ABC\textsuperscript{D2} Score Predicts Severity Rather Than Risk of Early Recurrent Events After Transient Ischemic Attack

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**Background and Purpose**—The ABC\textsuperscript{D2} score predicts the early risk of stroke after transient ischemic attack (TIA). However, data on the severity of recurrent events would also be useful. Do patients with high scores also have more severe early recurrent strokes, perhaps further justifying hospital admission? Do patients with low scores have a low early risk of recurrent TIA as well as recurrent stroke?

**Methods**—We completed a prospective, population-based study in Oxfordshire, England, of 500 consecutive patients presenting with TIA from April 1, 2002, by using multiple methods of case ascertainment (Oxford Vascular Study). Recurrent TIA, minor stroke, and major stroke (National Institutes of Health Stroke Scale score \textgreater{}3 at the time of first assessment) were identified by face-to-face follow-up. Predictive value was expressed as the area under the receiver operating characteristic curve.

**Results**—Of 500 patients with TIA, 55 had a recurrent TIA (11.0%; 95% CI, 8.3% to 13.7%) and 50 had a recurrent stroke (10.0%; 95% CI, 7.5% to 12.0%) within 7 days. The ABC\textsuperscript{D2} score was highly predictive of major recurrent stroke (area under the receiver operating characteristic curve=0.80; 95% CI, 0.72 to 0.87, \(P\textless{}0.0001\)), weakly predictive of minor stroke (area under the receiver operating characteristic curve=0.57; 95% CI, 0.43 to 0.71, \(P=0.26\)), and inversely related to risk of recurrent TIA (area under the receiver operating characteristic curve=0.37; 95% CI, 0.29 to 0.44, \(P=0.001\)) (overall heterogeneity, \(P=0.0001\)). The score predicted stroke-related disability, length of stay for recurrent stroke, and hence, overall acute hospital care costs.

**Conclusions**—The ABC\textsuperscript{D2} score predicts severity of recurrent events after TIA, high scores being associated with major recurrent stroke and low scores with high rates of recurrent TIA. These findings have implications for cost-benefit analyses of policies on hospital admission for patients with high scores and for the advice given to patients with low scores. (Stroke. 2010;41:00-00.)

**Key Words:** epidemiology \(|\) prevention \(|\) prognosis \(|\) transient ischemic attack

Recent hospital and population-based studies have shown a high early risk of stroke after a transient ischemic attack (TIA) or minor stroke.\textsuperscript{1–8} The ABCD score was developed to predict individual risk and to triage patients on first presentation to medical attention.\textsuperscript{7} The score is based on clinical characteristics detected at the time of first assessment (Age, Blood pressure, Clinical features, and Duration of symptoms). This score was further validated and refined with the addition of a point for diabetes (ABCD\textsuperscript{2} score).\textsuperscript{9} Since publication, the ABCD and ABCD\textsuperscript{2} scores have been independently validated in different clinical settings and have generally performed reasonably well.\textsuperscript{10–14} The ABCD\textsuperscript{2} score is now recommended for use in triaging patients with suspected TIA by several major clinical guidelines.\textsuperscript{15–18}

Despite rapid adoption of the ABCD\textsuperscript{2} score in clinical guidelines and in routine clinical practice, several important questions about its predictive value remain. First, although patients with high scores are at high risk of early recurrent stroke, there are no reliable data on the severity of recurrent strokes, long-term outcome, hospitalization, subsequent length of stay, and acute-care costs. Do patients with high scores have mainly minor strokes, or does the severity of stroke also increase with ABCD\textsuperscript{2} score? This information would have important implications for analyses of the clinical rationale and cost-effectiveness of hospital admission for patients with high scores to facilitate thrombolysis. Second, patients with low scores have a low early risk of recurrent stroke, but what about recurrent TIA? A low score could be falsely reassuring for patients if the risk of recurrent TIA remains high despite the risk of stroke. We aimed to answer these questions in a prospective, population-based study of all incident and recurrent TIAs and strokes, the Oxford Vascular Study (OXVASC).
Patients and Methods

The OXVASC is a population-based study of all strokes and TIAs in 91,105 individuals of all ages registered with 63 general practitioners in Oxfordshire, England. The present article includes the first 500 consecutive TIA cases, from April 1, 2002, to May 4, 2007. The study methods have been described elsewhere.19–21 In brief, multiple overlapping methods of “hot” and “cold” pursuit were used to achieve near-complete ascertainment of all individuals with TIA or stroke.19–21 These included the following procedures: (1) a daily, rapid-access “TIA clinic” to which participating general practitioners and the local accident and emergency departments refer all individuals with suspected TIA or stroke whom they would not normally admit to hospital; (2) daily searches of admissions to the medical, stroke, neurology, and other relevant wards; (3) daily searches of the local accident and emergency department attendance register; (4) monthly searches of general practitioner diagnostic coding and hospital discharge codes; and (5) monthly searches of all cranial and carotid imaging studies performed in local hospitals.

All patients gave informed consent to participate in the study and were seen by study physicians as soon as possible after their initial presentation. Event characteristics and risk factors were recorded, and all patients underwent brain imaging by computed tomography and/or magnetic resonance imaging. All cases were subsequently reviewed by the study senior neurologist (P.M.R.) and classified as TIA, stroke, or other condition, according to standard definitions.19–21 All patients presenting with stroke were asked about recent symptoms of TIA. All patients were followed up face-to-face at 30 days by a study nurse or physician. Patients were assessed for recurrent symptoms, medications, and disability scores. All patients with recurrent strokes and TIAs who presented to medical attention would also be identified in the short term by ongoing daily case ascertainment within OXVASC.

