Validation of the ABCD Score in Identifying Individuals at High Early Risk of Stroke After a Transient Ischemic Attack

A Hospital-Based Case Series Study

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Background and Purpose—A simple score derived in the Oxfordshire Community Stroke Project (ABCD score) was able to identify individuals at high early risk of stroke after a transient ischemic attack (TIA) both in a population-based and a hospital-referred clinic cohort. We aimed to further validate the former score in a cohort of hospitalized TIA patients.

Methods—We retrospectively reviewed the emergency room and hospital records of consecutive patients hospitalized in our neurological department with a definite TIA according to the World Health Organization (WHO) criteria during a 5-year period. The 6-point ABCD score (age ≤60 years, ≥60 years; blood pressure [systolic ≥140 mm Hg and diastolic ≤90 mm Hg, systolic >140 mm Hg and/or diastolic >90 mm Hg]; clinical features [unilateral weakness, speech disturbance without weakness, other symptom]; duration of symptoms [<10 minutes, 10 to 59 minutes, ≥60 minutes]) was used to stratify the 30-day stroke risk.

Results—The 30-day risk of stroke in the present case series (n=226) was 9.7% (95% CI, 5.8% to 13.6%). The ABCD score was highly predictive of 30-day risk of stroke (ABCD score 0 to 2: 0%, ABCD score 3: 3.5% [95% CI, 0% to 8.2%], ABCD score 4: 7.6% [95% CI, 1.2% to 14.0%], ABCD score 5: 21.3% [95% CI, 10.4% to 33.0%], ABCD score 6: 31.3% [95% CI, 8.6% to 54.0%]; log-rank test=23.09; df=6; P=0.0008; P for linear trend across the ABCD score levels <0.0001). After adjustment for stroke risk factors, history of previous TIA, medication use before the index TIA, and secondary prevention treatment strategies, an ABCD score of 5 to 6 was independently (P=0.001) associated with an 8-fold greater 30-day risk of stroke (hazard ratio, 8.01; 95% CI, 3.21 to 19.98).

Conclusions—Our findings validate the predictive value of the ABCD score in identifying hospitalized TIA patients with a high risk of early stroke and provide further evidence for its potential applicability in clinical practice. (Stroke. 2006;37:2892-2897.)

Key Words: ABCD score ■ prognosis ■ stroke ■ transient ischemic attack

Recent population-based studies have documented that transient ischemic attacks (TIAs) constitute a strong predictor of subsequent stroke, with the 90-day stroke risk following a TIA ranging from 9.5% to 14.6%. However, a substantial international variation in the acute management of individuals presenting to the emergency room (ER) with TIA (emergency inpatient care versus nonemergency outpatient clinic assessment) exists because of the inability to identify the patients who are at highest risk for early stroke. A simple score derived in the Oxfordshire Community Stroke Project (OCSP) on the basis of age, blood pressure (BP), clinical features, and duration of TIA symptoms (ABCD score) was validated both in a population-based and a hospital-referred clinic cohort as a practical tool able to identify individuals at high early risk for stroke after a TIA. Aim of the present hospital-based case series study was to further validate the former score in a cohort of hospitalized TIA patients.

Methods

Patient Selection

A series of 238 consecutive patients hospitalized in our institution between January 2000 and December 2004 with a diagnosis of definite TIA according to the World Health Organization standard definition were initially screened. All patients presenting at the ER of the Neurology Department of our institution are primarily screened by the attending neurologist. An initial brain CT scan is routinely performed in all TIA patients at the ER or within 24 hours from hospital admission. The diagnostic
work-up of the TIA patients during hospitalization includes extracranial Doppler/duplex ultrasonography in nearly all cases, whereas brain MRI, transthoracic or transesophageal echocardiography, and magnetic resonance or digital subtraction angiography and 24-hour heart rate monitoring are performed in selected cases. All TIA and stroke patients hospitalized in our Neurology Department are included in a computerized observational data bank and their demographic characteristics, risk factors, history of previous TIA, previous medications, and secondary prevention therapies during hospitalization and after discharge are documented as elsewhere described. More specifically, patients were diagnosed as having a history of hypertension, if they had evidence of systolic BP $\geq 140$ mm Hg or diastolic BP $\geq 90$ mm Hg or if they had received any antihypertensive medication at any time before presentation to the ED. Diabetes mellitus was specified as fasting serum glucose $\geq 7.0$ mmol/L, nonfasting serum glucose $\geq 11.1$ mmol/L, or use of oral blood sugar-lowering drugs or insulin. Hypercholesterolemia was defined as total cholesterol $>6.2$ mmol/L or use of lipid-lowering drugs. Smoking status was defined as current use. History of myocardial infarction, angioplasty, coronary artery bypass surgery, and angina pectoris was recorded. A positive history of coronary artery disease was defined by the presence of any of the previous conditions. Finally, atrial fibrillation was diagnosed on the basis of at least one ECG before or during hospitalization.

