, body mass index (BMI), and drinking and smoking habits), vascular risk factors (hypertension, dyslipidemia, and diabetes mellitus), usage of antithrombotic agent prior to the stroke incidence, and neurologic deficits at admission using the National Institutes of Health stroke scale (NIHSS) score. Hypertension was defined as the use of anti-hypertensive medications prior to admission or a confirmed blood pressure \geq 140/90 mmHg 2 weeks after stroke onset. Diabetes mellitus was defined as an HbA1c value of \geq 6.5%, a fasting blood sugar level \geq 126 mg/dL, or the use of anti-diabetic medications. Dyslipidemia was defined as a total cholesterol level \geq 220 mg/dL, low-density lipoprotein cholesterol level \geq 150 mg/dL at admission, or the use of anti-dyslipidemia medications. The mRS scores were evaluated 3 months after onset, and the patients were categorized into good outcome (mRS score, 0 and 1) or poor outcome (mRS score, 2–6).

Measurements of ABI and baPWV

The ABI and baPWV were evaluated within 5 days after hospitalization. Brachial-ankle arterial blood pressures were simultaneously measured using a noninvasive automatic device (model BP-203RPE-III; Nihon Colin, Tokyo, Japan) after a 5-minute rest in the supine position. The ABI was defined as the ratio of systolic blood pressure in the ankle (dorsalis pedis and posterior tibial arteries) and the higher side of the 2 brachial arteries. The laterality, which showed a lower ABI, was used for evaluation. The baPWV on each side was calculated as the transmission distance divided by the transmission time. The transmission time between the right arm and both ankles was calculated using the waveform. The transmission distance between the right brachium and ankle was automatically calculated according to the height of the patient. The baPWV was evaluated on the higher side. **Statistical analysis**

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The data are expressed as mean \pm standard deviation (SD) or median (25th and 75th percentiles) for continuous variables and as frequency and percentage for discrete variables. The statistical significance of intergroup differences was assessed by using the analysis of variance, Kruskal-Wallis test, or χ^2 test, as appropriate. Univariate and multivariate logistic regression analyses were performed to evaluate the association of factors with poor outcome, and the odds ratios and 95% confidence intervals were calculated. Receiver operation characteristic curve was used to determine a cutoff baPWV for predicting poor outcome. In multivariate logistic regression analysis, factors that showed intergroup difference on evaluation with p-values <0.2 in the univariate analysis were used for adjustment. Statistical significance was set at a p-value <0.05. All statistical analyses were performed using JMP 12.0.1 statistical software (SAS Institute Inc., Cary, NC, USA).

Results

The ABI was less than 0.9 in 72 (8.4%) patients. The mean baPWV was 2059 ± 491 cm/s. On plotting the values of the ABI and baPWV, there were linear associations between these values, separately for both a low ABI (<0.9) and high ABI (≥ 0.9) (Figure 2). Poor outcome 3 months after onset was noted in 254 (29.5%) patients. An ABI <0.9 and the baPWV were associated with poor outcome in the univariate analysis (p < 0.001 and p < 0.001, respectively). And, a cutoff of baPWV for predicting poor outcome was 1870 cm/s.

The patients were categorized into four groups by combination of ABI (ABI <0.9 or ≥ 0.9) and baPWV (baPWV >1870 cm/s or ≤ 1870 cm/s). We classified patients with ABI ≥ 0.9 and baPWV ≤ 1870 cm/s as group 1 (n=316), ABI ≥ 0.9 and baPWV >1870 cm/s as group 2 (n=473), ABI <0.9 and baPWV ≤ 1870 cm/s as group 3 (n=21), and ABI <0.9 and baPWV >1870 cm/s as group 4 (n=51). The baseline characteristics of the patients are presented in Table 1. Age, BMI, ischemic stroke subtype, NIHSS score on admission, smoking,

hypertension, diabetes mellitus, and usage of antithrombotic agent were significantly different among four groups. NIHSS score was higher in group 4 than group 1 (P =0.002). The proportions of poor outcome (3 months mRS, 2–6) were significantly higher in the group 3 and 4 (p <0.001, Figure 3). With multivariate logistic regression models adjusted with these factors, group 2 showed slightly high odds ratio compared with group 1, although there was no statistical significance. Group 3 and 4 significantly associated with poor outcome (Table 3).