Baseline characteristics were recorded for all patients, and assessments were made for severity of the event (according to the National Institutes of Health Stroke Scale [NIHSS]), territory, and clinical features. The NIHSS is a 15-item scale that measures the degree of neurologic impairment. Scores of the NIHSS range from 0 to 42, with higher values reflecting more severe neurologic deficit.22

A recurrent stroke was defined as a new or persistent neurologic symptom in a patient in whom the initial symptoms had already substantially or fully recovered. A recurrent TIA was defined as a new neurologic symptom of <24 hours’ duration in a patient in whom the initial symptoms had completely recovered. In patients who had multiple recurrent events, the end point was classified as the first recurrence after the index TIA. All patients with recurrent events were reassessed by a study physician and the case was reviewed by P.M.R. Severity of the recurrent event was based on clinical examination at the time of assessment by a study physician. Minor stroke was defined as an NIHSS score of 0 to 3 and major stroke as an NIHSS score >3. Stroke-related disability/handicap was assessed with the modified Rankin Scale (mRS) at the 1- and 6-month follow-up visits.23 Disabling stroke was defined by an mRS score >2. To account for those patients who had high premorbid mRS scores, we performed a separate analysis of the change in mRS status from the premorbid condition to 1 and 6 months.

Analysis

We restricted analyses to the risk of TIA or stroke after the first probable or definite TIA in the study period. Risk of recurrent stroke and TIA, severity of recurrent stroke (NIHSS and mRS scores), and acute-care costs were determined in relation to the ABCD² score,9 calculated as follows: ABCD² score = age >60 years +1, blood pressure >140 systolic and/or ≥90 diastolic mm Hg =1, clinical features (unilateral weakness =2, speech disturbance =1), duration of symptoms (≥60 minutes =2, 10 to 59 minutes =1, ≤10 minutes =0), and diabetes =1. Acute-care costs relating to recurrent strokes were calculated as reported previously.24,25 Predictive value was expressed as the area under the receiver operating characteristic curve (AUROC).

Results

Table 1 shows the baseline characteristics of all 500 consecutive patients with first TIAs in the study period from April 1, 2002, to May 4, 2007. The mean (range) age at the first event was 72 (24–98) years, with 174 (35%) patients whose age was >80.

Of the 500 patients with TIAs, 55 had a recurrent TIA (11.0%; 95% CI, 8.3% to 13.7%) and 50 had a recurrent stroke (10.0%; 95% CI, 7.5% to 12.0%) within 7 days of their first TIA. Forty-eight of 50 (96%) patients with recurrent strokes underwent brain imaging. The majority (44/50, 88%) had computed tomography as first-line imaging, and 11 went on to have magnetic resonance imaging. The ABCD² score was predictive of the 7-day risk of recurrent stroke (AUROC=0.71; 95% CI, 0.63 to 0.79, P<0.001). However, when the analysis was stratified by severity of the recurrent stroke (28 major strokes versus 22 minor strokes), the score was more highly predictive of the 7-day risk of major recurrent stroke (AUROC=0.80; 95% CI, 0.72 to 0.87, P<0.0001) but only weakly predictive of minor stroke, with an AUROC (0.57; 95% CI, 0.43 to 0.71, P=0.26) that was not significantly >0.50 (ie, chance). Moreover, the AUROC for the 7-day risk of recurrent TIA was significantly <0.50 (0.37; 95% CI, 0.29 to 0.44, P=0.001), indicating that the score was inversely related to risk. Formal testing of the differences in the predictive value of the score for these different outcomes showed statistically significant heterogeneity (P<0.0001), even when the comparison was limited to the predictive value for major stroke versus that for minor stroke (P=0.004). When TIA and stroke outcomes were combined, the predictive values cancelled each other out, such that the overall predictive value for any recurrent event was no greater than chance (0.54; 95% CI, 0.47 to 0.60, P=0.276).

Table 1. Baseline Clinical Characteristics of TIA Patients in the OXVASC Cohort

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>TIA (N=500)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>72.5 (12.7)</td>
</tr>
<tr>
<td>Male sex</td>
<td>219 (43.8%)</td>
</tr>
<tr>
<td>Systolic BP, mean (SD), mm Hg</td>
<td>152.7 (29.0)</td>
</tr>
<tr>
<td>Diastolic BP, mean (SD), mm Hg</td>
<td>82.1 (14.2)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>256 (52.8%)</td>
</tr>
<tr>
<td>Clinical features</td>
<td></td>
</tr>
<tr>
<td>Unilateral weakness</td>
<td>210 (42.0%)</td>
</tr>
<tr>
<td>Speech disturbance without weakness</td>
<td>203 (40.6%)</td>
</tr>
<tr>
<td>Duration of symptoms</td>
<td></td>
</tr>
<tr>
<td>&lt;10 min</td>
<td>105 (21%)</td>
</tr>
<tr>
<td>10–59 min</td>
<td>167 (33.4%)</td>
</tr>
<tr>
<td>&gt;60 min</td>
<td>228 (45.6%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>66 (13.2%)</td>
</tr>
<tr>
<td>Angina or myocardial infarction</td>
<td>95 (19.6%)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>29 (5.8%)</td>
</tr>
<tr>
<td>Previously diagnosed atrial fibrillation</td>
<td>78 (15.8%)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>69 (13.8%)</td>
</tr>
</tbody>
</table>

BP indicates blood pressure.
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Figure. Risk of recurrent events during the 7 days after a TIA stratified by ABCD² score. The top figure shows the proportionate severity of recurrent events at each score, and the bottom figure shows the absolute risks of events by severity.

