Prediction of Ischemic Stroke in Patients with Tissue-Defined Transient Ischemic Attack

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Background: The risk of future stroke after transient ischemic attack (TIA) has been widely studied, but most findings were obtained for classically defined TIA (time-defined TIA). A new definition of TIA, that is, tissue-defined TIA, which requires the absence of fresh brain infarction on magnetic resonance imaging, could change stroke risk assessments. We, therefore, aimed to evaluate the risk of future stroke in patients with tissue-defined TIA. *Methods:* We retrospectively reviewed 74 patients with tissue-defined TIA, who could be followed for 2 years. Clinical, laboratory, and radiological data were collected and compared between groups that did and did not develop ischemic stroke within the 2-year period. *Results:* Ischemic stroke occurred in 11 patients (14.9%). Increased age, hemiparesis, and/or dysarthria during the TIA, old cerebral infarction revealed by magnetic resonance imaging, and large-artery stenosis detected by magnetic resonance angiography and/or ultrasonography tended to increase the risk of future stroke, but no individual factor showed statistically significant effect. TIA etiology did not significantly affect the risk. ABCD2 score, an established score for predicting stroke after time-defined TIA, showed only a weak association with future stroke. In contrast, new scores that we created reliably predicted future stroke; these included the APO (age, paresis, and old cerebral infarction) and APOL (age, paresis, old cerebral infarction, and large-artery stenosis) scores. The areas under the receiver operating characteristic curves were .662, .737, and .807 for ABCD2, APO, and APOL, respectively. *Conclusions:* Compared with the established measures, our newly created scores could predict future stroke for tissue-defined TIA more reliably. **Key Words:** Clinical score—large-artery disease—old cerebral infarction—risk factor—stroke prediction—transient ischemic attack.

Introduction

Transient ischemic attack (TIA) is a medical emergency. Approximately 5% of the patients with TIA develop stroke within 48 hours, and 10%-20% of patients do so within 3 months.[1-3] Conversely, 7%-40% of patients with ischemic stroke have experienced a previous TIA episode.[3,4] The prompt evaluation of patients with TIA and appropriate medical intervention are, thus, mandatory.

Subsequent stroke is a matter of serious concern, and physicians are often asked to evaluate the probability of future stroke after TIA. As this issue is of great

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importance in a clinical setting, it has been extensively investigated. Many factors, such as age, symptoms and their duration, comorbidities, and radiological features have been shown to influence the risk of stroke.[1,5] To this end, the ABCD2 score, a risk stratification tool, was established and is now widely used as an aid for making medical decisions.[6]

In the meantime, a new definition of TIA was proposed by the American Heart Association/American Stroke Association as a Scientific Statement in 2009.[3] TIA had previously been operationally defined as a focal cerebral ischemic event that lasts less than 24 hours (time-defined TIA).[7] However, this definition does not reflect the pathobiological basis of the disease, and the time limit of 24 hours was considered too arbitrary. The absence of new cerebral infarction on diffusion-weighted image (DWI) in magnetic resonance imaging (MRI) is critical in discriminating between TIA and ischemic stroke, and this information was considered in the new definition of TIA (tissue-defined TIA).[3,8] This new definition better contributes to our understanding of the pathophysiology of TIA and aids clinicians in making medical decisions.[3,9]

Knowledge of future stroke risk, and the ABCD2 score system, has been based on findings obtained for time-defined TIA.[5,6,10] As the standard definition of TIA has changed from time defined to tissue defined, the risk evaluation system may need to be changed. In the present study, we aimed to evaluate the risks of future stroke in patients with tissue-defined TIA. Furthermore, we aimed to assess the reliability of the ABCD2 scoring system for tissue-defined TIA and, if necessary, develop new stratification tools.

Methods

This study was approved by our institutional ethics committee (Institutional Review Board at Saitama Medical University International Medical Center).

All patients who were admitted to our hospital with transient focal neurologic deficits underwent MRI, unless it was contraindicated. When the first MRI revealed no fresh lesions on DWI, a second MRI was performed 3-7 days later. Those without high-intensity lesions revealed by DWI on both scans were diagnosed with tissue-defined TIA. Patients with lasting focal neurologic deficits on admission that disappeared within 24 hours were also included, if repeated MRI after the neurologic deficits resolved demonstrated no new lesions. Patients with transient neurologic deficits and no DWI lesions by the first MRI, but caused cerebral infarction before the second MRI examination, were included. In total, there were 124 patents with tissue-defined TIA from April 2007 to December 2010, and among them, 74 patients could be followed for 2 years; these 74 patients were included in this study. Patients who did not undergo MRI were not included in the study.

We retrospectively reviewed patients' profiles (age and sex), risk factors for stroke (hypertension, diabetes mellitus, dyslipidemia, and smoking), symptoms (presence of hemiparesis and/or dysarthria during the transient attack), and symptom duration. Patients with blood pressure of 140/90 mm Hg or more or who were receiving antihypertensive medication were said to have hypertension.[11] Diabetes mellitus was defined as blood glucose level on admission of 200 mg/dL or more and HbA1c of 6.5% or more or if the patient was being treated with antidiabetic medication.[11] Dyslipidemia was diagnosed when the patient had any of the following: low-density lipoprotein cholesterol of 140 mg/dL or more, high-density lipoprotein cholesterol of 40 mg/dL or less, triglycerides of 150 mg/dL or more, or was being treated with lipid-lowering medication.[11] We also assessed the presence of any old cerebral infarction and large-artery stenosis, regardless of their relevance to the transient symptoms. Old cerebral infarction was investigated by MRI, and high-intensity lesions on T2 and fluid-attenuated inversion recovery images were considered old infarctions. Large-artery stenosis was investigated by magnetic resonance angiography and carotid ultrasonography and more than 50% stenosis as assessed according to the North American Symptomatic Carotid Endarterectomy Trial criteria was considered to be stenotic.[12,13] TIA etiology was categorized according to the Trial of Org 10172 in Acute Stroke Treatment.[14,15] Any subsequent use of antiplatelets, anticoagulants, statins, and stenting or bypass formation was also reviewed. ABCD2 score,[6] a stroke risk stratification tool developed for time-defined TIA, was assessed in all patients.

The above-mentioned variables were compared between the groups with and without subsequent ischemic stroke occurring within 2 years. Statistical analysis was performed using the PASW Statistics software (version 18; SPSS Inc., Chicago, IL). Differences in age between the groups were analyzed using the Wilcoxon test, and differences in other variables were assessed using the chi-square test.

Based on our results, we developed 2 new scales to predict future stroke risk. Factors with small P value by Wilcoxon or chi-square test were first selected, but to further confirm the pertinence, we carried out multivariate logistic regression analysis and determined the factors for the new scales. The predictive values of these scales, and that of ABCD2, were quantified using the area under the receiver operating characteristics curve (AUC) with a 95% confidence interval (CI).

Results

Of the 124 patients who fulfilled the criteria for tissue-defined TIA, 74 patients were followed-up for 2 years and included in our analyses.