# Risk Factors of Neurological Deterioration in Patients with Cerebral Infarction due to Large-Artery Atherosclerosis

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*Background:* In some patients with acute ischemic stroke, neurological deterioration (ND) is observed, and it is difficult to predict at the time of admission. Especially in some patients with large-artery atherosclerosis (LAA), aggressive medical treatments and surgical interventions might be helpful to prevent ND. Therefore, we investigated factors associated with ND in patients with LAA. *Methods:* We studied patients with LAA who were admitted to our hospital. We divided them into 2 groups with (group 1) and without deterioration (group 2), and evaluated their medical records, risk factors, and radiological findings, such as number of diffusion-positive lesion and degree of stenosis. *Results:* Our study population consisted of 171 patients; 71 (41.5%) did and 100 (58.5%) did not suffer deterioration. By univariate analysis, blood pressure (BP), heart rate, National Institutes of Health Stroke Scale (NIHSS) score, number of diffusion-positive lesion, count of red blood cell, high-density lipoprotein, and degree of stenosis differed significantly between the 2 groups. By multivariate analysis, systolic BP (≥170 mm Hg, odds ratio: 7.20, $P < .001$) was associated with ND. Furthermore, number of diffusion-weighted image (DWI)–positive lesion (≥8), degree of stenosis (>80.0%), and NIHSS score (≥4) were also independent factors associated with ND. *Conclusions:* High BP, severity of neurological deficit at the time of admission, and radiological findings, such as degree of stenosis and number of DWI-positive lesion, are independently associated with ND in patients with LAA. **Key Words:** Ischemic stroke—large-artery atherosclerosis—neurological deterioration—diffusion-weighted image—high blood pressure.
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## Introduction

Neurological deterioration (ND) in some patients with ischemic stroke is observed after hospitalization in spite of medical treatments, and ND makes their activity of life worsen. Therefore, it is important to prevent ND in patients with acute ischemic stroke. Previously, progressive ischemic stroke was reported to be associated with high blood pressure (BP), high serum glucose, ischemic lesions in the carotid artery territory, and basilar artery branch disease.[1-4] Especially, patients with large-artery atherosclerosis (LAA) can be treated by aggressive medical treatment or interventions such as carotid endarterectomy, carotid artery stenting, and percutaneous

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transluminal angioplasty to prevent ND. In this study, we investigated factors of ND in patients with acute ischemic stroke due to LAA.

Microembolism detected using transcranial Doppler ultrasonography, called microembolic signals (MES), was reported to be associated with recurrence of ischemic stroke and ND.[5,6] Liberman et al. reported that MES were present in 40% of patients with a watershed infarct pattern. Recurrence of cerebral ischemia was observed in 19% of included patients.[5] We speculated that the total number of ischemic lesions on diffusion-weighted image (DWI) might be associated with the frequency of MES detected by transcranial Doppler ultrasonography. Therefore, we studied the association between total number of ischemic lesions on DWI and ND during hospitalization.

## Methods

The study was approved by the local ethics committee and based on patients' consent. This retrospective analysis was based on a prospectively collected register of consecutive patients between January 2011 and December 2016. We extracted data of intended patients from the registry. Patients with cerebral infarction due to LAA within 24 hours from onset, who were diagnosed using magnetic resonance imaging (MRI) by experienced neurologists and neurosurgeons, were included. Patients were diagnosed as acute ischemic stroke due to LAA based on classification of the Trial of ORG 1072 in Acute Stroke Treatment criteria. Their degree of stenosis was measured by digital subtraction angiography (DSA). We excluded patients who were treated by intravenous tissue plasminogen activator or endovascular treatment, such as stent retrievers and aspiration catheters, at the time of admission.

We divided our patients into 2 groups: group 1, ND, indicating 2 points or more based on National Institutes of Health Stroke Scale (NIHSS) worsening during hospitalization; and group 2, no ND, indicating less than 2 points worsening based on NIHSS or neurological improvement during hospitalization. We compared clinical findings, laboratory data, and MRI findings between the 2 groups.

### *Definition and Complicated Diseases*

Continuous variables that were measured at the time of admission are expressed as mean ± standard deviation. Diabetes mellitus was defined as a hemoglobin A1C (National Glycohemoglobin Standardization Program) level greater than 6.5% or the current use of drugs for hyperglycemia; dyslipidemia was defined as a total cholesterol concentration greater than 220 mg/dL or low-density lipoprotein greater than 140 mg/dL or the current use of drugs for dyslipidemia. Hypertension was defined as the current use of antihypertensive drugs.

### *MR Imaging*

The standard MRI protocol in our hospital included DWI, $T_2$*-weighted gradient echo imaging ($T_2$*-WI), fluid-attenuated inversion recovery, and intra- and extracranial 3-dimensional time-of-flight MR angiography (MRA). MRI examinations were performed with a 3-tesla MRI scanner (Discovery MR 750; GE Healthcare, Milwaukee, WI) equipped with an 8-channel phased array head coil. All patients were examined with DWI, MRA, and $T_2$*-WI. The imaging sequences and parameters were as follows: DWI (field of view [FOV]: 24 cm, matrix: 128 × 128, repetition time [TR]: 6000 ms, echo time [TE]: 65 ms, slice thickness: 5 mm, gap: 0 mm, number of slices: 30, b-factor: 1000, number of excitations: 2, and acceleration factor: 2), MRA (FOV: 22 cm, matrix: 512 × 224, TR: 30 ms, TE: 2.8 ms, flip angle: 17°, slice thickness: 1.2 mm, and number of slices: 66), and $T_2$*-WI gradient echo (FOV: 24 cm, matrix: 320 × 192, TR: 400 ms, TE: 28 ms, flip angle: 28°, slice thickness: 6 mm, gap: 1.5 mm, and number of slices: 18).

We counted number of ischemic lesions on DWI on each slice. A single neurologist evaluated the MRI without referencing any patient information.

### *Statistical Analysis*

Comparisons were performed using the Mann–Whitney $U$ test for continuous variables and the $\chi^2$ test for categorical variables. Statistical significance was defined as $P < .05$. Values of $P$ less than .1 in the univariate analysis were used in the evaluation of the multivariate analysis. To calculate the sensitivity and specificity of parameters employed to evaluate risk factors associated with ND, we prepared a receiver operating characteristic curve. Cutoff values with the highest sensitivity and specificity were included in the final logistic regression analysis. We removed factors with higher $P$ values, which might influence each other in the multivariate analysis. Results are expressed as adjusted odds ratios and the corresponding 95% confidence interval (CI). Statistical significance was set at $P < .05$. All statistical analyses were performed with SPSS Statistics version 20.0 software package (IBM Corporation, Tokyo, Japan).

## Results

Between January 2011 and December 2016, 972 patients with acute ischemic stroke were admitted to our hospital; 171 of them (134 men and 37 women, age: 72.6 ± 10.0 years) who were diagnosed as having LAA were included in our study (Fig 1). Of these, 71 (41.5%, group 1) did and 100 (58.5%, group 2) did not manifest ND. In comparison of laboratory data, high-density lipoprotein levels were significantly different between the groups (group 1: 48.6 ± 12.5, group 2: 53.7 ± 15.2, $P = .028$). In clinical findings, severity of neurological deficit measured based on the NIHSS, heart rate, and BP at the time

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