The Figure shows the risks of TIA, minor stroke, and major stroke for different ABCD² scores. The 7-day risk of any stroke was 18.7% (36/193) in patients with ABCD² scores ≥5 versus 4.6% (14/307) in patients with a score of 4 or less (P<0.001). This difference in risk was due mainly to a difference in the risk of major stroke of 12.8% (24/193) versus 1.3% (4/307, P<0.001), with a smaller difference in the risk of minor stroke of 6.2% (12/193) versus 3.3% (10/307, P=0.12). The direction of the risk relation was reversed for recurrent TIA, patients with ABCD² scores ≥5 having a lower risk (5.7%, 11/193) than those with a score of 4 or less (14.3%, 44/307, P=0.004). No major strokes occurred in patients with an ABCD² score of <3, and no recurrent TIAs occurred in patients with an ABCD² score of 7 (Table 2). In the 55 patients who had a recurrent TIA, 1 went on to have a minor recurrent stroke within 7 days of the initial TIA, and 2 had a recurrent stroke (1 major, 1 minor) between 7 and 90 days after the initial TIA. The ABCD² scores of the initial and recurrent TIAs in these 3 cases were 1, 5, and 5, and 1, 5, and 6, respectively. The patient with the 2 TIAs with ABCD² scores of 1 was a 52-year-old woman with 2 sensory TIAs who was subsequently found to have cerebral vasculitis.

When the analysis was stratified by disability due to recurrent stroke at the 6-month follow-up visit (21 disabling versus 28 nondisabling), the score was highly predictive of the 7-day risk of disabling recurrent stroke (AUROC=0.78; 95% CI, 0.70 to 0.87, P<0.001) but less strongly predictive of nondisabling recurrent stroke (0.64; 95% CI, 0.53 to 0.76, P=0.01). Consequently, the proportion of recurrent strokes that were disabling was greater in patients with ABCD² scores ≥5 (18/36, 50%, versus 3/13, 23%; odds ratio=3.33; 95% CI, 0.8 to 14.2, P=0.10). The score remained highly predictive of the 7-day risk of disabling stroke when disability was defined by a 2-point deterioration in the mRS score at 6 months (AUROC=0.78; 95% CI, 0.69 to 0.87, P<0.001). Consequently, the proportion of recurrent strokes that resulted in at least a 2-point deterioration in the mRS score at 6 months was greater in patients with an ABCD² score ≥5 (14/36, 39%, versus 2/13, 15%; odds ratio=3.50; 95% CI, 0.7 to 18.2, P=0.15).

The average hospital costs for patients with recurrent stroke were stratified by ABCD² score. There was a trend for patients with ABCD² scores ≥5 to incur greater costs than those with lower scores (£8209 versus £2009, P=0.05), due to a greater likelihood of hospital admission after recurrent stroke (67% versus 43%; odds ratio=2.67; 95% CI, 0.8 to 9.4, P=0.12) and a longer mean hospital stay (31.3 versus 6.1 days, P=0.04).

Table 3 demonstrates the relation between the individual components of the ABCD² score and the 7-day risk of recurrent TIA, minor stroke, and major stroke. Age ≥60 years (hazard ratio=5.01; 95% CI, 0.68 to 36.87, P=0.12), hypertension (hazard ratio=3.33; 95% CI, 1.01 to 11.03, P=0.05), motor weakness (hazard ratio=6.35; 95% CI, 1.89 to 21.36, P=0.003), and duration of event ≥60 minutes (hazard ratio=2.64; 95% CI, 0.91 to 7.67, P=0.006) were significantly associated with recurrent major stroke. Recurrent TIA was more common in patients age <60 years (hazard ratio=1.76; 95% CI, 0.95 to 3.28, P=0.08), those without motor symptoms (hazard ratio=2.19; 95% CI, 1.22 to 3.93, P=0.009), and those with a duration of the initial event <10 minutes (hazard ratio=3.87; 95% CI, 1.84 to 8.13, P=0.001). The predictive power of these variables for risk of minor stroke was intermediate (Table 4).

In an additional univariate analysis of non-ABCD² score clinical features, patients with recurrent TIA were more likely to present with visual or sensory symptoms (Table 4). There were trends for previous stroke (P=0.06) and atrial fibrillation (P<0.001) to predict major stroke. In patients with recurrent TIA, 12 of 55 (21%) preceding TIAs were amaurosis fugax and 7 of 17 (41%) vertebrobasilar events were binocular visual disturbance. This was in contrast to recurrent strokes after TIA, for which only 2 of 49 (4%) preceding
events were amaurosis fugax and 1 of 12 (8%) preceding vertebrobasilar events was binocular visual disturbance.

Of the 55 patients with recurrent TIA, 47 had episodes similar to the index TIA, with motor symptoms in 15 (27%), speech symptoms in 14 (26%), sensory symptoms in 14 (26%), vertigo in 4 (7%), and visual symptoms (amaurosis fugax, binocular visual disturbance, hemianopia, or diplopia) in 23 (42%). Of the 55 patients with recurrent TIA, 49 (89%) were reviewed after the recurrent event such that the clinical details could be clarified.

**Discussion**

The ABCD² score has been shown to be highly effective in the prediction of recurrent stroke after TIA at 7 days. However, no previously published study has reported data on the relation between ABCD² score and the severity of recurrent stroke, and there are few published data on the risk of recurrent TIA. We have shown that the ABCD² score predicts severity of the recurrent event after TIA, with a stronger association with major recurrent stroke than with minor stroke and with a negative association with recurrent TIA.

In our study, the 7-day risk of recurrent TIA was high (≈11%). In a California cohort of 1707 patients, recurrent TIAs (identified by presentation to the Emergency Department rather than face-to-face follow-up) occurred in 191 patients (11.2%) within 90 days. In keeping with our findings, a shorter duration of the initial TIA and sensory symptoms only predicted recurrent TIA. Among those TIAs lasting ≤10 minutes and those with sensory symptoms alone, there was a 40% 90-day risk of recurrent TIA but no early recurrent strokes. We found a higher risk of recurrent TIAs in patients presenting with sensory or visual symptoms, age <60 years, normotension, and initial symptom duration ≤10 minutes.