Discussion

In our study, among first-ever non-cardioembolic stroke patients, an ABI <0.9 and baPWV was associated with the outcome 3 months after stroke onset. The outcome 3 months after stroke onset was poorer in patients with an ABI <0.9 than in those with an ABI \ge 0.9. Within the subjects with ABI \ge 0.9, baPWV >1870 cm/s had some prognostic value of poor outcome in comparison with the subjects with baPWV \le 1800 cm/s.

It has been reported that a low ABI of <0.9 has a prognostic value for mortality and the incidences of coronary artery disease and stroke in the general population^{18, 19)}. In our study, 68.1% of the patients with a low ABI showed poor outcome 3 months after the events. A low ABI showed high predictivity for poor outcome 3 months after the events. Kim et al. reported that, in acute first-ever stroke patients, an ABI <0.9 was a predictive factor for mRS 0-2 3 month after stroke onset⁷⁾. A previous study reported that the mortality rate of ischemic stroke patients increases when peripheral artery disease is also present²⁰⁾. Some studies showed an association between an ABI <0.9 and an increase in mortality or recurrence of stroke in acute stroke patients; therefore, poor outcome at 3 months may result from high mortality or recurrence of stroke^{18, 21-23)}. In our study, the mortality rate was 4.3% in the low ABI patients and was 1.6% in the high ABI patients. Additionally, the stroke severity at

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admission was higher in the low ABI patients than in the high ABI patients. Therefore, it may have an influence on poor outcome.

Peripheral artery disease has been shown to be present in 10.1% of cerebrovascular disease patients²⁴⁾. In the present study, an ABI <0.9 was noted in 8.4% of patients. A recent study showed that 20.1% of patients with acute ischemic stroke or transient ischemic attack were diagnosed with peripheral artery disease on computed tomography angiography, and the proportion of patients with a low ABI was $12.2\%^{25}$. The criterion of an ABI <0.9 may underestimate the presence of peripheral artery disease, although it is widely used as a surrogate marker for peripheral artery disease. In this study, we did not perform any additional evaluation for peripheral artery disease than was detected with a low ABI.

The findings of our study suggest that a high baPWV is a weak predictive factor for poor outcome when the ABI is ≥ 0.9 . Our scatter plot of the ABI and baPWV, and their regression lines suggested that the accuracy of the baPWV may diminish when the ABI is <0.9. Our results are supported by the findings of a previous study that reported associations of mortality with the ABI and baPWV in dialysis patients²⁶⁾. In this previous study, a high baPWV predicted mortality only in patients with an ABI ≥ 0.9 . Kim et al. reported an association between the baPWV and the long-term outcome of acute first-ever stroke, without consideration of the ABI⁸⁾. They showed that patients with the highest baPWV tertile had a significantly high OR of poor outcome in comparison to patients with the lowest tertile. The proportion of patients with an ABI <0.9 was slightly higher in this previous study (8.8%) than in our study (8.4%). Additionally, the proportion of patients with an ABI <0.9 was lower in their lowest baPWV tertile (<1755 cm/s, 6.3%) than in our lower baPWV (<1870 cm/s, 9.7%). Ishizuka K et al. also reported an association between baPWV and 3-month mRS in acute stroke patients without consideration of the ABI⁹). Their study population was relatively small (n=327), and a proportion of mRS \geq 3 was higher (32.1%) than our study (16.4%). It was not provided the proportion of low ABI or PAD in their subjects. Moreover, both of the previous reports included a stroke subtype of cardioembolic stroke. These differences might account for the inconsistent results between these previous studies and our study.

Our study indicates that the predictive power of the baPWV is weaker than that of the ABI for the outcome of non-cardioembolic stroke. There are several explanations for this result. First, the baPWV was under estimated when patients had peripheral artery disease, as mentioned above. Moreover, the baPWV reflects the arterial stiffness that increases because of atherosclerosis. On the other hand, the ABI reflects stenosis or obstruction of the artery that reflects a progressed stage of atherosclerosis. Therefore, the ABI may reflect severe atherosclerosis that has an impact on stroke outcome more directly than the baPWV.

Limitations

There are several limitations in this study. First, this study was a single hospital retrospective study. This setting may have caused selection bias in our results. Second, there were significant differences in stroke severity at admission among the groups. Especially, patients with an ABI <0.9 had a high NIHSS score at admission. Although we included the NIHSS score for adjustment in the models of multivariate analysis, the difference may have influenced the prediction of stroke outcome with the ABI and baPWV.

