Ankle-Brachial Index and Neurologic Deterioration in Acute Ischemic Stroke

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Background: Few studies have examined the relationship between abnormal ankle-brachial index (ABI) and short-term outcome in patients with acute ischemic stroke (AIS). *Methods:* We included 209 consecutive patients with AIS admitted to our hospital and divided them into abnormal ABI (≤.9) and normal ABI (>.9) groups. We defined neurologic deterioration (ND) as an increase of 1 or more points in the National Institutes of Health Stroke Scale score within 7 days of stroke onset. Clinical characteristics were compared between the 2 groups. Then, we performed a multiple logistic regression analysis to identify independent predictors of ND. In the multivariate analysis, the ABI values were used separately as binary variables in different cutoff thresholds (.9, 1.0, and 1.1). *Results:* Of the 209 patients, 24 (11.5%) had an abnormal ABI. The patients in abnormal and normal ABI groups showed significant differences in carotid arterial stenosis (37.5% versus 18.9%; $P = .040$), intracranial artery stenosis (54.2% versus 18.9%; $P < .001$), and previous use of antiplatelet drugs (58.3% versus 29.2%; $P = .004$). According to the multivariate analysis, ABIs of .9 or less and 1.0 or less were positively associated with ND (odds ratio [OR], 1.74; 95% confidence interval [CI], 1.03-2.89; $P = .034$ and OR, 1.63; 95% CI, 1.05-2.54; $P = .027$, respectively), whereas an ABI value of 1.1 or less was not an independent predictor of ND (OR, 1.17; 95% CI, 0.79-1.74; $P = .43$). *Conclusions:* Not only an ABI of .9 or less but also an ABI of 1.0 or less can be a predictor of ND in patients with AIS. **Key Words:** Acute ischemic stroke—ankle-brachial index—atherosclerosis—neurologic deterioration—progressive stroke.

Introduction

The ankle-brachial index (ABI) is an easy and reliable tool for identifying patients with subclinical peripheral arterial disease (PAD) and is used as an indicator of generalized atherosclerosis.[1-3] An abnormal ABI (≤.9) is broadly used as an indicator of lower limb PAD[4] and has been shown to predict all-cause mortality, vascular-related deaths, and nonfatal cardiovascular events, even after adjusting for conventional vascular risk factors.[1,3,5]

Recent studies have suggested a high prevalence of low ABI among patients with acute ischemic stroke (AIS) or transient ischemic attack, with prevalence estimates ranging from 24%-51%.[6-10] In patients with AIS, low ABI has been shown to be an independent predictor of subsequent stroke, myocardial infarction, or death.[7,9,11] Furthermore, it was reported that low ABI may be a predictive factor of the initial severity and long-term functional outcomes of AIS.[11-13] However, few data exist on the relationship between abnormal ABI and early neurologic deterioration (ND) during the acute phase of ischemic stroke. This study aimed to determine if the ABI predicted the risk of ND in patients with AIS, independently of other potential confounding factors.

Materials and Methods

Study Protocol

The ethics committee of our institution approved the study protocol. We conducted a hospital-based

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retrospective study involving 250 consecutive patients with AIS hospitalized in the Department of Neurology at the Tokyo Women's Medical University Hospital between May 2009 and August 2012. The subjects were eligible if they (1) were recruited within 1 week of the onset of stroke and (2) underwent ABI measurement during hospitalization. Of 250 patients, 209 were eligible.

Our hospital maintains a registry of all consecutive patients, and data were collected from a computerized observational database. We used a standardized case report form and abstracted several demographic and clinical variables, including date of the event, past medical history, risk factors for stroke, previous medications, findings of physiological examination, and neurologic symptoms. We also documented the results of all diagnostic tests and details of treatment performed during the hospitalization. The person imputing the data was blinded to the purpose of this study.

AIS was defined as the sudden onset of acute neurologic deficits with evidence of acute infarction on brain computed tomography or magnetic resonance imaging. The severity of the event was assessed according to the National Institutes of Health Stroke Scale (NIHSS) score. ND was defined as an increase of 1 or more points in the NIHSS score during the 7 days after admission.

