

Original Paper

Clinical, Laboratory, and Imaging Characteristics of Transient Ischemic Attack Caused by Large Artery Lesions: A Comparison between Carotid and Intracranial Arteries

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Key Words

Acute ischemic lesions · Carotid artery · Intracranial artery · Ischemic stroke · Stenosis · Transient ischemic attack

Abstract

Background/Aims: The aims of this study were to determine the differences in clinical characteristics and the risk of ischemic stroke between patients with transient ischemic attack (TIA) attributable to extracranial carotid and intracranial artery occlusive lesions. **Methods:** Among 445 patients admitted to our stroke care unit within 48 h of TIA onset between April 2008 and December 2013, 85 patients (63 men, mean age 69.4 years) with large artery occlusive lesions relevant to symptoms were included in this study. The primary endpoints were ischemic stroke at 2 and 90 days after TIA onset. **Results:** Twenty-eight patients had carotid artery occlusive lesions (extracranial group), and 57 patients had intracranial artery occlusive lesions (intracranial group). Patients in the intracranial group were significantly younger, had lower levels of fibrinogen, and were less likely to have occlusion when compared with those in the extracranial group. Eleven patients in the extracranial group and none in the intracranial group underwent revascularization procedures within 90 days of TIA onset. The 2-day risk (14.2 vs. 0%, $p = 0.044$) and the 90-day risk (17.1 vs. 0%, $p = 0.020$) of ischemic stroke after TIA onset were significantly higher in the intracranial group than in the extracranial group. **Conclusions:** Among our patients with TIA caused by large artery disease, patients with intracranial artery occlusive lesions were more frequent and were at higher risk of early ischemic stroke than those with extracranial carotid artery occlusive lesions. These data highlight the importance of prompt assessment of intracranial artery lesions in patients with TIA.

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Introduction

Transient ischemic attack (TIA) is a medical emergency that is associated with a high risk of early ischemic stroke. Carotid artery occlusive lesions [1, 2] or intracranial artery occlusive lesions [3–6] were associated with subsequent stroke after TIA. The Fukuoka Stroke Registry (FSR) examining 693 patients with definite TIA showed that not only carotid arterial stenosis but also intracranial arterial stenosis was significantly associated with stroke in the short and long term for up to 3 years [7]. We also previously reported that large arterial occlusive lesions were significantly associated with recurrent TIA or subsequent ischemic stroke [8].

It is well known that the distribution of atherosclerotic lesions in the cervicocephalic vascular systems varies among different race/ethnic groups. In Caucasians, atherosclerosis develops frequently in the extracranial carotid arteries, whereas intracranial atherosclerosis is a common cause of stroke in Asians [9–11]. Thus, it is presumed that TIA attributable to intracranial atherosclerosis is more frequent than that attributable to extracranial carotid atherosclerosis in Japanese.

Several therapeutic strategies, including antiplatelet therapy, statin use, carotid endarterectomy (CEA), and carotid artery stenting (CAS), have been proven to reduce the risk of recurrent stroke in patients with symptomatic extracranial carotid stenosis [12].

In contrast, patients with symptomatic intracranial artery stenosis are still at high risk of stroke recurrence despite medical therapy, including antiplatelet therapy, and risk factor modification. Annual recurrence rates of ischemic stroke were reported to be as high as 15% in the aspirin arm of the Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) trial [13, 14] and as high as 12% in the aggressive medical treatment arm of the Stenting and Aggressive Medical Management for Preventing Recurrent stroke in Intracranial Stenosis (SAMMPRIS) trial [15, 16]. The SAMMPRIS trial also demonstrated that angioplasty and stenting in addition to aggressive medical therapy were significantly inferior in terms of safety and efficacy when compared with aggressive medical therapy alone [15, 16].

Therefore, we hypothesized that, among TIA patients receiving immediate diagnosis and treatment at a stroke center, those with intracranial artery occlusive lesions would be at higher risk of subsequent ischemic stroke compared with those with extracranial carotid artery occlusive lesions. We aimed to determine the differences in clinical characteristics and the risk of subsequent ischemic stroke between patients with TIA caused by extracranial carotid artery occlusive lesions versus those with TIA caused by intracranial artery occlusive lesions among the patients admitted to our stroke care unit.