One explanation for the predictive value of the ABCD² score for recurrent stroke is that the score may be acting as a diagnostic tool, identifying patients who are more likely to have had a true TIA, as a clinical diagnosis of TIA can be unreliable. However, in both the derivation and validation of the ABCD system, when the analysis was limited to patients with neurologist-confirmed TIA, the score remained predictive. Our observation that patients with lower scores are more likely to have minor stroke than major stroke also

<table>
<thead>
<tr>
<th>ABCD² Score</th>
<th>Patients, n (%)</th>
<th>TIA, n (%)</th>
<th>% Risk (95% CI)</th>
<th>Minor Stroke, n (%)</th>
<th>% Risk (95% CI)</th>
<th>Major Stroke, n (%)</th>
<th>% Risk (95% CI)</th>
<th>Combined Stroke/TIA, n (%)</th>
<th>% Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>29 (6%)</td>
<td>5 (9%)</td>
<td>17.2 (3.5–30.9)</td>
<td>2 (9%)</td>
<td>6.9 (0–16.1)</td>
<td>0</td>
<td>0</td>
<td>7 (7%)</td>
<td>24.1 (8.6–39.6)</td>
</tr>
<tr>
<td>2</td>
<td>73 (15%)</td>
<td>13 (24%)</td>
<td>17.8 (9.0–26.6)</td>
<td>2 (9%)</td>
<td>2.7 (0–6.4)</td>
<td>0</td>
<td>0</td>
<td>15 (14%)</td>
<td>20.5 (11.3–29.7)</td>
</tr>
<tr>
<td>3</td>
<td>90 (18%)</td>
<td>13 (24%)</td>
<td>14.4 (7.1–21.7)</td>
<td>4 (18%)</td>
<td>4.4 (0.1–8.7)</td>
<td>2 (7%)</td>
<td>2.2 (0–5.3)</td>
<td>19 (18%)</td>
<td>21.1 (12.7–29.5)</td>
</tr>
<tr>
<td>4</td>
<td>115 (23%)</td>
<td>13 (24%)</td>
<td>11.5 (5.4–17.2)</td>
<td>2 (9%)</td>
<td>1.7 (0–4.1)</td>
<td>2 (7%)</td>
<td>1.7 (0–4.1)</td>
<td>17 (16%)</td>
<td>14.8 (8.3–21.3)</td>
</tr>
<tr>
<td>5</td>
<td>95 (19%)</td>
<td>5 (9%)</td>
<td>5.3 (0.8–9.8)</td>
<td>4 (18%)</td>
<td>4.2 (0.1–8.3)</td>
<td>8 (29%)</td>
<td>8.4 (2.7–14.1)</td>
<td>17 (16%)</td>
<td>17 (9.4–24.6)</td>
</tr>
<tr>
<td>6</td>
<td>92 (18%)</td>
<td>6 (11%)</td>
<td>6.5 (1.4–11.6)</td>
<td>8 (36%)</td>
<td>8.7 (2.4–15.0)</td>
<td>14 (50%)</td>
<td>15.2 (7.6–22.8)</td>
<td>28 (27%)</td>
<td>30.4 (21.0–39.8)</td>
</tr>
<tr>
<td>7</td>
<td>6 (1%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2 (7%)</td>
<td>33.3 (0–70.9)</td>
<td>2 (2%)</td>
<td>33.3 (0–70.9)</td>
</tr>
<tr>
<td>Total</td>
<td>500 (100%)</td>
<td>55 (100%)</td>
<td>11.0 (8.3–13.7)</td>
<td>22 (100%)</td>
<td>4.4 (2.6–6.2)</td>
<td>28 (100%)</td>
<td>5.8 (3.6–8.0)</td>
<td>105 (100%)</td>
<td>21 (17.5–24.5)</td>
</tr>
</tbody>
</table>

Table 2. Seven-Day Risk of Recurrent Events After TIA, Stratified by ABCD² Score and Severity of the Recurrent Event

<table>
<thead>
<tr>
<th>TIA</th>
<th>Minor Stroke</th>
<th>Major Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;60 y</td>
<td>HR (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>SBP &gt;140 or DBP &gt;90 mm Hg</td>
<td>1.41 (0.74–2.67)</td>
<td>0.30</td>
</tr>
</tbody>
</table>

Clinical features

<table>
<thead>
<tr>
<th>No weakness or speech disturbance</th>
<th>1.00</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral weakness</td>
<td>0.46 (0.26–0.82)</td>
</tr>
<tr>
<td>Speech disturbance</td>
<td>0.42 (0.23–0.77)</td>
</tr>
<tr>
<td>Combined motor or speech symptoms</td>
<td>0.40 (0.23–0.68)</td>
</tr>
</tbody>
</table>

Duration of symptoms

| >60 min                      | 0.26 (0.12–0.54) | 0.001 |
| 10–59 min                    | 0.81 (0.48–1.47) | 0.005 |
| <10 min                      | 1.00             | 1.00 |

Diabetes                      | 1.29 (0.63–2.63) | 0.49 |

HR indicates hazard ratio; SBP, systolic blood pressure; and DBP, diastolic blood pressure.
argues against a major diagnostic element, because clinical and imaging diagnosis of minor stroke is much more reliable than for TIA. Moreover, a recent collaborative, multicenter study showed that the ABCD² score is still highly predictive of recurrent stroke in TIA patients with an acute ischemic lesion on diffusion-weighted brain imaging (P.M. Rothwell, unpublished data, 2009), indicating that the prognostic value is not purely related to diagnostic certainty. It has also been shown that TIA patients who have no acute lesions on diffusion-weighted brain imaging have a low risk of recurrent stroke but a high risk of recurrent TIA during the following year.28

One could also argue that in clinical practice, patients with lower ABCD² scores might be managed less aggressively, but in our cohort, the vast majority were seen in the daily OXVASC clinic, most were also nested within the EXPRESS study, and so they would have received standard management, that is, antiplatelet treatment, 40 mg simvastatin, and Coversyl plus, when appropriate. However, it is true that clinical patients with ABCD² scores <5 were somewhat less likely to receive clopidogrel in addition to aspirin than those with higher scores (81/270, 30%, versus 58/150, 39%, P=0.07). However, this small absolute difference in clopidogrel use would not explain such a striking trend in TIA risk in relation to ABCD² score.