Conclusion

Our study suggests that the stroke outcome can be predicted with the ABI, and slightly with baPWV when ABI \geq 0.9 in non-cardioembolic stroke patients. Further studies evaluating the ABI or baPWV for their association with stroke outcome should be designed considering their inter-relationship.

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References

- Cacoub PP, Abola MT, Baumgartner I, Bhatt DL, Creager MA, Liau CS, Goto S, Röther J, Steg PG, Hirsch AT: Cardiovascular risk factor control and outcomes in peripheral artery disease patients in the Reduction of Atherothrombosis for Continued Health (REACH) Registry. Atherosclerosis, 2009; 204:e86-92
- Meadows TA, Bhatt DL, Hirsch AT, Creager MA, Califf RM, Ohman EM, Cannon CP, Eagle KA, Alberts MJ, Goto S, Smith SC Jr, Wilson PW, Watson KE, Steg PG: Ethnic differences in the prevalence and treatment of cardiovascular risk factors in US outpatients with peripheral arterial disease: insights from the reduction of atherothrombosis for continued health (REACH) registry. Am Heart J, 2009; 158:1038-1045
- 3) Tanaka H, Munakata M, Kawano Y, Ohishi M, Shoji T, Sugawara J, Tomiyama H, Yamashina A, Yasuda H, Sawayama T, Ozawa T: Comparison between carotid-femoral and brachial-ankle pulse wave velocity as measures of arterial stiffness. J Hpertens, 2009; 27:2022-2027
- Tsuchikura S, Shoji T, Kimoto E, Shinohara K, Hatsuda S, Koyama H, Emoto M, Nishizawa Y: Brachial-ankle pulse wave velocity as an index of central arterial stiffness. J Atheroscler Thromb, 2010; 17:658-665
- 5) Torii S, Arima H, Ohkubo T, Fujiyoshi A, Kadota A, Takashima N, Kadowaki S, Hisamatsu T, Saito Y, Miyagawa N, Zaid M, Murakami Y, Abbott RD, Horie M, Miura K, Ueshima H; SESSA Research Group: Association between Pulse Wave Velocity and Coronary Artery Calcification in Japanese men. J Atheroscler Thromb, 2015; 22:1266-1277
- Tomiyama H, Matsumoto C, Shiina K, Yamashina A: Brachial-Ankle PWV: Current Status and Future Directions as a Useful Marker in the Management of

Cardiovascular Disease and/or Cardiovascular Risk Factors. J Atheroscler Thromb, 2016; 23:128-146

- 7) Kim J, Lee DH, Cha MJ, Song TJ, Park JH, Lee HS, Nam CM, Nam HS, Kim YD, Heo JH: Low ankle-brachial index is an independent predictor of poor functional outcome in acute cerebral infarction. Atherosclerosis, 2012; 224:113-117
- 8) Kim J, Song TJ, Kim EH, Lee KJ, Lee HS, Nam CM, Song D, Nam HS, Kim YD, Heo JH: Brachial-ankle pulse wave velocity for predicting functional outcome in acute stroke. Stroke, 2014; 45:2305-2310
- 9) Ishizuka K, Hoshino T, Shimizu S, Shirai Y, Mizuno S, Toi S, Maruyama K,
 Uchiyama S, Kitagawa K: Brachial-ankle pulse wave velocity is associated with
 3-month functional prognosis after ischemic stroke. Atherosclerosis, 2016; 255:1-5
- Milionis H, Vemmou A, Ntaios G, Makaritsis K, Koroboki E, Papavasileiou V, Savvari P, Spengos K, Elisaf M, Vemmos K: Ankle-brachial index long-term outcome after first-ever ischaemic stroke. Eur J Neurol, 2013; 20:1471-1478
- Feigelson HS, Criqui MH, Fronek A, Langer RD, Molgaard CA: Screening for peripheral arterial disease: the sensitivity, specificity, and predictive value of noninvasive tests in a defined population. Am J Epidemiol, 1994; 140:526-534
- 12) Lehmann ED: Clinical value of aortic pulse-wave velocity measurement. Lancet, 1999; 354:528-529
- Asmar R, Benetos A, Topouchian J, Laurent P, Pannier B, Brisac AM, Target R,
 Levy BI: Assessment of arterial distensibility by automatic pulse wave velocity
 measurement. Validation and clinical application studies. Hypertension, 1995;
 26:485-490
- 14) Kempczinski RF: Segmental volume plethysmography in the diagnosis of lower extremity arterial occlusive disease. J Cardiovasc Surg (Torino), 1982; 23:125-129