**ABCD Score**

For the needs of the present study, 2 investigators (G.T. and K.S.) blinded to the follow-up events retrospectively reviewed both the ER and hospital records of all 238 patients. The 6-point ABCD score (age $[<60$ years $=0$, $\geq 60$ years $=1$]; BP (systolic $\leq 140$ mm Hg and diastolic $\geq 90$ mm Hg $=0$, systolic $>140$ mm Hg and/or diastolic $\geq 90$ mm Hg $=1$]; clinical features [unilateral weakness $=2$, speech disturbance without weakness $=1$, other symptom $=0$]; duration of symptoms $[<10$ minutes $=0$, 10 to 59 minutes $=1$, $\geq 60$ minutes $=2]$) was computed in 231 cases. BP measurements at the ER were performed using standard mercury sphygmomanometer by the attending physicians. Clinical features were categorized as motor weakness (focal, usually unilateral, weakness of one or more of face, arm, hand, or leg) versus speech disturbance (defined as dysarthria or dysphasia or both) versus all other symptoms (numbness, change in vision, dizziness or vertigo, gait disturbance) according to the OCSP definition of the ABCD score. Seven patients with unavailable BP recordings (n=5) or duration of TIA symptoms (n=2) at the ER records were excluded from further evaluation.

**Patient Outcome**

All surviving stroke or TIA patients hospitalized in our institution were followed-up prospectively at 1 month, as previously described. Follow-up was routinely performed at the outpatient clinics of our department. The outcome events of interest in case of stroke and TIA patients were recurrent and subsequent strokes respectively, defined as a cerebrovascular events of sudden onset, lasting for $>24$ hours, clearly resulting in an increase of an existing or in a new neurological deficit. They were determined after evaluation of all the available information obtained from our and other hospital records, physicians’ notes in private practice, necropsy findings, or death certificates, and the patients’ clinical presentation at the regular follow-up assessments. Brain imaging visualizing a new lesion involving an anatomic site or vascular territory that was unaffected on the admission CT scan was mandatory to support the diagnosis of subsequent stroke in TIA patients. According to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria, ischemic stroke was classified based on etiopathogenetic mechanisms into the following groups: large artery atherosclerotic stroke, cardioembolic stroke, small artery occlusion or lacunar infarction, infarction of other determined origin, and infarction of undetermined cause. A total of 5 patients who were lost from follow-up were excluded from further evaluation.

**Statistical Analysis**

Statistical comparisons were performed between subgroups of patients using the $\chi^2$ test (or the Fisher exact test) and the unpaired $t$ test (or Mann-Whitney U test) as indicated. The Kaplan-Meier product-limit method was used to estimate the cumulative probability of subsequent stroke after 1 month from the index TIA. Differences in stroke-free survival between groups stratified by the ABCD score were assessed for statistical significance with the log-rank test. Sensitivities and specificities of prediction were determined at each cut-off of the score and the receiver operating characteristic curve was plotted. Cox proportional hazards regression modeling was used to identify factors that increased the risk of subsequent stroke after a TIA. In the initial univariate analyses the association of demographic characteristics, stroke risk factors, previous medication use, secondary prevention therapies, and the ABCD score with the 30-day risk of stroke was investigated. All factors that contributed to the outcome in the initial univariate analyses at $P<0.1$ were included in the multivariate model as candidate variables and then removed by backward stepwise selection procedure. In the final multivariate analyses, statistical significance was achieved if $P<0.05$. To confirm the robustness of multivariate models, we repeated all multivariate analyses using a forward-selection procedure. Associations are presented as hazard ratios (HR) with corresponding 95% confidence intervals (95% CI). The Statistical Package for Social Science (version 10.0 for Windows; SPSS Inc) was used for statistical analyses.