In our study, 24 of 29 (83%) major stroke recurrences within 7 days were preceded by a TIA with an ABCD² score ≥5. Previous studies in patients with stroke rather than TIA have shown that some of the factors that are included in the ABCD² score, including motor or speech symptoms, hypertension, and age, are associated with a worse functional outcome after stroke.30–32 However, the mechanism of the associations with severity of stroke after TIA that we have observed is uncertain. The ability of the ABCD² score to predict severity of subsequent recurrent events is an additional benefit of its use in early triage of TIA patients and would support admission for patients with higher scores on the basis of a greater opportunity to administer early thrombolysis if a stroke occurs. In our cohort, 53% (19/36) of recurrent strokes in patients with an ABCD² score ≥5 would have been thrombolyzable by standard criteria.

Our study had some potential limitations. First, our analysis of the severity of recurrent stroke was based on only 51 stroke outcomes. Although this is more than in the vast majority of published validations of the ABCD or ABCD² scores and our analysis had sufficient statistical power, further studies would help confirm or refute our findings. Second, we may have underestimated the risk of severe stroke because some patients with a major stroke with a preceding TIA may not have been identified because we excluded those in whom it was impossible to obtain a definite history of TIAs because they were aphasic, confused, or unconscious. Third, the mechanism of the association between the ABCD² score and severity of recurrent events is uncertain. Further work is required to determine risk of recurrent events stratified by ABCD² score, severity of recurrence, and underlying etiology, but such a 3-way stratification will require larger collaborative studies.

In summary, strictly speaking, the ABCD² score appears to predict severity of recurrent events rather than risk of any recurrent event. The strong association between high ABCD² score and severe recurrent stroke adds to the case for admission of patients with high ABCD² scores to maximize preventive treatment and allow early thrombolysis if a recurrence occurs. Patients with low ABCD² scores should be warned that they are at appreciable risk of recurrent TIA, but the subsequent risk of stroke remains low.

Table 4. Univariate Associations of Non-ABCD² Score Clinical Characteristics and Risk of Recurrent Events Within 7 Days

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>TIA HR (95% CI)</th>
<th>P Value</th>
<th>Minor Stroke HR (95% CI)</th>
<th>P Value</th>
<th>Major Stroke HR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>0.68 (0.40–1.16)</td>
<td>0.16</td>
<td>0.98 (0.43–2.24)</td>
<td>0.97</td>
<td>0.66 (0.31–1.38)</td>
<td>0.27</td>
</tr>
<tr>
<td>Amaurosis fugax</td>
<td>2.26 (1.20–4.29)</td>
<td>0.01</td>
<td>0.34 (0.05–2.82)</td>
<td>0.34</td>
<td>0.29 (0.04–2.16)</td>
<td>0.23</td>
</tr>
<tr>
<td>Binocular visual disturbance</td>
<td>1.57 (0.68–3.67)</td>
<td>0.29</td>
<td>0.04 (0–43.27)</td>
<td>0.37</td>
<td>0.04 (0–19.67)</td>
<td>0.32</td>
</tr>
<tr>
<td>Sensory symptoms</td>
<td>1.72 (1.00–2.97)</td>
<td>0.05</td>
<td>1.39 (0.57–3.42)</td>
<td>0.47</td>
<td>0.82 (0.33–2.02)</td>
<td>0.66</td>
</tr>
<tr>
<td>Vertigo</td>
<td>0.86 (0.31–2.38)</td>
<td>0.77</td>
<td>0.51 (0.07–3.76)</td>
<td>0.51</td>
<td>0.82 (0.19–3.43)</td>
<td>0.78</td>
</tr>
<tr>
<td>Other risk factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>1.02 (0.44–2.37)</td>
<td>0.97</td>
<td>0.04 (0–14.85)</td>
<td>0.29</td>
<td>2.23 (0.90–5.49)</td>
<td>0.08</td>
</tr>
<tr>
<td>Previous TIA</td>
<td>0.88 (0.43–1.80)</td>
<td>0.74</td>
<td>1.36 (0.50–3.69)</td>
<td>0.55</td>
<td>1.01 (0.38–2.05)</td>
<td>0.99</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>0.51 (0.18–1.41)</td>
<td>0.19</td>
<td>0.34 (0.05–2.51)</td>
<td>0.29</td>
<td>2.35 (1.00–5.53)</td>
<td>0.50</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>0.92 (0.29–2.94)</td>
<td>0.89</td>
<td>0.78 (0.11–5.83)</td>
<td>0.81</td>
<td>1.25 (0.30–5.27)</td>
<td>0.16</td>
</tr>
<tr>
<td>Angina</td>
<td>0.78 (0.35–1.72)</td>
<td>0.54</td>
<td>0.26 (0.04–1.93)</td>
<td>0.19</td>
<td>1.81 (0.77–4.26)</td>
<td>0.17</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.13 (0.67–1.91)</td>
<td>0.65</td>
<td>0.93 (0.40–2.15)</td>
<td>0.87</td>
<td>1.67 (0.77–3.61)</td>
<td>0.20</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1.02 (0.50–2.09)</td>
<td>0.95</td>
<td>0.26 (0.04–1.96)</td>
<td>0.19</td>
<td>3.61 (1.69–7.70)</td>
<td>0.001</td>
</tr>
<tr>
<td>Current smoker</td>
<td>1.13 (0.55–2.31)</td>
<td>0.75</td>
<td>1.34 (0.46–3.94)</td>
<td>0.60</td>
<td>1.11 (0.38–3.20)</td>
<td>0.85</td>
</tr>
</tbody>
</table>

HR indicates hazard ratio.
Sources of Funding
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None.