Methods

Patient Selection

Between April 2008 and December 2013, 445 patients were admitted to our stroke care unit within 48 h of TIA onset. As a general rule, TIA patients were hospitalized for urgent workup and treatment in our unit if they presented to the hospital within 48 h of TIA onset. An attending physician experienced in stroke medical care made the ultimate diagnosis of TIA and was responsible for management decisions. The diagnosis of TIA was made if focal neurological symptoms ascribable to a vascular etiology lasted <24 h, irrespective of the presence of ischemic insults on imaging. Patients receiving intravenous thrombolysis or catheter interventions were not included. The carotid and intracranial arteries were assessed by ultrasonography, magnetic resonance angiography (MRA), CT angiography (CTA), and/or digital subtraction angiography (DSA) in all 445 patients.

In this study, a significant occlusive lesion was defined as the presence of $\geq 50\%$ stenosis or occlusion in the extracranial carotid or intracranial arteries, as detected by any modality. Extracranial carotid arteries included the extracranial internal carotid artery (ICA), and intracranial arteries included the ICA, middle cerebral artery, anterior cerebral artery, vertebral artery, basilar artery, and posterior cerebral artery. In the results of vascular imaging, 138 patients had carotid or intracranial occlusive lesions, including symptomatic and asymptomatic lesions. Of these, 105 patients were considered as having extracranial carotid or intracranial artery occlusive lesions in an appropriate territory to explain their neurological symptoms. Eight patients who were diagnosed as having cervicocephalic artery disease other than atherosclerosis (including dissection and cerebral angiitis) and 12 patients with potential cardioembolic sources, such as atrial fibrillation, were excluded. Finally, a total of 85 patients (63 men, mean age 69.4 ± 11.7 years) were included in this study. We categorized the 85 subjects into two different groups: patients with TIA attributable to extracranial carotid artery occlusive lesions (extracranial group) and those with TIA attributable to intracranial artery occlusive lesions (intracranial group). The hospital's ethics committee approved the study protocol.

Patient Characteristics

The following patient demographic and clinical characteristics were obtained from review of our stroke database and medical records: sex, age, history of ischemic stroke, ischemic heart disease, hypertension (blood pressure of $\geq 140/90$ mm Hg or use of antihypertensive medications), diabetes mellitus (fasting blood glucose ≥ 126 mg/dl, positive 75-gram oral glucose tolerance test result, or use of insulin or oral hypoglycemic agents), and dyslipidemia [serum low-density lipoprotein cholesterol (LDL-Chol) ≥ 140 mg/dl, high-density lipoprotein cholesterol (HDL-Chol) < 40 mg/dl, triglycerides (TG) ≥ 150 mg/dl, or use of antidyslipidemic medications], and current smoking and drinking habits. Multiple TIA was defined as the occurrence of at least two TIAs (the qualifying TIA and one other TIA) within the 90 days prior to the qualifying TIA. We also calculated the ABCD² score for each patient.

Blood Tests

Peripheral venous blood samples were obtained on admission. Tests included measurement of white blood cell count, hemoglobin, hematocrit, platelets, aspartate aminotransferase, alanine aminotransferase, γ -glutamyl transpeptidase, alkaline phosphatase, creatinine, total cholesterol, LDL-Chol, HDL-Chol, TG, glucose, high sensitivity C-reactive protein, and fibrinogen.

Imaging

We used the results of the diffusion-weighted imaging (DWI) examination to evaluate whether acute ischemic lesions were present on admission. Extracranial carotid and intracranial arteries were estimated by ultrasonography, MRA, CTA, and/or DSA. The degree of occlusive lesions was classified into three grades: moderate (50–69% stenosis), severe (70–99% stenosis), and occlusion. DSA data were used whenever available. The degree of extracranial carotid artery stenosis was estimated according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method [17], and the degree of intracranial artery stenosis was estimated according to the WASID trial [13, 14]. The grade of the degree of intracranial artery stenosis on MRA was identified according to a previously published scoring scheme [9, 18].

Clinical Outcomes

All 85 patients underwent follow-up at 90 days via direct clinical visit or telephone interview. The outcome measure was the occurrence of ischemic stroke within 2 and 90 days of TIA onset. Ischemic stroke was defined by focal neurological deficit lasting > 24 h. Treat-

ments after the qualifying TIA event with oral agents (including aspirin, dual antiplatelet therapy, anticoagulant agents, and statins) and any revascularization procedures (including CEA, CAS, stenting of intracranial artery, and bypass surgery) were recorded.