**Results**

The final studied population consisted of 226 patients hospitalized with a diagnosis of TIA. The elapsed time from symptom onset to hospital admission was $<48$ hours in all cases (87.6% within 24 hours). Demographic characteristics, stroke risk factors, medications before hospitalization, and secondary prevention therapies during hospital stay and after hospital discharge are presented in Table 1. The distribution of the ABCD scores at the time of presentation at the ER is shown in Table 2. The median length of hospitalization was 8 days (interquartile range, 7 days). The diagnostic evaluation of TIA patients at the ER and during hospital stay included a brain CT scan (100% of cases within 24 hours after presentation to the ER), extracranial Doppler/duplex ultrasonography (96.9%), transthoracic or transesophageal echocardiography (38.1%), cerebral magnetic resonance or digital subtraction angiography (14.6%), and 24-hour heart rate monitoring (33.6%). Evidence of cerebral infarction was identified on admission CT scan in 31 patients (13.7%), whereas ultrasonography disclosed carotid stenosis ($\geq 50\%$ reduction in lumen diameter) relevant to the patient’s presenting symptoms in 16 cases (7.1%). Patients with ABCD score $<5$ had fewer ($P<0.05$, Fisher exact test) ischemic lesions on brain CT scan (10.4%) and less carotid stenoses (4.9%) than patients with an ABCD score of 5 to 6 (22.2% and 12.7%, respectively). Carotid endarterectomy was performed in 2 patients (12.5%) with symptomatic carotid disease during the follow-up period.

Within 30 days of the index TIA, 22 (9.7%) patients had a subsequent stroke (18 during hospitalization and 4 after discharge), 16 (7.1%) experienced a recurrent TIA, and 13 were dead (n=2, 0.9%) or dependent (n=11, 4.9%). The subtypes of ischemic stroke (IS) had the following distribution: large artery atherosclerotic stroke (45.5%, n=10), cardioembolic stroke (13.6%, n=3), lacunar infarction (22.7%, n=5), and infarction of undetermined cause (18.2%, n=4). During the follow-up period no hemorrhagic cerebral events ocurred.
were documented. A total of 3 (1.3%) and 18 (8.0%) stroke events occurred within 1 and 7 days after hospital admission. The ABCD score was highly predictive of both the 7-day (ABCD=0 to 2: 0%, ABCD=3: 3.5% [95% CI, 0% to 8.2%], ABCD=4: 7.6% [95% CI, 1.2% to 14.0%], ABCD=5: 21.3% [95% CI, 10.4% to 33.0%], ABCD=6: 31.3% [95% CI, 8.6% to 54.0%]; log-rank test=23.09; df=6; P=0.0008; P for linear trend across the ABCD score levels <0.00001) risk of stroke (Table 2). The area under the receiver operating characteristic curve (Figure 1) was 0.78 (95% CI, 0.69 to 0.87; P<0.001).

The association of demographic characteristics, stroke risk factors, previous medications, secondary prevention therapies during hospitalization and after discharge, and ABCD score at the time of presentation at the ER with the risk of subsequent stroke was evaluated using univariate Cox proportional hazards analyses. The following variables were significantly (P<0.1) related to stroke recurrence and were therefore selected for entry into the final multiple-variable model: ABCD score >4 (HR, 6.12; 95% CI, 2.49 to 15.02), hypercholesterolemia (HR, 4.22; 95% CI, 1.80 to 9.89), diabetes mellitus (HR, 3.01; 95% CI, 1.27 to 6.77), arterial hypertension (HR, 2.65; 95% CI, 0.98 to 7.19), lipid-lowering medications during hospitalization and/or after discharge (HR, 0.38; 95% CI, 0.15 to 0.96), and antihypertensive medications during hospitalization and/or after discharge (HR, 0.46; 95% CI, 0.19 to 1.09). The multivariate Cox regression analyses (performed both with the backward-selection and forward-selection procedure) revealed only an ABCD score of 5 to 6, hypercholesterolemia, and diabetes mellitus as independent predictors of the 30-day risk of stroke (Table 3). More specifically, an ABCD score of 5 to 6 at the ED was associated (P<0.001) with an 8-fold greater 30-day risk of stroke (HR, 8.01; 95% CI, 3.21 to 19.98; Figure 2). Furthermore, an ABCD score of 5 to 6 was also independently (P<0.001) associated with the 7-day risk of stroke (HR, 8.94; 95% CI, 2.72 to 29.32).

Because evidence for infarction on CT-scans of TIA patients had been associated with an increased risk of subsequent stroke, we repeated the analyses after including this potential confounder in the multivariable model. An ABCD score of 5 to 6 remained an independent (P<0.001) predictor of the 30-day risk of stroke (HR, 7.31; 95% CI, 2.98 to 17.94). In addition, the exclusion of the TIA patients who experienced a recurrent stroke within 24 hours after hospital admission (n=3), did not attenuate the predictive value of the ABCD score (HR, 12.59; 95% CI, 4.43 to 35.80; P<0.001). Finally, we included the patients who were lost during the follow-up period in our dataset and performed the Cox regression analyses based on the worst-case scenario (assuming that all 5 patients had experienced a subsequent stroke). The association between ABCD score and risk of stroke recurrence retained its statistical significance (HR, 4.86; 95% CI, 2.23 to 10.66; P<0.001).

