Validation of the ABCD³-I Score to Predict Stroke Risk After Transient Ischemic Attack

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Background and Purpose—The Age, Blood Pressure, Clinical Features, Duration, and Diabetes plus Dual TIA (ABCD³-I) score is recommended to predict the risk of early stroke after transient ischemic attack. The aim of this study was to validate the predictive value of the ABCD³-I score and compare the accuracy of the Age, Blood Pressure, Clinical Features, Duration, and Diabetes (ABCD²) and ABCD³-I scores in a Chinese population.

Methods—Data were prospectively collected from patients who had transient ischemic attack, as defined by the World Health Organization time-based criteria. ABCD² and ABCD³-I scores were available within 7 days of the index transient ischemic attack. The predictive outcome was stroke occurrence at 90 days. The receiver-operating characteristic curves were plotted, and the C statistics were calculated as a measure of predictive ability. The comparison of the area under the receiver-operating characteristic curve (area under the curve) was performed by Z test.

Results—Among 239 eligible patients, the mean age was 57.4±13.32 years, and 40.2% of the patients were women. The incidence of stroke at 90 days was 12.1%, which ranged from 0% in patients with lower ABCD³-I scores (0–3) to 40.91% in those with higher scores of 8 to 13 (P for trend <0.0001). Moreover, the C statistic of ABCD³-I scores (0.825; 95% confidence interval, 0.752–0.898) was statistically higher than that of ABCD² scores (0.694; 95% confidence interval, 0.601–0.786; P<0.001).

Conclusions—The ABCD³-I score had a higher predictive value than the ABCD² score for assessing the risk of early stroke after transient ischemic attack in a Chinese population. (Stroke. 2013;44:1244-1248.)

Key Words: prognosis ■ risk prediction ■ risk score ■ stroke ■ transient ischemic attack

 transient ischemic attack (TIA) is associated with a high risk of early recurrent stroke, with stroke rates as high as 14.6% in some subgroups at 90 days after index TIA.¹ The value of the Age, Blood Pressure, Clinical Features, Duration, and Diabetes (ABCD²) score in predicting the risk of early stroke after TIA (diagnosed according to the World Health Organization time-based criteria)² has been validated by many studies,³⁻⁵ and has been recommended for use in international guidelines to improve early stroke risk stratification after TIA.⁶⁻⁸ However, the ABCD² score was originally intended to help primary care and emergency clinicians to triage TIA patients, to rapidly identify patients in need of hospital admission.⁹⁻¹⁰ This score deliberately does not include brain and carotid imaging often obtained in secondary care that might improve predictive accuracy.⁸,¹⁰⁻¹⁶ A multicenter observational study¹⁷ developed the Age, Blood Pressure, Clinical Features, Duration, and Diabetes plus Dual TIA (ABCD³-I) score by adding the parameters of dual TIA, brain, and carotid imaging into the ABCD² score. Compared with the ABCD² score, the ABCD³-I score pays close attention to responsible arteries and brain tissue damage and is appropriate for hospitalized patients.

The design of the previous study¹⁷ was a retrospective case series, and there has not been any prospective validation of the ABCD² score so far. Moreover, the ABCD³-I model used carotid artery stenosis as a score index, which is more appropriate for whites: intracranial artery stenosis is much more common in the Chinese population.¹⁸,¹⁹ Thus, it is important to validate the ABCD³-I score in different ethnic groups. This study aims to prospectively validate the predictive value of the ABCD³-I score and compare the accuracies of the ABCD² score and ABCD³-I score in identifying the 90-day risk of stroke in a cohort of consecutive patients admitted with TIA.

Methods

Patient Selection

Patients included in this study were from the database of the first affiliated hospital of Zhengzhou University, which is a prospective hospital-based cohort study of consecutive patients who had TIA. Detailed baseline data were registered prospectively using paper case report forms designed specifically for this study, including: age, sex, clinical features, medical history, physical examination, laboratory tests, electrocardiography, transcranial duplex, diffusion-weighted imaging (DWI), carotid imaging, and ABCD² and ABCD³-I scores. TIA registry forms were completed by neurologists with similar levels of training and experience.