- 15) Motobe K, Tomiyama H, Koji Y, Yambe M, Gulinisa Z, Arai T, Ichihashi H, Nagae T, Ishimaru S, Yamashina A: Cut-off value of the ankle-brachial pressure index at which the accuracy of brachial-ankle pulse wave velocity measurement is diminished. Circ J, 2005; 69:55-60
- 16) http://www.mhlw.go.jp/file/
 06-Seisakujouhou-10600000-Daijinkanboukouseikagakuka/0000080278.pdf
- Adams HP Jr, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, Marsh EE
 3rd: Classification of subtype of acute ischemic stroke. Definitions for use in a
 multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment.
 Stroke, 1993; 24:35-41
- 18) Fowkes FG, Murray GD, Butcher I, Heald CL, Lee RJ, Chambless LE, Folsom AR, Hirsch AT, Dramaix M, deBacker G, Wautrecht JC, Kornitzer M, Newman AB, Cushman M, Sutton-Tyrrell K, Fowkes FG, Lee AJ, Price JF, d'Agostino RB, Murabito JM, Norman PE, Jamrozik K, Curb JD, Masaki KH, Rodríguez BL, Dekker JM, Bouter LM, Heine RJ, Nijpels G, Stehouwer CD, Ferrucci L, McDermott MM, Stoffers HE, Hooi JD, Knottnerus JA, Ogren M, Hedblad B, Witteman JC, Breteler MM, Hunink MG, Hofman A, Criqui MH, Langer RD, Fronek A, Hiatt WR, Hamman R, Resnick HE, Guralnik J, McDermott MM: Ankle brachial index combined with Framingham Risk Score to predict cardiovascular events and mortality: a meta-analysis. JAMA, 2008; 300:197-208
- Gronewold J, Hermann DM, Lehmann N, Kröger K, Lauterbach K, Berger K,
 Weimar C, Kälsch HI, Moebus S, Jöckel KH, Bauer M, Erbel R: Ankle-brachial
 index predicts stroke in the general population in addition to classical risk factors.
 Atherosclerosis, 2014; 233:545-550

- 20) Koton S, Tanne D, Green MS, Bornstein NM: Mortality and predictors of death 1 month and 3 years after first-ever ischemic stroke: data from the first national acute stroke Israeli survey (NASIS 2004). Neuroepidemiology, 2010; 34:90-96
- 21) Newman AB, Shemanski L, Manolio TA, Cushman M, Mittelmark M, Polak JF, Powe NR, Siscovick D: Ankle-arm index as a predictor of cardiovascular disease and mortality in the Cardiovascular Health Study. The Cardiovascular Health Study Group. Arterioscler Thromb Vasc Biol, 1999; 19:538-545
- 22) O'Hare AM, Katz R, Shlipak MG, Cushman M, Newman AB: Mortality and cardiovascular risk across the ankle-arm index spectrum: results from the Cardiovascular Health Study. Circulation, 2006; 113:388-393
- 23) Tsivgoulis G, Bogiatzi C, Heliopoulos I, Vadikolias K, Boutati E, Tsakaldimi S, Al-Attas OS, Charalampidis P, Piperidou C, Maltezos E, Papanas N: Low ankle-brachial index predicts early risk of recurrent stroke in patients with acute cerebral ischemia. Atherosclerosis, 2012; 220:407-412
- Bhatt DL, Steg PG, Ohman EM, Hirsch AT, Ikeda Y, Mas JL, Goto S, Liau CS,
 Richard AJ, Röther J, Wilson PW: International prevalence, recognition, and
 treatment of cardiovascular risk factors in outpatients with atherothrombosis. JAMA,
 2006; 295:180-189
- 25) Naito H, Naka H, Kobayashi M, Kanaya Y, Naito K, Kurashige T, Tokinobu H, Matsumoto M: Prevalences of peripheral arterial disease diagnosed by computed tomography angiography in patients with acute ischemic stroke. J Stroke Cerebrovasc Dis, 2016; 25:1128-1134
- 26) Kitahara T, Ono K, Tsuchida A, Kawai H, Shinohara M, Ishii Y, Koyanagi H,Noguchi T, Matsumoto T, Sekihara T, Watanabe Y, Kanai H, Ishida H, Nojima Y:

Impact of brachial-ankle pulse wave velocity and ankle-brachial blood pressure index on mortality in hemodialysis patients. Am J Kidney Dis, 2005; 46:688-696

	Group 1	Group 2	Group 3	Group 4	
	ABI <u>2</u> 0.9	ABI <u>2</u> 0.9	ABI<0.9	ABI<0.9	D 1
	baPWV≤1870	baPWV>1870	baPWV≤1870	baPWV>1870	P value
	cm/s	cm/s	cm/s	cm/s	
	N=316	N=473	N=21	N=51	
Age, years	63.2 ± 11.8	74.1 ± 9.1	72.5 ± 14.4	76.9 ± 8.7	< 0.001
Female, n (%)	101 (32.0)	160 (33.8)	9 (42.9)	15 (29.4)	0.679
BMI	23.9±3.6	23.2 ± 3.4	23.3 ± 2.8	23.0±3.7	0.019
Ischemic stroke					<0.001
Subtype					<0.001
LAA, n (%)	76 (24.1)	127 (26.9)	11 (52.3)	27 (53.0)	
SVO, n (%)	129 (40.8)	166 (35.1)	4 (19.1)	10 (19.6)	
Other, n (%)	24 (7.6)	19 (4.0)	2 (9.5)	2 (3.9)	
Undetermined, n (%)	87 (27.5)	161 (34.0)	4 (19.1)	12 (23.5)	
NIHSS score on					
admission	2 [1-3]	2 [1-4]	3 [1-4]	4 [2–5]	0.002
(median [IQR])					
Drinking, n (%)	143 (45.4)	190 (40.6)	6 (28.6)	20 (39.2)	0.310
Smoking, n (%)	177 (56.0)	178 (38.4)	11 (52.4)	23 (45.1)	< 0.001
Hypertension, n (%)	211 (69.6)	374 (81.1)	16 (76.2)	47 (92.2)	< 0.001
Dyslipidemia, n (%)	189 (60.4)	272 (58.0)	12 (57.1)	28 (56.0)	0.889
Diabetes	00(215)	176 (27 5)	11 (52 4)	27(52.0)	0.008
mellitus, n (%)	99 (SI.S)	1/0 (37.3)	11 (32.4)	27 (32.9)	0.008
Antithrombotic	23 (7.3)	60 (12.7)	5 (23.8)	13 (25.5)	<0.001
agent, n (%)					~0.001

Table 1. Characteristics among the patients categorized with the ABI and baPWV

ABI, ankle brachial index; baPWV, brachial-ankle pulse wave velocity; LAA, large artery atherosclerosis; SVO, small vessel occlusion; NIHSS, National Institutes of Health stroke scale; IQR, interquartile raange; 3M mRS, modified Rankin scale 3-month after onset

	ABI≥0.9	ABI<0.9
	Group 1	Group 3
baPWV≤1870	N=316	N=21
	1.0 (reference)	5.19 (1.85-15.14)
	Group 2	Group 4
baPWV>1870	N=473	N=51
	1.46 (0.95-2.27)	3.37 (1.63-7.08)

Table 2. Odds ratio for poor outcome of groups categorized with ABI and baPWV

Odds ratio (95% confidence intervals) was calculated with multivariate logistic regression analysis adjusted with age, body mass index, large artery atherosclerosis, National Institute of Health stroke scale on admission, smoking, diabetes mellitus, and antithrombotic agent, which associated with poor outcome.

ABI, ankle brachial index; baPWV, brachial-ankle pulse wave velocity.

Figure Legends

Figure 1. Flow chart of inclusion and exclusion criteria

Figure 2. Scatter plot of the ABI and baPWV, and their regression lines

There are linear associations between these factors, separately for both a low ABI (<0.9) and

a high ABI (≥0.9).

ABI, ankle brachial index; baPWV, brachial-ankle pulse wave velocity

Figure 3. Proportion of subjects who showed poor outcome (3M mRS 2-6) and mortality

Figure 1.



Figure 2.



Figure 3.

