Prevalence of Positive Diffusion-Weighted Imaging Findings and Ischemic Stroke Recurrence in Transient Ischemic Attack

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Background: The relationship between transient ischemic attack (TIA) clinical etiology, positive diffusion-weighted imaging (DWI) findings, and stroke recurrence is controversial. This study aimed to clarify the prevalence of positive DWI findings and TIA recurrence in relation to TIA patient characteristics. *Methods:* The subjects were patients admitted to our stroke unit within 7 days after symptom onset between January 2006 and July 2013. We examined DWI findings and TIA recurrence according to etiologic subtypes. *Results:* We enrolled 139 patients with lacunar TIA (n = 17), atherothrombotic TIA (n = 35), cardioembolic TIA (n = 25), TIA due to other causes (n = 32), or TIA with undetermined etiology (n = 30). The prevalence of positive DWI findings was highest among the cardioembolic TIA patients (56.0%). No association was found between the prevalence of positive DWI findings and symptom duration, motor presence, or $ABCD^2$ score. Plasma D-dimer level was significantly higher in the DWI-positive group than that in the DWI-negative group ($P = .01$). The prevalence of TIA recurrence was highest (5 of 35, 14.3%) among the atherothrombotic TIA patients, regardless of positive DWI findings. None of the patients treated with the anticoagulant and antiplatelet combination therapy experienced a recurrence. In contrast, almost all patients with cardioembolic TIA received anticoagulant treatment and none experienced recurrence. *Conclusions:* The prevalence of positive DWI findings was high among the cardiogenic TIA patients. TIA recurrence was often observed among the atherothrombotic TIA patients treated with antiplatelets. Management of patients with atherothrombotic TIA requires further aggressive antithrombotic strategy. **Key Words:** Transient ischemic attack—etiology—diffusion-weighted imaging—D-dimer—ischemic stroke recurrence.

Transient ischemic attack (TIA) has been defined as the sudden loss of neurologic function that recovers completely within 24 hours. The definition of TIA has changed during these several years owing to advances in imaging technology. In the traditional definition, the phenomenon was called time-based TIA as symptoms completely resolve within 24 hours. By contrast, in the new definition, it is called tissue-based TIA, without any evidence of infarction in imaging examination using modern technology.[1]

Previous reports have shown that by the traditional definition, 30%-50% of TIA patients have diffusion-weighted imaging (DWI) abnormality.[2,3] During recent years, with the dissemination of imaging technology, many studies have shown the relationship between DWI abnormality and the clinical characteristics of TIA. Some reports suggested that high $ABCD^2$ score, motor weakness, and TIA duration of 60 minutes or more were associated with DWI abnormality,[2,4,5] and other reports suggested that DWI abnormality was related to

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the risk of acute stroke recurrence after TIA.[6] However, these relationships remain controversial. Furthermore, only few reports evaluated the association between DWI abnormality, TIA subtypes, and stroke recurrence. Patients with TIA have extremely high risk of subsequent stroke; therefore, managing the risk stratification according to clinical parameters after TIA is highly important. The aim of this study was to clarify the prevalence of positive DWI findings and ischemic stroke recurrence among TIA etiological subtypes.

Methods

Patients

We retrospectively studied 1289 consecutive patients who were admitted to the stroke unit of Osaka University Hospital for acute cerebrovascular diseases between January 2006 and July 2013. The subjects were selected from among patients within 7 days after symptom onset. Patients who underwent diffusion-weighted magnetic resonance imaging (MRI) at the time of hospitalization were included. TIA was diagnosed according to the National Institute of Neurological Disorders and Stroke criteria,[7] and we classified TIA etiology according to the Trial of Org 10172 in Acute Stroke Treatment classification.[8] The subjects gave informed consent, and this study was approved by the Ethics Committee for Clinical Research at Osaka University Hospital.

Clinical Variables

The following clinical data were retrospectively obtained from the clinical records of all the patients: age, sex, body mass index, TIA symptom, TIA duration, history of stroke, history of ischemic heart disease, history of peripheral artery disease, arterial fibrillation, use of statin, use of antihypertensive drugs, $ABCD^2$ score, and vascular risk factors, including hypertension, diabetes mellitus, hypercholesterolemia, smoking, and drinking. All the patients had baseline blood samples drawn at the time of hospitalization, and the samples were analyzed for the following: white blood cell count, platelet counts, estimated glomerular filtration rate, and levels of hemoglobin, hematocrit, fibrinogen, D-dimer, creatinine, glucose, hemoglobin A1c, total cholesterol, triglycerides, low-density lipoprotein, high-density lipoprotein, and C-reactive protein.

Imaging

Three-tesla MRI was performed at the time of hospitalization. DWIs, T1-weighted images, fluid-attenuated inversion recovery images, T2-weighted images, and the accompanying magnetic resonance angiograms with 3-dimensional time-of-flight images were obtained. The presence of abnormality on DWI was assessed independently by a neurologist and a neuroradiologist who were blinded to the clinical data.

Vascular Risk Factors

Hypertension was defined as the use of antihypertensive medications, a systolic blood pressure of 140 mm Hg or more, or a diastolic blood pressure of 90 mm Hg or more. Hyperlipidemia was defined as the use of cholesterol-lowering therapy, a fasting total serum cholesterol level of 220 mg/dL or more, a triglyceride level of 150 mg/dL or more, or a low-density lipoprotein cholesterol level of 140 mg/dL or more. Diabetes mellitus was defined as a fasting blood glucose level of 126 mg/dL or greater, a glycosylated hemoglobin A1c concentration of 6.1% or more according to the Japan Diabetes Society criteria, or the use of glucose-lowering agents. Estimated glomerular filtration rate was used in accordance with the Modification of Diet in Renal Disease Study method[7] modified by the Japanese coefficient.[9] Body mass index was calculated as weight in kilograms divided by the square of height in meters. Smoking was defined as currently smoking. Habitual alcohol intake was defined as alcohol drinking of 20 g/day or greater.

Classification of Etiological TIA Subtypes

Lacunar TIA (Small-Vessel Disease)

Patient should have one of the traditional clinical lacunar syndromes (pure motor syndrome, pure sensory syndrome, sensory motor syndrome, clumsy hand and dysarthria syndrome, and ataxic hemiparesis) and should not have evidence of cortical signs, including occlusive lesions in the major cerebral artery or embolic source in the heart.

Atherothrombotic TIA (Large-Artery Atherosclerosis [LAA])

Patients should have clinical and brain imaging findings of either significant (>50%) stenosis or occlusion of a major brain artery or branch cortical artery.

Cardioembolic TIA

Patients should have arterial occlusions presumably because of an embolus arising in the heart, without significant (>50%) stenosis in the cerebral arteries.

TIA of Other Determined Etiology

Patients with rare causes of stroke, such as nonatherosclerotic vasculopathies, hypercoagulable states, arterial dissection, or hematologic disorders.

TIA of Undetermined Etiology

Patients should have no definite etiology despite an elaborate evaluation. This category also includes patients