Statistical Analysis

All analyses were performed using JMP 10 software (SAS Institute Inc.). Continuous variables were expressed as the mean \pm standard deviation (age, blood pressure on admission, and blood test findings) and as the median and interquartile range (IQR; ABCD² score). Categorical data are summarized as percentages. Differences between groups were analyzed using the Student t test and Mann-Whitney U test for continuous values and the Pearson χ^2 test and Fisher exact test for categorical variables, as appropriate. The risk of ischemic stroke after TIA onset was estimated by Kaplan-Meier event-free survival curves. Statistical test results were considered significant when $p < 0.05$.

Results

All 85 patients in this study underwent carotid ultrasonography and intracranial MRA. DSA was performed in 42 patients (49.4%). One of 85 patients had both carotid and intracranial artery occlusive lesions. This patient was considered as having extracranial carotid artery occlusive lesions relevant to symptoms because he had severe stenosis in the extracranial carotid artery but moderate stenosis in the intracranial artery. Therefore, 28 patients were considered as having extracranial carotid artery occlusive lesions relevant to symptoms (extracranial group), and 57 patients were considered as having intracranial artery occlusive lesions relevant to symptoms (intracranial group). Intracranial artery occlusive lesions relevant to symptoms were found in middle cerebral artery in 30 patients, ICA in 13 patients, basilar artery in 9 patients, vertebral artery in 4 patients, and anterior cerebral artery in 1 patient.

Table 1 shows a comparison of patient characteristics between the carotid and intracranial groups. Patients in the intracranial group were younger, were less frequently prescribed premorbid antiplatelet agents and statins, had lower levels of fibrinogen, and were less likely to have occlusion when compared with those in the extracranial group. A history of ischemic heart disease tended to be less common, multiple TIA to be more common, and systolic and diastolic blood pressure on admission to be higher in the intracranial group than in the extracranial group. Patients in the intracranial group were less frequently prescribed statins after TIA onset when compared with those in the extracranial group. In the extracranial group, 11 patients underwent revascularization procedures, including seven CEA and four CAS. The timing of these procedures ranged from 13 to 80 days (mean, 33.6 days) after onset of TIA. In the intracranial group, no patient underwent revascularization procedures.

In the extracranial group, no patient had ischemic stroke within 90 days of TIA onset. In the intracranial group, 10 patients had subsequent ischemic stroke within 90 days of TIA onset, and ischemic strokes occurred within 2 days of TIA onset in 8 of these 10 patients. All ten infarcts were found in the territory of arteries with occlusive lesions responsible for the neurological symptoms of qualifying TIA. Cerebral infarctions were detected in the carotid system of 8 patients and in the vertebrobasilar system of 2 patients. Figure 1 shows Kaplan-Meier ischemic stroke-free survival curves of the extracranial and intracranial groups. Both the 2-day risk (14.2 vs. 0%, $p = 0.044$) and 90-day risk (17.1 vs. 0%, $p = 0.020$) of ischemic stroke after TIA onset were significantly higher in the intracranial group than in the extracranial group.

Table 1. Comparison of patients' characteristics between the extracranial and intracranial groups