References
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ORIGINAL CONTRIBUTIONS

ABCD² Score Predicts Severity Rather Than Risk of Early Recurrent Events After Transient Ischemic Attack

Arvind Chandratheva, BM, MRCP; Olivia C. Geraghty, MBBS, MRCP; Ramon Luengo-Fernandez, DPhil; Peter M. Rothwell, MD, PhD, FRCP, FMedSci; for the Oxford Vascular Study

Background and Objectives: ABCD² score was developed to predict the risk of early recurrent events (within 7 days) after a TIA. However, it is also useful to predict the severity of recurrent events, i.e., whether patients with high scores had severe strokes rather than minor strokes. ABCD² score was developed based on the Oxford Vascular Study (OXVASC), which is a population-based prospective study including all TIAs and recurrent events.

Methods: This study was conducted on 500 patients with TIA from Oxford, UK, recruited from 2002 to 2004. The patients were followed up to identify recurrent TIAs, minor and major strokes (NIHSS > 3). The ABCD² score was used to predict the risk of recurrent strokes. The receiver operating characteristic (ROC) curve was used to assess the predictive power of the ABCD² score.

Results: In 500 TIA patients, 55 patients (11.0%; 95% CI, 8.3%-13.7%) had recurrent TIAs within 7 days, and 50 patients (10.0%; 95% CI, 7.5%-12.0%) had recurrent strokes (NIHSS > 3). The ABCD² score had a high predictive value for major strokes (ROC area under the curve = 0.80; 95% CI, 0.72-0.87, P < 0.0001), while its predictive value for minor strokes was lower (ROC area under the curve = 0.57; 95% CI, 0.43-0.71, P = 0.26). The ABCD² score was negatively correlated with the risk of recurrent TIAs (ROC area under the curve = 0.37; 95% CI, 0.29-0.44, P = 0.001).

Conclusions: ABCD² score can predict the severity of recurrent events after TIA, with higher scores associated with major strokes and lower scores with minor strokes. The score is also predictive of recurrent TIAs, which is important for clinical decision-making.

Keywords: Epidemiology, Prevention, Prognosis, Transient Ischemic Attack
登记所有的卒中和 TIA 患者。本研究纳入从 2002 年 4 月 1 日到 2007 年 5 月 4 日的第一批 TIA 患者。研究方法在其他文献中已有描述 [19,20]。简单来说，多重叠的“热”和“冷”方法的采用力求对所有 TIA 或卒中的患者达到近乎完整的诊断 [19-21]。包括：(1) 每日在 “TIA 诊所” 由参加的全科医生和当地急诊室快速诊断所有疑似 TIA 或卒中患者，这些患者通常不去医院就诊；(2) 每天搜索内科、卒中病房、神经科或其他相关科室的患者；(3) 每天搜索当地急诊就诊登记；(4) 每月对全科医生的诊断编码和医院出院代码进行搜索；(5) 每月对当地医院所有颅颈影像资料进行搜索。

所有参加本研究的患者均签署了知情同意书，当出现首次症状时会尽快的到研究者处就诊。事件特征和危险因素都进行了记录，所有患者均进行了脑部 CT/MRI 检查。接下来，所有病例均接受资深神经病学家（P.M.R）的复审后根据标准定义划分为 TIA、卒中或其他情况 [19-21]。包括：(1) 每日在 “TIA 诊所” 由参加的全科医生和当地急诊室快速诊断所有疑似 TIA 或卒中患者，这些患者通常不去医院就诊；(2) 每天搜索内科、卒中病房、神经科或其他相关科室的患者；(3) 每天搜索当地急诊就诊登记；(4) 每月对全科医生的诊断编码和医院出院代码进行搜索；(5) 每月对当地医院所有颅颈影像资料进行搜索。

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记录所有患者的基线特征及评估事件的严重程度 (根据国立卫生研究院卒中量表 [NIHSS])、部位和临床特征。NIHSS 是一个有 15 项标准的量表来评估神经功能缺损程度，评分从 0-42 分，分值越高表明神经功能缺损程度越重 [23]。

卒中复发定义为在最初症状已有大部分或完全恢复的基础上又出现了新的或持续的神经症状。TIA 复发定义为在最初症状完全消失后新出现的持续时间小于 24 小时的神经症状。对于多发性复发事件，终点定义为首次 TIA 后的第一次复发。本研究的医生会对所有复发患者进行再评估，P.M.R. 会对病例进行复审。通过本研究医生的临床评估来确定复发事件的严重程度。小卒中定义为 NIHSS 评分 0-3。大卒中定义为 NIHSS 评分大于 3。随访患者 1 月和 6 月后的情况，采用改良 Rankin 量表 (mRS) 对卒中相关残疾进行评分 [24]。残疾定义为 mRS > 2。为了解释有些患者发病前的高 mRS 评分，我们从病前到 1 月和 6 月的 mRS 的变化分别作了分析。

分析
研究阶段我们侧重于首次发生可能或确定 TIA 后发生或卒中的风险。确定卒中复发和 TIA 的风险、卒中复发的严重程度 (NIHSS 和 mRS 评分) 以及急救医护费用和 ABCD² 评分的关系，计算如下：ABCD² 评分 - 年龄 > 60 岁 =1，血压收缩压 > 140 mmHg 和 / 或舒张压 ≥ 90 mmHg =1，临床表现 (≥ 60 分钟 =2，10-59 分钟 =1，<10 分钟 =0)，糖尿病 =1。卒中复发的急救医护费用也通过既往报道过的方法进行计算 [24,25]。预测值通过受试者工作特征曲线下面积 (AUROC) 进行测定。

结果
表 1 所示从 2002 年 4 月 1 日到 2007 年 5 月 4 日连续登记的 500 名首次 TIA 患者的基线特征。首次发作时间平均年龄 72(24-98) 岁，174 名 (35%) 患者年龄超过 80 岁。