The elapsed time from last episode to registry was <7 days. Exclusion criteria included patients who did not undergo DWI or carotid imaging for the index TIA (ABCD³-I scores for these patients

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were unavailable), patients who could not describe the characteristics of the attack or provide their past medical history because of cognitive impairment or other causes, patients who refused to participate in the research, and patients who failed to complete the follow-up protocol. The study was approved by the ethics committee of the First Affiliated Hospital of Zhengzhou University, and informed consent was obtained from all the patients or their legally authorized representatives.

**ABCD² and ABCD³-I Scores**

The ABCD² score (Table 1) is a simple score that combined 5 clinical variables (age, blood pressure, clinical features, duration of symptoms, and a history of diabetes mellitus) into a 7-point scale and stratified them into low-risk (0–3), medium-risk (4–5), and high-risk (6–7) categories. The ABCD³-I score is derived by assigning 2 points for dual TIA (an earlier TIA within 7 days of the index event), 2 points for ipsilateral ≥50% stenosis of internal carotid artery, and 2 points for acute DWI hyperintensity to the ABCD³-I score, which is separated into low-risk (0–3), medium-risk (4–7), and high-risk (8–13) categories.

**Definitions**

The TIA diagnosis was based on World Health Organization TIA diagnostic criteria, which defines a TIA as an acute loss of focal cerebral or ocular function lasting <24 hours and attributed to embolic or thrombotic vascular disease. The index TIA was defined as the most recently preceding assessment by a stroke specialist. Duration of symptoms was calculated from the last time the patient was known to be well. Dual TIA was defined as the occurrence of ≥2 TIA:s: the index TIA and another TIA in the 7 days before the index event. Carotid stenosis was defined as ≥50% narrowing of the ipsilateral internal carotid artery on carotid imaging (including carotid artery ultrasound, magnetic resonance angiography, computed tomography angiography, or digital subtraction angiography), and the percentage of stenosis was calculated using the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method. DWI imaging was done within 7 days for the index TIA. Acute DWI hyperintensity was defined as lesions consistent with acute cerebral ischemia identified by the treating neurologists. Information on demographic characteristics and vascular risk factors was obtained from patients’ self-reports on their past medical history.

**Predictive Outcomes**

All registered patients were followed up prospectively for 90 days. Follow-up involved face-to-face assessments by 2 neurologists blinded to the scoring. Stroke was defined as the sudden onset of neurological symptoms that persisted for ≤24 hours based on the World Health Organization criteria. Survival time of patients during follow-up was calculated as the duration of occurrence of event (from the beginning of follow-up time after last TIA to the time of occurrence of the stroke). Survival time of those patients who did not have a stroke was recorded as 90 days.

**Statistical Analysis**

Kaplan–Meier analysis was used to calculate the cumulative incidence, and Cochran–Armitage trend test was performed for patients for each risk category of the ABCD² and ABCD³-I scores; risk of stroke (stratified according to the scores) was compared by the log-rank test. We examined risk reclassification from strata of ABCD² to ABCD³-I scores by cross-tabulation, and the net reclassification improvement from ABCD² to ABCD³-I score was calculated. The receiver-operating characteristic curves were plotted, and the C statistics were calculated as a measure of predictive ability. Cox proportional hazards regression modeling was performed to identify factors that increased the risk of subsequent stroke after TIA. All factors that contributed to the outcome in the univariate analyses at P<0.1 were included in the multivariate model as candidate variables and then removed by a backward selection procedure. In the final multivariate analyses, statistical significance was achieved at P<0.05. Associations were presented as hazard ratios (HRs) with corresponding 95% confidence intervals (95% CIs). All statistical analyses were performed using SPSS software for Windows (version 16.0; SPSS), and P<0.05 was considered statistically significant.

**Results**

From October 2010 to December 2011, there were 239 (96.4%) eligible patients after excluding 3 patients (1.2%) without DWI or carotid imaging and 6 patients (2.4%) without a complete 90-day follow-up. The average age of the patients was 57.40±13.32, of whom 96 patients (40.2%) were women. Table 2 shows the clinical characteristics and risk of stroke in relation to risk factors in patients who had TIA. There were 29 patients (12.1%) who had an ischemic stroke at 90-day follow-up, and 15 out of 29 strokes (51.7%) occurred in the first 48 hours after TIA.