	All patients (n = 85)	Carotid group (n = 28)	Intracranial group (n = 57)	p value
<i>Background characteristics</i>				
Males	63 (74.1)	23 (82.1)	40 (70.2)	0.236
Age, years	69.4±11.7	73.5±9.3	67.5±12.3	0.014
<i>History of</i>				
Ischemic stroke	18 (21.1)	7 (25.0)	11 (19.3)	0.446
Ischemic heart disease	15 (17.6)	8 (28.6)	7 (12.3)	0.064
Hypertension	73 (85.9)	26 (92.9)	47 (82.5)	0.196
Diabetes mellitus	26 (30.6)	8 (28.6)	18 (31.6)	0.777
Dyslipidemia	51 (60.0)	20 (71.4)	31 (54.4)	0.132
Multiple TIA	27 (31.8)	5 (17.9)	22 (37.6)	0.054
Current smoking	19 (22.4)	5 (17.9)	14 (24.6)	0.486
Current drinking	35 (41.2)	11 (39.3)	24 (42.1)	0.803
<i>Premorbid treatment</i>				
Antiplatelets	34 (40.0)	16 (57.2)	18 (31.6)	0.024
Antihypertensives	40 (47.1)	17 (60.7)	23 (40.4)	0.077
Statins	24 (28.2)	12 (42.9)	12 (21.1)	0.039
<i>ABCD² score</i>				
SBP on admission, mm Hg	155.8±26.0	148.6±29.3	159.5±23.6	0.094
DBP on admission, mm Hg	84.0±16.7	78.8±17.7	86.6±15.8	0.053
<i>Clinical features</i>				
Unilateral weakness	66 (77.6)	25 (89.3)	41 (71.9)	0.167
Speech disturbance without weakness	10 (11.8)	1 (3.6)	9 (15.8)	0.528
<i>Duration of symptoms</i>				
≥60 min	33 (38.8)	13 (46.4)	20 (35.1)	
10–59 min	39 (45.9)	12 (42.9)	27 (47.4)	
ABCD ² score	5 [4–6]	5 [4–6]	5 [4–6]	0.424
<i>Blood test findings</i>				
WBC, ×10 ³ /μl	7.5±2.7	8.1±3.4	7.2±2.3	0.222
Hb, g/dl	13.5±1.9	13.3±2.1	13.7±1.88	0.375
Hct, %	40.1±5.6	39.4±6.0	40.5±5.4	0.408
Platelets, ×10 ³ /μl	222.7±75.5	232.8±76.9	217.8±75.0	0.399
AST, U/l	26.0±18.7	29.0±29.8	24.5±9.6	0.437
ALT, U/l	20.7±17.0	22.5±25.3	19.9±11.1	0.609
γ-GTP, U/l	44.0±68.5	38.4±26.7	46.8±81.7	0.484
ALP, U/l	235.4±66.2	241.5±62.1	232.4±68.5	0.542
Cre, mg/dl	0.93±0.41	1.01±0.46	0.89±0.39	0.239
T-Chol, mg/dl	193.4±39.1	184.3±34.0	197.9±40.9	0.111
LDL-Chol, mg/dl	116.4±36.6	108.9±36.9	119.8±36.2	0.213
HDL-Chol, mg/dl	48.7±14.5	47.4±12.0	49.4±15.6	0.518
TG, mg/dl	165.2±142.9	148.8±97.9	173.3±160.6	0.387
Glucose, mg/dl	137.6±51.7	147.1±70.7	132.9±39.1	0.328
hs-CRP, mg/dl	0.68±2.28	1.33±3.23	0.36±1.56	0.143
Fibrinogen, mg/dl	342.4±90.0	378.9±116.4	323.9±67.1	0.026
<i>Imaging findings</i>				
Grade of occlusive lesions				0.019
Moderate	28 (33.3)	10 (35.7)	18 (32.1)	
Severe	39 (46.4)	8 (28.6)	31 (55.4)	
Occluded	17 (20.3)	10 (35.7)	7 (12.5)	
DWI lesions	27 (31.8)	7 (25.0)	20 (35.1)	0.348

Table 1 (continued)

	All patients (n = 85)	Carotid group (n = 28)	Intracranial group (n = 57)	p value
<i>Acute treatment with oral agents</i>				
Aspirin	78 (91.8)	26 (92.9)	52 (91.2)	0.797
DAPT	29 (34.1)	9 (32.1)	20 (35.1)	0.788
Anticoagulant agents	0	0	0	
Statins	51 (60.0)	22 (78.6)	29 (50.9)	0.014
Revascularization procedures within 90 days	11 (12.9)	11 (39.3)	0	<0.001

Values are mean ± SD, n (%) or median [IQR]. SBP = Systolic blood pressure; DBP = diastolic blood pressure; WBC = white blood cells; Hb = hemoglobin; Hct = hematocrit; AST = aspartate aminotransferase; ALT = alanine aminotransferase; γ -GTP = γ -glutamyl transpeptidase; ALP = alkaline phosphatase; Cre = creatinine; T-Chol = total cholesterol; hs-CRP = high-sensitivity C-reactive protein; DAPT = dual antiplatelet therapy.