这 500 例 TIA 患者中，首次 TIA 后 7 天内 TIA 复发 55 例 (11.0%；95% CI，8.3%-13.7%)，卒中复发 50 例 (10.0%；95% CI，7.5%-12.0%)。50 例卒中复发患者中 48 例 (96%) 接受了头颅影像检查。大多数患者 (44/50，88%) 接受了作为一线影像检查的头颅 CT，11 名患者接受了头颈 MRI。ABCD² 可预测 7 天内卒中复发的风险 (AUROC=0.71；95% CI，0.63-0.79, P<0.001)，然而对卒中复发严重程度 (28 例卒中 vs.22 例小卒中) 进行分层分析后发现，评分对 7 天的大卒中复发有很强的预测作用 (AUROC=0.80；95% CI，0.72-0.87, P<0.0001)，对小卒中的预测作用相对较弱，结果没有显著性差异 (AUROC=0.57；95% CI，0.43-0.71, P=0.26)。进一步分析发现，7
天 TIA 复发风险的 AUROC 小于 0.50(AUROC=0.37; 95% CI: 0.29-0.44, \( P=0.001 \)), 表示评分和风险呈反比。对不同结局测试其不同的预测变量发现有很大的异质性 (\( P<0.0001 \)), 特别是在比较卒中和小卒中预
测价值的时候 (\( P=0.004 \))。当把 TIA 和卒中结局合并的时候，预测值相互抵消，因此对任何复发事件而言均是机遇 (0.54; 95% CI: 0.47-0.60, \( P=0.276 \))。

图显示的是不同 ABCD^2 评分相应的 TIA、小
卒中和大卒中的风险。ABCD^2 评分 \( \geq 5 \) 的患者 7 天
卒中复发风险是 18.7%(36/193), ABCD^2 评分 \( \leq 4 \)
者的风险是 4.6%(14/307)(\( P<0.001 \))。风险不同主要是
大卒中风险不同，12.8%(24/193) 对比 1.3%(4/307,
\( P<0.001 \)), 而小卒中风险差别较小，6.2% (12/193)

di 绝对风险。ABCD^2 评分与 TIA 复发风险呈负相关, ABCD^2 评分 \( \geq 5 \) 的患者风险 (5.7%, 11/193) 比 ABCD^2 评分 \( \leq 4 \) (14.3%, 44/307, \( P=0.004 \))
的患者更低。ABCD^2 评分 \( <5 \) 分的患者中没有大卒
中，ABCD^2 评分为 7 分的患者中没有 TIA 复发 (图 2).

在 55 例 TIA 复发患者中，1 例在首发 TIA 的 7
t 天内进展为小卒中，2 例在 7 天到 90 天之间卒中复
发 (大卒中和小卒中各 1 例)。在这三个病例中首发
和复发 TIAs 的 ABCD^2 评分为 1、5、5 和 1、5、6。一位 52 岁的妇女有两次 TIAs，ABCD^2 评分均为 1，
均为感觉性 TIA，后来被发现为颅内血管炎。

根据 6 月时随访对残疾情况 (21 例残疾 vs. 28 例非残疾) 进行分层分析时发现，7 天伴残疾的卒中复发
(AUROC=0.78; 95% CI, 0.70-0.87, \( P<0.001 \)) 比
非残疾的卒中复发 (AUROC=0.64; 95% CI, 0.53-
0.76, \( P=0.01 \)) 的预测性更强。结果，卒中复发中残
疾的比例在 ABCD^2 评分 \( \geq 5 \) 的患者中的比例更大
(18/36, 50% vs. 3/13, 23%; OR=3.33; 95% CI, 0.8-
14.2, \( P=0.10 \))。当残疾被定义为 6 个月内 mRS 评
分恶化至少 2 分时，评分仍然对 7 天伴残疾的卒中
有更高的预测作用 (AUROC=0.78; 95% CI, 0.69-0.87,
\( P<0.001 \))。卒中复发导致 6 月内 mRS 恶化至少 2
者在 ABCD^2 评分 \( \geq 5 \) 的患者中比例更大 (14/36,39%
vs. 2/13,15%; OR=3.50; 95% CI, 0.7-18.2, \( P=0.15 \))。

卒中复发的平均入院花费通过 ABCD^2 进行分层，有这样一个趋势，ABCD^2 评分 \( \geq 5 \) 比其他评分
低的花费更多 (\£8209 vs. \£2090, \( P=0.05 \))，因为前
者有更大的入院可能性 (67% vs. 43%; OR=2.67; 95%
CI, 0.8-9.4, \( P=0.12 \)) 以及有更长的平均住院时间 (31.3
vs. 6.1 天, \( P=0.04 \))。

表 3 所示 ABCD^2 评分各组成部分和 7 天 TIA 复
发、小卒中以及大卒中发病风险的关系。年龄 \( \geq 60
\) 岁 (HR=5.01; 95% CI, 0.68-36.87, \( P=0.12 \))、高
血压 (HR=3.33; 95% CI, 1.01-11.03, \( P=0.05 \))、运
动障碍 (HR=6.35; 95% CI, 1.89-21.36, \( P=0.003 \)) 和症
状持续时间 \( \geq 60 \) 分钟 (HR=2.64; 95% CI, 0.91-7.67,
\( P=0.06 \)) 与大卒中复发联系密切。TIA 复发在年龄
\( <60 \) 岁 (HR=1.76; 95% CI, 0.95-3.28, \( P=0.08 \))、无
运动障碍 (HR=2.19; 95% CI, 1.22-3.93, \( P=0.009 \))
和首发事件持续时间 \( <10 \) 分钟 (HR=3.87; 95% CI,
1.84-8.13, \( P=0.001 \)) 的患者中更多见。这些变量对
小卒中的预测强度居于两者之间 (表 4)。