The 90-day risk of stroke stratified by individuals according to their ABCD²/ABCD³-I scores revealed that there was a steady increase in the rate of stroke with increasing risk categories (Table 3). There was found to be a linear trend of occurrence rates with the Cochran–Armitage trend test (ABCD², Z=−3.7306, P=0.0002; ABCD³-I, Z=−5.9124, P<0.0001). Survival-free of stroke curves categorized by ABCD² and ABCD³-I scores are shown in Figures 1 and 2. Survival curves were significantly different among the low-, medium-, and high-risk categories of both scores when overall comparisons were made (ABCD², log-rank test=15.366, P<0.001; ABCD³-I, log-rank test=49.619, P<0.001).

Of the 6 patients who had a stroke within 90 days and were classified as low risk (0–3) by the ABCD² score, all 6 patients were classified as medium risk by the ABCD³-I score; of the 20 patients who had a stroke within 90 days and were classified as medium risk (4–5) by the ABCD² score, 15 patients (75%) were classified as high risk by the ABCD³-I score. Risk reclassification from strata of ABCD² to ABCD³-I scores was calculated by cross-tabulation; movement of patients from low- to medium-risk categories of the ABCD² score and further to the high-risk category of the ABCD³-I risk categories was associated with a net reclassification improvement of 44.1% (P<0.001).

Predictive ability improved when the ABCD³-I score was compared with the ABCD² score using the receiver-operating...
characteristic curve analysis. The area under the curve (AUC) was 0.825 (95% CI, 0.752–0.898) by the ABCD3-I score and 0.694 (95% CI, 0.601–0.786) by the ABCD2 score for the prediction of 90-day stroke occurrence (Figure 3). The comparison of the AUC was performed by Z testing, which revealed that the C statistic for ABCD3-I score was higher than that for the ABCD2 score (Z = −3.369; P < 0.001).

Cox regression analysis was performed to determine whether there was an association between potential risk factors and recurrent stroke. In the ABCD3-I scoring classification, no events occurred in the low-risk (0–3) reference category, and thus, an HR could not be calculated. Therefore, a threshold value of 7 was assigned, and a score of 0 to 7 (low- and medium-risk categories) was taken as a reference category to find out the relationship between the high-risk category of ABCD3-I and the occurrence of stroke within 90 days. In the initial univariate analyses of the association of the clinical features, ABCD3-I score (8–13 vs 0–7), stroke risk factors, previous medications, and secondary prevention therapies during hospitalization and after discharge with the risk of subsequent stroke were investigated using Cox proportional regression analyses. The following variables were related to stroke occurrence and were therefore selected for entry into the final multivariate model (P < 0.1): an ABCD3-I score of 8 to 13 (HR, 8.844; 95% CI, 4.165–18.783), hypertension (HR, 2.489; 95% CI, 1.014–6.114), atrial fibrillation (HR, 5.846; 95% CI, 1.384–24.691), stroke history (HR, 4.700; 95% CI, 2.005–11.021), history of using antihypertensive medications (HR, 0.346; 95% CI, 0.157–0.759), antihypertensive medications after discharge (HR, 0.462; 95% CI, 0.222–0.961), and lipid-lowering medication use after discharge (HR, 0.162; 95% CI, 0.049–0.537). These variables were included in the multivariate model as candidate variables and then removed by the backward regression procedure. The final multivariate analyses revealed that an ABCD3-I score of 8 to 13 (HR, 7.897; 95% CI, 3.659–17.041) and lipid-lowering drugs after discharge (HR, 0.180; 95% CI, 0.054–0.597) were independent predictors of stroke risk (P < 0.05). More specifically, an ABCD3-I score of 8 to 13 was associated with a ≈8-fold greater 90-day risk of stroke after adjustment for potential confounders, including stroke risk factors and secondary prevention therapies (HR, 6.317; 95% CI, 2.667–14.963).