**Discussion**

The findings of the current hospital-based case series of TIA patients add to the mounting evidence of an early risk of subsequent stroke following the index TIA. The rate of IS during hospitalization in our study (7.9%) was practically identical to the in-hospital stroke incidence (8.0%) recorded in a multicenter prospective observational study.\textsuperscript{15} In addi-
tion, the 30-day risk of stroke in our cohort was substantially high (9.7%) and only slightly lower to the equivalent risk documented in population-based studies conducted in Oxfordshire (11.5%) and the greater Cincinnati metropolitan region (11.2%). Hence, our data underscore the brief time window available for stroke prevention in TIA patients and emphasize the importance of urgent assessment and effective management in this specific subgroup of patients.

Because TIA patients are a highly heterogeneous group in terms of symptoms, risk factors, underlying pathology, and early prognosis, different models for the stratification of stroke risk have been recently developed. Our results provide for the first time evidence for the external validity of the OCSP-derived ABCD score. More specifically, an ABCD score of 5 to 6 was associated with 8-fold greater 30-day risk of stroke after adjustment for potential confounders including stroke risk factors and secondary prevention therapies. However, only 7 strokes (4.3%) were documented in the subgroup of patients with an ABCD score ≤4. The consistency of the predictive power of the ABCD score both in a population-based and hospital-referred clinic cohort of TIA patients, as well as in the current hospital-based cases series, underlines the high reliability of the score for the prediction of stroke risk after a TIA in different clinical settings. In contrast to our findings, Cucchiara et al after assessing the ABCD score in a North American series of hospitalized TIA patients (n=117) found little predictive value of the ABCD risk score and concluded that its discriminatory capacity was not optimal. Of note, though, is that the outcome chosen in the former study was a composite one including stroke, death, ipsilateral carotid stenosis >50%, or a cardioembolic source warranting coagulation. Notably, only 2 patients experienced a stroke event during the 90-day follow-up period and consequently the risk of stroke was substantially low (<2%).

We also documented a higher prevalence of cerebral infarction and ipsilateral carotid stenosis in patients with an ABCD score of 5 to 6 than in subjects with an ABCD score ≤4. Interestingly, evidence of ischemic lesions on baseline brain CT scan has been previously associated with an adverse outcome in hospitalized TIA patients, whereas the early (90-day) risk of stroke was particularly high (20.1%) in TIA patients with internal carotid artery disease.

Given that the ABCD score seems to constitute a valuable tool able to identify in the ED the subgroup of TIA patients which is at greatest need for emergent evaluation and effective treatment, the applicability of the former score in clinical practice may raise certain potential therapeutic implications. A recent meta-analysis of individual patient data from randomized control trials of carotid endarterectomy versus medical treatment alone showed that the benefit from surgery was time-dependent and demonstrated that carotid endarterectomy was most effective when performed within 2 weeks from the qualifying ischemic event (stroke/TIA). However, only 12.5% of cases with symptomatic carotid disease underwent carotid revascularization during the first month after the

### Table 2. The 7- and 30-Day Risks of Stroke Stratified According to the ABCD Score

<table>
<thead>
<tr>
<th>ABCD Score</th>
<th>Patients</th>
<th>Strokes</th>
<th>Risk (%, 95% CI)*</th>
<th>Strokes</th>
<th>Risk (%, 95% CI)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5 (2.2%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>12 (5.3%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>22 (9.7%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>58 (25.7%)</td>
<td>1 (6.6%)</td>
<td>1.7 (0–5.1)</td>
<td>2 (9.1%)</td>
<td>3.5 (0–8.2)</td>
</tr>
<tr>
<td>4</td>
<td>66 (29.2%)</td>
<td>5 (27.8%)</td>
<td>7.6 (1.2–14.0)</td>
<td>5 (22.7%)</td>
<td>7.6 (1.2–14.0)</td>
</tr>
<tr>
<td>5</td>
<td>47 (20.8%)</td>
<td>9 (50.0%)</td>
<td>19.1 (7.8–30.4)</td>
<td>10 (45.5%)</td>
<td>21.3 (10.4–33.0)</td>
</tr>
<tr>
<td>6</td>
<td>16 (7.1%)</td>
<td>3 (16.7%)</td>
<td>18.8 (0–37.9)</td>
<td>5 (22.7%)</td>
<td>31.3 (8.6–54.0)</td>
</tr>
<tr>
<td>Total</td>
<td>226 (100%)</td>
<td>18 (100%)</td>
<td>8.0 (4.5–11.5)</td>
<td>22 (100%)</td>
<td>9.7 (5.8–13.6)</td>
</tr>
</tbody>
</table>

*Log-rank test = 17.46; df = 6; P = 0.0077; P for linear trend across the ABCD score levels = 0.0003; †Log-rank test = 23.09; df = 6; P = 0.0008; P for linear trend across the ABCD score levels < 0.00001.