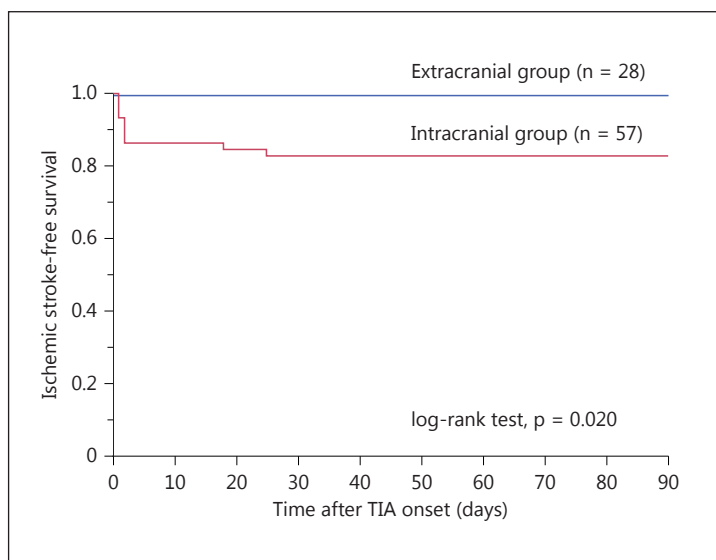


Fig. 1. Kaplan-Meier ischemic stroke-free survival curves following TIA in the extracranial and intracranial groups.

Discussion

This study showed that, among 445 patients admitted to our stroke care unit within 48 h of TIA onset, 28 patients (6.3%) had extracranial carotid artery occlusive lesions and 57 patients (12.8%) had intracranial artery occlusive lesions responsible for the neurological symptoms. In a prospective study that enrolled 510 patients with TIA and minor stroke, extracranial carotid artery occlusion or stenosis $\geq 50\%$ was detected on CTA in 9.4%, and intracranial artery occlusion or stenosis $\geq 50\%$ was detected on CTA in 20.8% [4]. The FSR showed that 21.8% of patients had carotid stenosis and 22.4% of patients had intracranial stenosis [7]. The incidence of extracranial carotid and intracranial artery occlusive lesions in our study was lower than that in those previous studies. This discrepancy may be partially explained by the fact that we excluded patients diagnosed as having cervicocephalic artery occlusive disease other than atherosclerosis and patients with potential cardioembolic sources. We

confirmed that intracranial artery occlusive lesions were more common than extracranial carotid artery occlusive lesions in TIA patients with large artery disease.

Patients in the intracranial group were significantly younger, had lower levels of fibrinogen, and were less likely to have occlusion when compared with those in the extracranial group. Several studies have revealed that risk factors are different between extracranial carotid atherosclerosis and intracranial atherosclerosis [10]. To the best of our knowledge, however, no study has investigated the difference in patient characteristics between those with extracranial carotid atherosclerosis and those with intracranial atherosclerosis among TIA patients.

We observed that no patient had a subsequent ischemic stroke within 90 days of TIA onset in the extracranial group, although the extracranial group included only 28 patients. When compared with patients in the intracranial group, patients in the extracranial group were prescribed statins more frequently. In addition, approximately 40% of patients in the extracranial group underwent revascularization procedures within 90 days of TIA onset. Therefore, the revascularization procedures could reduce the 90-day risk of subsequent ischemic stroke in patients with extracranial carotid artery occlusive lesions. However, because the timing of these procedures ranged from 13 to 80 days after TIA onset, we believe that TIA patients with extracranial carotid artery occlusive lesions were at a lower 2-day risk of ischemic stroke when compared with those with intracranial artery occlusive lesions, regardless of the revascularization procedures.

This study showed that in the intracranial group, the 2-day and 90-day risk of subsequent ischemic stroke after TIA was 14.2 and 17.1%, respectively. The WASID trial enrolled patients with TIA or nondisabling stroke within the preceding 3 months and demonstrated a corresponding 50–99% stenosis in a major intracranial artery on angiography [13, 14]; in that study, the 7-day and 90-day risk of ischemic stroke in the arterial territory after TIA was 1.4 and 6.9%, respectively. In the SAMMPRIS trial [15, 16], in which patients with 70–99% intracranial artery stenosis who had stroke or TIA within the preceding 30 days were randomly assigned to aggressive medical management plus angioplasty and stenting or aggressive medical management alone for stroke prevention, the 30-day rate of stroke or death was 5.8% in the aggressive medical treatment arm. The risk of subsequent ischemic stroke in our patients with intracranial artery occlusive lesions was much higher than that in the WASID and SAMMPRIS trials. The median time from the qualifying event to randomization was 17 days in the WASID trial and 7 days in the SAMMPRIS trial. Therefore, it is conceivable that some patients at higher risk of stroke were excluded from the WASID and SAMMPRIS trials because they were not randomized due to early recurrence. In contrast, subjects in our study were patients who were admitted to our stroke care unit within 48 h of TIA onset, and 80% of recurrent ischemic stroke events occurred within 2 days of TIA onset.

