Factors Associated with Proximal Carotid Axis Occlusion in Patients with Acute Stroke and Atrial Fibrillation

Yuki Sakamoto, MD,* Shoichiro Sato, MD,* Yuka Kuronuma, MD,* Kazuyuki Nagatsuka, MD,† Kazuo Minematsu, MD,* and Kazunori Toyoda, MD*

Background: Patients with atrial fibrillation (AF) are more likely to exhibit proximal carotid axis occlusion than those without AF. However, clinical characteristics associated with proximal arterial occlusion (PAO) in acute stroke patients with AF are not fully known. This study was aimed to elucidate the factors correlated with PAO. *Methods:* Consecutive patients with acute ischemic stroke developed in the middle cerebral artery (MCA) territory and AF who underwent magnetic resonance angiography (MRA) within 24 h from onset were retrospectively enrolled. Prior users of warfarin were excluded. Patients were divided into 3 groups based on the site of arterial occlusion: occlusion at the internal carotid artery (ICA), at the horizontal segment of the MCA (M1), and at the MCA branch or no identifiable occlusion. Clinical characteristics were compared between the 3 groups, and the factors associated with proximal vessel occlusion were evaluated with ordinal logistic regression analysis. All variables identified on univariable analyses with *P* values less than .1 were entered into the model. *Results:* A total of 244 patients (124 women, median 80 years old [interquartile range 72-87], median National Institutes of Health Stroke Scale [NIHSS] score 16 [7-22]) were studied. MRA was performed median 2.7 h (1.5-8.9) after stroke onset. Occlusion site was the ICA in 34 patients, M1 in 78, and MCA branch or no occlusion in the remaining 132. As the occlusion site was more proximal, patients were older and more female, the initial NIHSS score was higher, levels of D-dimer and brain natriuretic peptide (BNP) were higher, and histories of heart failure and systemic embolism were more common. On multivariable ordinal logistic regression analysis, female sex (odds ratio [OR] 1.83, 95% confidence interval [CI] 1.03-3.26), advanced age (OR 1.37, 95% CI 1.02-1.84 for every 10 years), history of systemic embolism (OR 14.9, 95% CI 1.41-157.75), and higher BNP level (OR 1.03, 95% CI 1.01-1.07 for every 100 pg/mL) were independent factors associated with the risk of occlusion at more proximal arteries. The risk was 2.68-fold higher (95% CI 1.28-5.61) in patients having 2 of the following factors: female sex, age more than 80 years, systemic embolism, and BNP greater than 250 pg/mL; and 4.50-fold (2.11-9.59) higher in those having 3 or 4 of the 4 factors compared with those without any of these factors. *Conclusions:* Female sex, advanced age, history of systemic embolism, and higher BNP level were independently associated with more proximal carotid axis occlusion. Patients with AF having

From the *Department of Cerebrovascular Medicine; and †Department of Neurology, National Cerebral and Cardiovascular Center, Suita, Japan.

Received May 14, 2013; revision received June 30, 2013; accepted July 5, 2013.

Sources of funding: This study was supported in part by an Intramural Research Fund (H24-6-30) for Cardiovascular Diseases of National Cerebral and Cardiovascular Center and Grants-in-Aid (H23-Junkanki-Ippan-010 and H24-Junkanki-Ippan-011) from the Ministry of Health, Labor and Welfare, Japan.

Disclosures None.

Address correspondence to Shoichiro Sato, MD, Department of Cerebrovascular Medicine, National Cerebral and Cardiovascular Center, 5-7-1 Fujishirodai, Suita, Osaka 565-8565, Japan. E-mail: sato.shoichiro@ncvc.go.jp.

1052-3057/$ - see front matter

http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2013.07.002

these factors may be prone to have relatively large thrombi in the heart. **Key Words:** Acute ischemic stroke—magnetic resonance angiography—atrial fibrillation—arterial occlusion.