Table 2. Baseline Clinical Characteristics and Risk of Stroke in Relation to Risk Factors in Patients Who Had TIA

<table>
<thead>
<tr>
<th>N (%)</th>
<th>HR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>96 (40.2)</td>
<td>1.044 (0.498–2.185)</td>
</tr>
<tr>
<td>Age ≥60 y</td>
<td>113 (47.3)</td>
<td>1.025 (0.995–1.005)</td>
</tr>
<tr>
<td>Blood pressure ≥140/90 mmHg</td>
<td>127 (53.1)</td>
<td>1.264 (0.604–2.647)</td>
</tr>
</tbody>
</table>

Clinical features

| Speech impairment without weakness | 25 (10.5) | 8.794 (0.983–78.681) | 0.052 |
| Unilateral weakness               | 161 (67.4) | 8.355 (1.130–61.765) | 0.038 |

Duration

<table>
<thead>
<tr>
<th>Duration</th>
<th>N (%)</th>
<th>HR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration 10–59 min</td>
<td>95 (39.7)</td>
<td>1.744 (0.755–4.029)</td>
<td>0.193</td>
</tr>
<tr>
<td>Duration ≥60 min</td>
<td>42 (17.6)</td>
<td>1.653 (0.588–4.644)</td>
<td>0.340</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>34 (14.2)</td>
<td>1.234 (0.471–3.235)</td>
<td>0.668</td>
</tr>
<tr>
<td>Dual transient ischemic attack</td>
<td>146 (61.1)</td>
<td>3.213 (1.226–8.421)</td>
<td>0.018</td>
</tr>
<tr>
<td>Acute DWI hyperintensity</td>
<td>79 (33.1)</td>
<td>2.234 (1.507–3.313)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ipsilateral ≥50% stenosis of ICA</td>
<td>38 (15.9)</td>
<td>1.595 (1.076–2.364)</td>
<td>0.020</td>
</tr>
<tr>
<td>Hypertension</td>
<td>23 (9.6)</td>
<td>1.484 (0.516–4.265)</td>
<td>0.464</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>4 (1.7)</td>
<td>5.846 (1.384–24.691)</td>
<td>0.016</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>23 (9.6)</td>
<td>1.099 (0.333–3.631)</td>
<td>0.877</td>
</tr>
<tr>
<td>History of stroke</td>
<td>18 (7.5)</td>
<td>4.700 (2.005–11.021)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Current smoker</td>
<td>73 (30.5)</td>
<td>1.672 (0.798–3.500)</td>
<td>0.173</td>
</tr>
<tr>
<td>Timing of DWI ≤72 h</td>
<td>189 (79.1)</td>
<td>1.305 (0.498–4.241)</td>
<td>0.588</td>
</tr>
</tbody>
</table>

DWI indicates diffusion-weighted imaging; ICA, internal carotid injury; and TIA, transient ischemic attack.

Table 3. ABCD3-I Score and ABCD2 Score Cutoff Values and Risk Stratification

<table>
<thead>
<tr>
<th>Score</th>
<th>Patient No.</th>
<th>Stroke No.</th>
<th>Risk, % (95% CI)</th>
<th>Score</th>
<th>Patient No.</th>
<th>Stroke No.</th>
<th>Risk, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–3</td>
<td>130</td>
<td>6</td>
<td>4.62 (1.01–8.22)</td>
<td>0–3</td>
<td>49</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4–5</td>
<td>96</td>
<td>20</td>
<td>20.83 (12.71–28.96)</td>
<td>4–7</td>
<td>146</td>
<td>11</td>
<td>7.53 (3.25–11.82)</td>
</tr>
<tr>
<td>6–7</td>
<td>13</td>
<td>3</td>
<td>23.08 (17.1–45.98)</td>
<td>8–13</td>
<td>44</td>
<td>18</td>
<td>40.91 (26.38–55.44)</td>
</tr>
</tbody>
</table>

CI indicates confidence interval.
Discussion

Our data validated the usefulness of the ABCD3-I score to predict the 90-day risk of stroke after an index TIA. The rate of 90-day stroke in our study (12.13%) was substantially higher than the stroke incidence documented in a multicenter retrospective observational study17 (3.9%) carried out in the secondary care settings. Differences in ethnic factors and underlying pathology, in addition to other demographics, may explain the variations between studies. Nevertheless, the incidence of stroke occurrence in our study was practically identical to the pooled risk (9.2%), based on a random effects model in a published systematic review.21

