Predictors of Neurologic Deterioration in Patients with Small-Vessel Occlusion and Infarcts in the Territory of Perforating Arteries

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Background: It is difficult to predict neurologic deterioration in patients with small-vessel occlusion (SVO), that is, small infarcts in the territory of cerebral perforating arteries. *Methods:* We reviewed 110 patients with SVO who were admitted to our hospital. We divided them into groups with (n = 32, group 1) and without deterioration (n = 78, group 2) and evaluated their medical records, risk factors, magnetic resonance imaging findings, grade of periventricular hyperintensity (PVH), maximum diameter of the infarct area, and the number of slices showing infarcts on diffusion-weighted images (DWI). *Results:* Our study population consisted of 110 patients (71 males and 39 females; mean age 69.2 years): 32 (29%) did and 78 (71%) did not suffer deterioration. By univariate analysis, the age, current smoking, history of stroke, maximum diameter of the infarcted area, number of DWI slices with infarcts, frequency of PVH, and PVH grade based on Fazekas classification differed significantly between the 2 groups. By multivariate analysis, conventional risk factors other than PVH and history of stroke were not associated with neurologic deterioration (PVH grade ≥ 2 versus PVH grade ≤ 1, odds ratio 6.72, $P = .006$; with stroke versus without stroke, odds ratio .21, $P = .049$). We also found that higher the PVH grade, the worse the National Institutes of Health Stroke Scale score at the time of discharge. *Conclusions:* PVH and without history of stroke are independently associated with neurologic deterioration in patients with SVO. **Key Words:** PVH grade—small-vessel occlusion—predictors—neurologic deterioration.

Introduction

Small-vessel occlusion (SVO) may be divided into branch atheromatous disease[1] because of atheromatous changes at the origin of perforating arteries[2] and lacunar infarction attributable to endothelial dysfunction of perforating arteries.[1-6] However, these stroke subtypes are based on pathologic findings. Branch atheromatous disease may be one of the most important causes of neurologic deterioration and factors associated with neurologic deterioration. Clinically, it is difficult to predict neurologic deterioration after onset of stroke. Whereas the prognosis of most SVO patients tends to be good with no or only minor neurologic deficits,[7] some

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suffer neurologic deterioration after hospitalization.[8-10] In some SVO patients, there is deterioration of neurologic function, and their ability to pursue activities of daily living is significantly impeded.[11] Therefore, it is important to prevent neurologic deterioration in patients with acute ischemic stroke. Progressive ischemic stroke has been reported to be associated with high blood pressure, high serum glucose, ischemic lesions in the carotid artery territory, and basilar artery branch disease.[9,10,12-14] We studied the characteristics of patients with acute ischemic stroke who had neurologic deterioration after hospitalization. Present study was performed based on the local ethics committee.

Patients and Methods

We retrospectively studied 110 consecutive SVO patients who were diagnosed according to the Trial of Org 10172 in Acute Stroke Treatment classification between April 2008 and July 2012 within 2 days from onset of acute ischemic stroke. The diagnosis was based on clinical signs, magnetic resonance imaging scan, especially diffusion-weighted image (DWI) findings, and physiological examinations, such as ultrasound cardiogram and electrocardiogram Holter monitor test. Patients with MRI evidence of infarcts in the territory of perforating arteries, for example, paramedian lesions of the pons, corona radiata, and posterior limb of the internal capsule and thalamus, were included.[10,15]

We investigated their medical records and evaluated risk factors, such as current smoking, hypertension (HT), diabetes mellitus (DM), dyslipidemia (DL), and atrial fibrillation. DM was defined as a hemoglobin A1C level greater than 6% or current use of drugs for hyperglycemia and DL as a total cholesterol concentration greater than 220 mg/dL and/or triglyceride greater than 200 mg/dL or current use of drugs for hyperlipidemia. HT was defined as systolic blood pressure greater than 140 mm Hg, diastolic blood pressure greater than 90 mm Hg, or current use of depressor drugs. Chronic kidney disease (CKD) was defined by the estimated glomerular filtration rate, calculated with the Cockcroft–Gault equation, as lower than 60 mL/min. We also used the National Institutes of Health Stroke Scale (NIHSS) as a clinical sign.

We divided our 110 SVO patients into groups, with (group 1, n = 32) and without neurologic deterioration (group 2, n = 78). Neurologic deterioration was defined as 1 point or more worsening of the NIHSS score during hospitalization.

We compared the groups for risk factors, MRI characteristics, maximum diameter of the infarct area, the number of lesion-positive DWI slices, Fazekas grade of the periventricular white matter region,[16] the number of cerebral microbleeds, and laboratory data acquired at the time of admission.

Magnetic Resonance Imaging

All patients underwent MRI and MR angiographic studies on admission. MRI scans were acquired on a 3-T Signa EXITE HD 3.0 T scanner (GE, Milwaukee, WI). All MRIs were acquired within 2 days after onset. The scan parameters for standard DWI echo-planar imaging (EPI) were repetition time (TR): 6000 ms/echo time (TE): 70 ms; b values, 0 and 1000 sec/mm^2; field of view, 24 cm; acquisition matrix; and EPI factor, 37. For T2-weighted image (T2-WI), they were TR: 3500 ms/TE: 100 ms, and for $T_2^* - WI$ gradient-echo, they were TR: 400 ms/TE: 30 ms in the axial plane. The slice thickness was 7 mm. Cerebral microbleeds were defined as small hypointense signals on $T_2^* - WI$ scans. We ignored symmetrical signal loss in the basal ganglia and cerebellum because of potential iron deposition or calcification.

Statistical Analysis

Continuous variables are expressed as the mean ± standard deviation. Comparisons were with the independent samples t test; 1-way analysis between the groups was with analysis of variance or the Mann–Whitney U test for continuous or ordinal variables; the χ^2 test for categorical variables was used for univariate analysis; and P values less than .10 by multivariate logistic regression analysis were used. In multiple comparison, differences were assessed with Bonferroni multiple comparison procedure. To calculate the sensitivity and specificity of parameters employed to evaluate risk factors associated with neurologic deterioration, we prepared a receiver operator characteristic curve. Cutoff values with the highest sensitivity and specificity were included in the final logistic regression analysis. Results were expressed as the adjusted odds ratios and corresponding 95% confidence intervals (CIs). Statistical significance was set at P less than .05. All statistical analyses were with the SPSS program, version 20.0 (SPSS; IBM Corporation, Tokyo, Japan) for Windows 7.

Results

Between April 2008 through July 2012, 452 patients with acute ischemic stroke were admitted to our hospital, of which 110 patients (71 men and 39 women, age 69.2 ± 12.1 years) were included in our study. Of these, 32 (29%, group 1) did and 78 did not manifest neurologic deterioration (group 2). The NIHSS score at the time of admission was not different (group 1: 3.6 ± 2.8, group 2: 3.2 ± 2.2, $P = .628$), but it was significantly different at the time of discharge (group 1: 5.7 ± 3.9, group 2: 1.5 ± 1.7, $P < .001$). With the exception of age, history of stroke, and current smoking, there was no significant difference in the patients' baseline characteristics (Table 1). Patients in group 1 were significantly older (74.0 ± 11.6