In this study, the diagnosis of TIA was made if focal neurological symptoms ascribable to a vascular etiology lasted <24 h, irrespective of the presence of ischemic insults on imaging, according to the classical definition of TIA [19]. The advent of brain imaging techniques has led to the understanding that up to one third of patients with symptoms lasting <24 h actually has an infarction [20]. This resulted in a new tissue-based definition of TIA, that is, ‘a transient episode of neurological dysfunction caused by focal brain, spinal cord or retinal ischemia, without acute infarction’ [20], which is different from the traditional time-based definition. In present study, DWI lesions were found in 7 (25.0%) of 28 patients in the extracranial group and 20 (35.1%) of 57 patients in the intracranial group. There was no statistically significant difference in DWI positivity between the two groups.

Our study had several limitations. First, the sample size of this study was too small to avoid types 1 and 2 errors. Second, we analyzed only inpatients with TIA using a retrospective

design, which might lead to a selection bias. However, most TIA patients were hospitalized for urgent workup and treatment in our unit if they presented to the hospital within 48 h of TIA onset. Therefore, our study patients were essentially consecutive cases. Finally, this study was conducted in a single center. It is necessary to confirm these findings in large multicenter settings to determine if they can be generalized.

In conclusion, among patients with TIA caused by large artery disease, patients with intracranial artery occlusive lesions were more frequent and at a higher risk of early ischemic stroke than those with extracranial carotid artery occlusive lesions. These data highlight the importance of prompt assessment of intracranial artery lesions in patients with TIA.

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Disclosure Statement

The authors have no conflicts of interest to disclose.

References

- 1 Sheehan OC, Kyne L, Kelly LA, Hannon N, Marnane M, Merwick A, McCormack PM, Duggan J, Moore A, Moroney J, Daly L, Harris D, Horgan G, Williams EB, Kelly PJ: Population-based study of ABCD2 score, carotid stenosis, and atrial fibrillation for early stroke prediction after transient ischemic attack. *The North Dublin TIA Study. Stroke* 2010;41:844–850.
- 2 Purroy F, Montaner J, Molina CA, Delgado P, Ribo M, Varez-Sabin J: Patterns and predictors of early risk of recurrence after transient ischemic attack with respect to etiologic subtypes. *Stroke* 2007;38:3225–3229.
- 3 Poisson SN, Nguyen-Huynh MN, Johnston SC, Furie KL, Lev MH, Smith WS: Intracranial large vessel occlusion as a predictor of decline in functional status after transient ischemic attack. *Stroke* 2011;42:44–47.
- 4 Coutts SB, Modi J, Patel SK, Demchuk AM, Goyal M, Hill MD; Calgary Stroke Program: CT/CT angiography and MRI findings predict recurrent stroke after transient ischemic attack and minor stroke: results of the prospective CATCH study. *Stroke* 2012;43:1013–1017.
- 5 Ssi-Yan-Kai G, Nasr N, Faury A, Catalaa I, Cognard C, Larrue V, Bonneville F: Intracranial artery stenosis or occlusion predicts ischemic recurrence after transient ischemic attack. *AJNR Am J Neuroradiol* 2013;34:185–190.
- 6 Purroy F, Jiménez-Caballero PE, Mauri-Capdevila G, Torres MJ, Gorospe A, Ramírez Moreno JM, de la Ossa NP, Cánovas D, Arenillas J, Alvarez-Sabín J, Martínez Sánchez P, Fuentes B, Delgado-Mederos R, Martí-Fàbregas J, Rodríguez Campello A, Masjuán J; PROMAPA study: Stroke Project, Cerebrovascular Diseases Study Group, Spanish Neurological Society: Predictive value of brain and vascular imaging including intracranial vessels in transient ischaemic attack patients: external validation of the ABCD3-I score. *Eur J Neurol* 2013;20:1088–1093.
- 7 Kiyohara T, Kamouchi M, Kunai Y, Ninomiya T, Hata J, Yoshimura S, Ago T, Okada Y, Kitazono T: ABCD3 and ABCD3-I scores are superior to ABCD2 score in the prediction of short- and long-term risks of stroke after transient ischemic attack. *Stroke* 2014;45:418–425.
- 8 Kobayashi J, Uehara T, Toyoda K, Endo K, Ohara T, Fujinami J, Nagatsuka K, Minematsu K: Clinical significance of fluid-attenuated inversion recovery vascular hyperintensities in TIA. *Stroke* 2013;44:1635–1640.
- 9 Uehara T, Tabuchi M, Hayashi T, Kurogane H, Yamadori A: Asymptomatic occlusive lesions of carotid and intracranial arteries in Japanese patients with ischemic heart disease: evaluation by brain magnetic resonance angiography. *Stroke* 1996;27:393–397.
- 10 Minematsu K, Bang O, Uehara T: Risk factors; in Kim JS, Caplan LR, Wong KS (eds): *Intracranial Atherosclerosis*, ed 1. Chichester, Wiley-Blackwell, 2008, pp 45–54.
- 11 Uehara T, Tabuchi M, Mori E: Frequency and clinical correlates of occlusive lesions of cerebral arteries in Japanese patients without stroke: evaluation by MR angiography. *Cerebrovasc Dis* 1998;8:267–272.