Stroke subtypes were classified on the basis of the Trial of ORG 10172 in Acute Stroke Treatment classification.[14] Diagnosis of large artery atherosclerosis (LAA) required significant (>50%) stenosis of a large artery, which was relevant to the infarct lesion. Cardioembolism was diagnosed when a patient had at least 1 potential cardiac source of embolism that was based on the Trial of ORG 10172 in Acute Stroke Treatment classification. Small vessel occlusion was diagnosed when a patient presented with a classic lacunar syndrome, a small infarct lesion (<15 mm) in the perforating artery territory, no stenosis of large artery, and no potential cardiac sources of embolism and LAA.

Risk Factors

Patients were diagnosed with a history of hypertension if they had evidence of systolic blood pressure of 140 mm Hg or more or diastolic blood pressure of 90 mm Hg or more, or if they had received any antihypertensive medication. Diabetes mellitus was specified as fasting serum glucose of 126 mg/dL or more, serum glucose of 200 mg/dL or more on 2 random measurements, glycated hemoglobin (HbA1c) of 6.5% or more, or use of antidiabetic therapy (oral hypoglycemic agents or insulin). Dyslipidemia was diagnosed if the patient had low-density lipoprotein cholesterol of 140 mg/dL or more or total cholesterol of 220 mg/dL or more, or if the patient had been treated with lipid-lowering agents after diagnosis of dyslipidemia. Smoking status was defined as current use. The estimated glomerular filtration rate was calculated using the modification of diet in renal disease formula by the Japanese coefficient. Chronic kidney disease was defined as an estimated glomerular filtration rate less than 60 mL/minute·per 1.73 m^2. Intracranial arterial stenosis of 50% or more on magnetic resonance angiography, 3-dimensional computed tomography angiography, or digital subtraction angiography was considered a significant finding. Findings of carotid artery ultrasonography were evaluated by appropriately trained neurologists, and stenosis of 50% or more was defined as significant extracranial arterial stenosis. Patients with either significant intra- or extracranial arterial stenosis were considered to have major artery lesions. Coronary artery disease was defined as a history of either angina pectoris or myocardial infarction, with or without coronary artery bypass surgery or percutaneous transluminal coronary angioplasty. Atrial fibrillation was diagnosed using the findings of at least 1 electrocardiogram (ECG) obtained before or during hospitalization. Routine cardiac tests included an initial 12-lead ECG, transthoracic echocardiography, and a Holter ECG; transesophageal echocardiography was also performed if indicated.

ABI Measurement

ABI was measured using a noninvasive automatic pulse wave analyzer (Form PWV/ABI; Colin Co Ltd, Komaki, Japan) after a 5-minute rest in the supine position. According to the recommendations of the American Heart Association,[15] ABI was calculated as the ratio of the systolic pressure in the posterior tibial artery and the highest systolic pressure in the 2 brachial arteries. After the individual calibration process, blood pressure was measured simultaneously using cuffs on both upper limbs (brachial arteries) and lower limbs (posterior tibial arteries). ABI was then calculated automatically and expressed as a ratio of systolic blood pressure in the ankle to that in the arm. An abnormal ABI was defined as ABI .9 or less than .9 on either the right or the left side.

Statistical Analysis

Descriptive statistics were obtained using the JMP statistical software package (version 10; SAS Institute, Cary, NC). Statistical significance of intergroup differences was assessed by the χ^2 test for categorical variables and the Student *t* test or the Mann–Whitney *U* test for continuous variables. To identify predictors of ND, we performed the multiple logistic regression analysis. Mulvariate adjustments were done using following variables: age, sex, hypertention, diabetes mellitus, smoking status, AF, prior use of antithrombotic drugs, carotid aterial stenosis, intracranial arterial stenosis, and ABI value. ABI values were used as binary variables in different cutoff thresholds (.9, 1.0, and 1.1) separately (models A, B, and C, respectively). Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. In all analyses, $P < .05$ was considered significant.