Our data revealed that the risk of recurrent stroke had a significant linear correlation with the increasing ABCD3-I risk categories (Table 3), and an ABCD3-I score of 8 to 13 (high-risk category) was found to be an independent predictor of risk of stroke. The results of our research provide evidence for the external validity of the ABCD3-I score. More specifically, after adjustment for potential confounders, including stroke risk factors and secondary prevention therapies, patients in the high-risk category were found to have a 8-fold greater risk of stroke than those in the low-risk and medium-risk categories. The predictive reliability of the ABCD2 score in our study with an AUC of 0.694 is similar to a collaborative analysis of 4574 patients (0.66)5 and a multicenter observational study of 3886 patients (0.60).17

Compared with the predictive accuracy of the ABCD2 score and ABCD3-I score, we found that the ABCD3-I score with an AUC of 0.825 had higher accuracy than the ABCD2 score with an AUC of 0.694 for the prediction of 90-day recurrent stroke (Figures 1 and 2). This indicates that the addition of dual TIA, DWI, and carotid imaging into the ABCD2 score improves the prediction value for 90-day risk of recurrent stroke after the index TIA. Although the ABCD2 score is a simple, quick, inexpensive, and easily available test for the early risk of recurrent stroke after TIA,4,10,11 several other variables might be useful markers of unstable vascular disease that are associated with higher risk of early stroke after TIA.14,15,22,23 It has been proved that carotid stenosis is associated with increased stroke risk after TIA, probably because of recurrent embolization from unstable carotid plaques24–26; acute DWI hyperintensity after TIA is associated with predictors of stroke risk and early stroke in several studies.13–15 These evidences may explain the better predictive value of ABCD3-I score than ABCD2 score.

This prospective study validates the value of the ABCD3-I score to predict stroke occurrence up to 90 days after TIA. We investigated and reported that ABCD3-I can predict 90-day stroke risk after TIA in a Chinese population, although there are racial differences in the distribution of intracranial or extracranial arteriostenosis in southeast Asians compared with whites.19 Because stroke risk is highest in the first 48 hours after TIA onset, it is recommended that brain and carotid imaging be done as early as possible for maximum benefit in patients who had TIA.17 Our study provides further evidence that the ABCD3-I score can increase the accuracy of the score and, therefore, could help clinicians to select appropriate patients for hospitalization and discharge after initial hospital assessment, and to determine individualized secondary prevention strategies for the purpose of reducing the risk of stroke after TIA.

The use of DWI has shown that some patients with a clinical definition of TIA have neuroimaging evidence of brain injury on DWI.15,27 Therefore, a new tissue–based definition was proposed by the American Heart Association (2009), which
defines TIA as a transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction. However, there have been many arguments against the new definition. Therefore, this study adopted the classic definition of TIA and stroke, using the same end points as a previous ABCD\textsuperscript{3}-I study, to identify the predictive accuracy of the model and make appropriate comparisons.

As observational research, the limitations of this study also cannot be avoided. First, the risk of recurrent stroke had a significant linear correlation with the increasing ABCD\textsuperscript{3}-I risk categories. However, the efficiency of the statistics was low because of the small sample size and low number of stroke incidence. Second, we evaluated only hospitalized patients at a single center, which can lead to selective bias. Multicenter validation of this score is required, especially in patients who had TIA who are referred to community and outpatient settings. Third, there is evidence confirming that taking pathogenesis into account improves the prediction of the early risk of stroke after TIA. However, subgroup analysis of pathogenesis and young patients with nonatherosclerotic TIA syndromes was not done in this study because of the small sample size. Thus, further validation of this score in different cohorts of patients with a larger sample size is needed to confirm the results.

In conclusion, our study prospectively validates the predictive accuracy of the ABCD\textsuperscript{3}-I score in Chinese patients by identifying the 90-day risk of stroke in hospitalized patients who had TIA. Furthermore, the study provides further evidence for the potential practical use of the ABCD\textsuperscript{3}-I score in clinical practice.

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Disclosures
All authors participated in the interpretation of study results and in the drafting, critical revision, and approval of the final version of the article. Dr Song was responsible for study design, data analyses, and drafting/revising the article; Drs Zhao, Gao, Tan, and Chandra were involved in revising the article for important intellectual content; Drs Lu, Sun, and Wang conducted the statistical analysis; Dr Xu was responsible for study concept or design, technical, material support, administrative, and supervision.

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