### Table 3. Multivariate Cox Regression Analysis of Predictors of 30-Day Risk of Stroke

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>Comparison</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABCD score</td>
<td>5–6 vs 0–4</td>
<td>8.01 (3.21–19.98)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>Yes vs no</td>
<td>3.83 (1.47–9.96)</td>
<td>0.006</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Yes vs no</td>
<td>2.98 (1.28–6.94)</td>
<td>0.015</td>
</tr>
</tbody>
</table>

Figure 1. Receiver operating characteristic curves (ROC) for predictive value of ABCD score.
index TIA in our cohort, whereas the results of a recent population-based study are more alarming, because they indicate that carotid surgery was performed within 2 weeks from TIA/stroke onset in 6% of patients with symptomatic carotid stenosis. Furthermore, among patients who were enrolled within 1 week in the MATCH (Management of ATherothrombosis with Clopidogrel in High-risk patients) trial, the risk of recurrent stroke appeared to be substantially (but not significantly because of small numbers) reduced with combination therapy (clopidogrel plus aspirin) versus clopidogrel alone, compared with the lack of risk reduction in the subgroup of patients who were enrolled later. The former observation suggests that the risk-benefit ratio of combination therapy compared with monotherapy may be greatest when double antiplatelet therapy is initiated early and continued only for a short period after the ischemic event. Notably, such a policy was associated with promising results in the recently published CARESS (Clopidogrel and Aspirin for Reduction of Emboli in Symptomatic Carotid Stenosis) trial.

Additionally, in the MIRACL (Myocardial Ischemia Reduction with Acute Cholesterol Lowering trial), statin treatment initiated immediately after an unstable angina or a non-Q wave myocardial infarction was associated with a significant reduction of stroke. Because statins seem to reduce the incidence of all strokes and the progression of carotid intima-media thickening, it was postulated that aggressive cholesterol reduction with statins in patients with recent IS or TIA may decrease stroke recurrence. This hypothesis was supported by the shortly presented final results of the SPARCL (Stroke Prevention by Aggressive Reduction in Cholesterol Levels) trial. Finally, in view of the extremely high (31.3%) early risk of stroke in the TIA patients of our cohort with an ABCD score of 6, admission of this TIA subgroup to a stroke unit with a ready access to immediate thrombolysis in case of subsequent stroke appears to be another aggressive albeit potentially effective treatment option. The substantial benefit of thrombolysis when given within 1 hour of stroke onset could be amplified in stroke patients treated within a few minutes of ictus. The results of the German multicenter hospital-based observational study that had identified admission to stroke unit as a valid predictor for survival and functional independence both in IS and TIA patients, lend support to the former assumption.

Certain methodological limitations of the present report should be addressed. First, the ABCD score of the studied patients at the time of their presentation at the ER was identified retrospectively from inspection of medical records and thus the risk of incomplete case ascertainment cannot be excluded. Second, we were unable to complete follow-up in all patients. However, our additional analyses have already addressed this potential shortcoming and indicate that it is unlikely that patients lost to follow-up may have biased the documented association between the ABCD score and the risk of stroke. Third, there is accruing evidence confirming that TIA patients with diffusion-weighted imaging ischemic lesions on MRI are at substantially higher risk of stroke than those without. Because diffusion-weighted brain MRI was available in an extremely limited number of patients in our cohort (5.7%), this potential confounder was not included in the multivariable Cox-regression model. Fourth, because we evaluated only hospitalized patients, it should be acknowledged that the present study validated the ABCD score in a different cohort of patients from those for which the model was intended to be used. More specifically, the ABCD model was developed in the outpatient setting, to predict risk for all TIA patients. Thus, further validation of this score is needed especially in patients with TIA that were referred to the ED but not hospitalized.

In conclusion, the present study validates the predictive value of the ABCD score in identifying hospitalized TIA patients with a high risk of early stroke and provides further evidence for its potential applicability in clinical practice. Our findings advocate the use of the simple and practical ABCD score in the emergency setting to triage TIA patients that may benefit the most from hospital admission, expedited diagnos-
tic evaluation, and early instigation of effective treatment strategies such as early carotid endarterectomy, close monitoring in a stroke unit with ready access to thrombolysis, and more aggressive risk factor modification.

Disclosures

None.

References

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