- 12 Kernan WN, Ovbiagele B, Black HR, Bravata DM, Chimowitz MI, Ezekowitz MD, Fang MC, Fisher M, Furie KL, Heck DV, Johnston SC, Kasner SE, Kittner SJ, Mitchell PH, Rich MW, Richardson D, Schwamm LH, Wilson JA, et al: Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2014; 45:2160–2236.
- 13 Chimowitz MI, Lynn MJ, Howlett-Smith H, Stern BJ, Hertzberg VS, Frankel MR, Levine SR, Chaturvedi S, Kasner SE, Benesch CG, Sila CA, Jovin TG, Romano JG; Warfarin-Aspirin Symptomatic Intracranial Disease Trial Investigators: Comparison of warfarin and aspirin for symptomatic intracranial arterial stenosis. *N Engl J Med* 2005;352:1305–1316.
- 14 Ovbiagele B, Cruz-Flores S, Lynn MJ, Chimowitz MI: Early stroke risk after transient ischemic attack among individuals with symptomatic intracranial artery stenosis. *Arch Neurol* 2008;65:733–737.
- 15 Chimowitz MI, Lynn MJ, Derdeyn CP, Turan TN, Fiorella D, Lane BF, Janis LS, Lutsep HL, Barnwell SL, Waters MF, Hoh BL, Hourihane JM, Levy EI, Alexandrov AV, Harrigan MR, Chiu D, Klucznik RP, Clark JM, McDougall CG, Johnson MD, Pride GL Jr, Torbey MT, Zaidat OO, Rumboldt Z, Cloft HJ: Stenting versus aggressive medical therapy for intracranial arterial stenosis. *N Engl J Med* 2011;365:993–1003.
- 16 Derdeyn CP, Chimowitz MI, Lynn MJ, Fiorella D, Turan TN, Janis LS, Montgomery J, Nizam A, Lane BF, Lutsep HL, Barnwell SL, Waters MF, Hoh BL, Hourihane JM, Levy EI, Alexandrov AV, Harrigan MR, Chiu D, Klucznik RP, Clark JM, McDougall CG, Johnson MD, Pride GL Jr, Lynch JR, Zaidat OO, Rumboldt Z, Cloft HJ: Aggressive medical treatment with or without stenting in high-risk patients with intracranial artery stenosis (SAMMPRIS): the final results of a randomised trial. *Lancet* 2014;383:333–341.
- 17 North American Symptomatic Carotid Endarterectomy Trial Collaborators: Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med* 1991;325:445–453.
- 18 Uehara T, Mori E, Tabuchi M, Ohsumi Y, Yamadori A: Detection of occlusive lesion in intracranial arteries by three-dimensional time-of-flight magnetic resonance angiography. *Cerebrovasc Dis* 1994;4:365–370.
- 19 Special report from the National Institute of Neurological Disorders and Stroke. Classification of cerebrovascular diseases III. *Stroke* 1990;21:637–676.
- 20 Easton JD, Saver JL, Albers GW, Alberts MJ, Chaturvedi S, Feldmann E, Hatsukami TS, Higashida RT, Johnston SC, Kidwell CS, Lustep HL, Miller E, Sacco RL, et al: Definition and evaluation of transient ischemic attack: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association Stroke Council; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; and the Interdisciplinary Council on Peripheral Vascular Disease: The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists. *Stroke* 2009;40:2276–2293.