Introduction

The site of arterial occlusion plays a key role in neurologic severity and outcome in patients with acute ischemic stroke. Patients with proximal arterial occlusion (PAO) show more severe symptoms,[1,2] poorer outcomes,[3] and more limited response to intravenous tissue plasminogen activator therapy than those with distal artery occlusion.[4,5] The factors associated with PAO are not fully known, and related factors are considered to differ according to the etiologies. Embolic PAO seems to be correlated with embolus size. Patients with atrial fibrillation (AF) often develop severe ischemic stroke and poor outcomes,[6,7] even after thrombolytic therapy,[8] mainly because they are more likely to have PAO on admission than patients without AF.[8] However, clinical factors associated with PAO in patients with AF are not well known.

The aim of this study was to clarify the clinical characteristics related to PAO in acute stroke patients with AF.

Methods

A prospective database of consecutive patients with acute stroke treated in the Stroke Care Unit in the National Cerebral and Cardiovascular Center was created (National Cerebral and Cardiovascular Center Stroke Registry).[9] From April 2006 to May 2012, consecutive acute stroke patients (<24 h from onset) with AF who fulfilled the following criteria were retrospectively enrolled from the registry: (1) underwent magnetic resonance imaging (MRI) examinations including diffusion-weighted imaging (DWI) and time-of-flight magnetic resonance angiography (MRA) on admission and (2) developed ischemic stroke in the middle cerebral artery (MCA) territory confirmed on initial DWI with compatible acute neurologic deficits. Patients with contraindications to MRI (eg, cardiac pacemakers or mechanical heart valve replacements) were excluded. Stroke patients having concomitant etiology other than AF (eg, >50% stenosis on the responsible artery) and patients on anticoagulant therapy were also excluded because anticoagulant therapy could reduce intracardiac thrombi and then affect the site of arterial occlusion in subjects with AF.[10] The institutional ethics committee approved this study.

Clinical Background Characteristics

Clinical background characteristics, including sex, age, cardiovascular risk factors, and medical history, were obtained on admission. Cardiovascular risk factors were defined as: (1) hypertension, history of using antihypertensive agents, systolic blood pressure of 140 mm Hg or more, or diastolic blood pressure of 90 mm Hg or more before or 2 or more weeks after stroke onset; (2) diabetes mellitus, use of hypoglycemic agents, random glucose level of 200 mg/dL or more, or glycosylated hemoglobin of 6.5% or more on admission; (3) hyperlipidemia, use of antihyperlipidemic agents, or a serum total cholesterol level of 220 mg/dL or more; and (4) current smoking habit. Routine blood biochemistry examinations were performed on admission. Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS), and functional outcome was estimated by the modified Rankin scale[11] score at hospital discharge or 30 days from onset. AF was diagnosed on 12-lead electrocardiogram or a history of AF was confirmed.

Neuroimaging

MRI studies including DWI and time-of-flight MRA were performed on admission using a commercially available echo planar instrument operating at 1.5 T (Siemens MAGNETOM Vision or MAGNETOM Sonata scanner, Erlangen, Germany). DWI was obtained using the following parameters: repetition time/echo time, 4000/100 ms; *b* values, 0 and 1000 s/mm^2; field of view, 24 cm; acquisition matrix, 96 × 128; and slice thickness, 4.0 mm, with a 1.0-mm intersection gap. The occluded vessel was determined on initial MRA. All patients were divided into 3 groups based on the occluded site: at the internal carotid artery (ICA) group, at the MCA horizontal segment (M1 group), and at the MCA branch occlusion or no identifiable occlusion (Branch group).

Statistical Analysis

First, clinical background characteristics were compared among the 3 groups. Univariable analyses were performed using the chi-square test, Fisher exact test, or the Kruskal–Wallis test, as appropriate. The data are presented as median values (interquartile range) or frequencies (%). Next, multivariable ordinal logistic regression analysis was performed to identify independent factors associated with more proximal arterial occlusion. This model allows the outcome variable to have more than 2 categories and estimates a proportional odds ratio (OR) for each predictor of shifting to a more proximal arterial occlusion category (eg, the ICA group versus the M1 and Distal groups or the ICA and M1 groups versus the Distal group). Sex, age, and all clinical characteristics identified on univariable analyses with *P* values less