此外，对非 ABCD^2 评分的临床症状行单因素
表2 TIA后7天复发事件的风险，以ABCD²评分和复发事件的严重程度进行分层

<table>
<thead>
<tr>
<th>ABCD²评分</th>
<th>病例数</th>
<th>TIA，n(%)</th>
<th>小卒中，% (95% CI)</th>
<th>大卒中，% (95% CI)</th>
<th>合并卒中/TIA，% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>29(6%)</td>
<td>5(9%)</td>
<td>17.2 (3.5–30.9)</td>
<td>0</td>
<td>7 (7%)</td>
</tr>
<tr>
<td>2</td>
<td>73(15%)</td>
<td>13(24%)</td>
<td>17.8 (9.0–26.6)</td>
<td>2(9%)</td>
<td>0 (9%)</td>
</tr>
<tr>
<td>3</td>
<td>90(18%)</td>
<td>14.7(21.1)</td>
<td>4(18%)</td>
<td>4.4 (0.1–8.7)</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>4</td>
<td>115(23%)</td>
<td>24(20%)</td>
<td>11.3 (5.4–17.2)</td>
<td>2(9%)</td>
<td>17 (16%)</td>
</tr>
<tr>
<td>5</td>
<td>95(19%)</td>
<td>5(9%)</td>
<td>5.3 (0.8–9.8)</td>
<td>8(29%)</td>
<td>8.4 (2.7–14.1)</td>
</tr>
<tr>
<td>6</td>
<td>92(18%)</td>
<td>6(11%)</td>
<td>6.5 (1.4–11.6)</td>
<td>8(36%)</td>
<td>15.2 (7.6–22.8)</td>
</tr>
<tr>
<td>7</td>
<td>6(1%)</td>
<td>0</td>
<td>4(2%)</td>
<td>2 (7%)</td>
<td>33.3 (0–70.9)</td>
</tr>
<tr>
<td>总数</td>
<td>500(100%)</td>
<td>55(100%)</td>
<td>11.0 (8.3–13.7)</td>
<td>22(100%)</td>
<td>4.4 (3.6–8.0)</td>
</tr>
</tbody>
</table>

表3 TIA后7天复发TIA或卒中和ABCD²评分各组成部分的关系

<table>
<thead>
<tr>
<th>年龄 &gt;60岁</th>
<th>HR(95% CI)</th>
<th>P值</th>
<th>HR(95% CI)</th>
<th>P值</th>
<th>HR(95% CI)</th>
<th>P值</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP&gt;140或DBP&gt;90mmHg</td>
<td>1.41 (0.74–2.67)</td>
<td>0.30</td>
<td>2.54 (0.75–8.57)</td>
<td>0.13</td>
<td>3.33 (1.01–11.03)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

讨论

ABCD²评分显示了对TIA发作后7天内卒中复发的预测作用非常有效[7,9,10,12,14]。然而，既往的研究没有报道ABCD²评分和卒中复发的严重程度之间的关系，有关TIA复发风险的报道也很有限。本研究已经证实ABCD²评分能预测TIA后事件复发的严重程度，与大卒中的关系比与小卒中的关系密切，和TIA复发呈负相关。

本研究中7天TIA复发的风险很高（约11%）。在加利福利亚队列中的1707例中有191例在90天内TIAs复发（通过急诊科而不是面对面的随访来诊断）[26]。和我们的研究一致，首次TIA持续时间越短和感觉症状可预测TIA复发。TIAs持续时间≤10分和只有感觉症状者，90天TIA复发风险为40%，但是没有早期卒中复发[26]。我们发现有感觉或视觉症状、年龄<60岁、血压正常和最初症状持续时间<10分钟的TIAs患者复发风险高。

ABCD²评分可以预测卒中复发的一个可能解释是评分可作为一个诊断工具来识别真正的TIA，因为TIA的临床诊断可能不甚可靠[27]。然而，在ABCD系统的发展和验证中，当分析局限于神经科医生证实的TIA时，评分有预测作用[7,9]。我们发现

HR，危险比；SBP，收缩压；DBP，舒张压。
评分低的患者更容易患小卒中而不是大卒中,这也反驳了一个诊断的主要因素,因为临床和影像学诊断小卒中比 TIA 更可靠。此外,一个新近的多中心合作研究发现 ABCD² 评分对在弥散加权脑成像中显示有急性缺血灶的卒中复发的 TIA 患者中仍然有很高的预测作用 ((P.M. Rothwell, 数据未发表,2009),显示预测价值不仅与明确诊断有关。在随访中发现对于弥散加权脑成像上没有发现急性病灶的 TIA 患者卒中复发风险低而 TIA 复发风险高 [28]。

在临床实践中处理 ABCD² 评分低的患者也许不那么积极,但是在我们的队列中,大多数患者在每天 OXVASC 诊所就诊,其中很多还参加了 EXPRESS 研究,所以他们都得到了标准化的治疗,比如抗血小板治疗和 40 mg 辛伐他汀,必要时加上培哚普利。然而,临床上除了阿司匹林外,氯吡格雷用于 ABCD² 评分<5 分患者比评分高的患者少 (81/270, 30%, vs. 58/150, 39%, P=0.07)。但氯吡格雷应用方面的微小差异不能解释与 ABCD² 评分相关的 TIA 风险的显著趋势。本研究中 29 例卒中复发中有 24 例 (83%) 之前 TIA 发作的 ABCD² 评分≥5。既往关于脑卒中而不是 TIA 的研究发现 ABCD² 评分中包含的几项因素,如运动或语言症状 [29],糖尿病和年龄,与卒中后严重的功能障碍有关 [30-32]。然而,对于本研究观察到的 TIA 和其后发生严重卒中之间的关系的机制仍然不清楚。

ABCD² 评分能预测再发事件的严重程度是其额外的优点,可早期分流 TIA 患者,支持评分高的患者入院治疗,在卒中发生时能尽早的接受溶栓治疗。在本队列中,53%(19/36) 的 ABCD² 评分≥5 的卒中复发能根据统一标准进行溶栓。

本研究仍有一些潜在的局限性。第一,我们对卒中复发的严重程度的分析只是基于 51 个卒中结局。虽然这比绝大多数已发表的验证 ABCD 或 ABCD² 评分的研究样本大,而且我们的分析有足够的检验效能,但进一步的研究可以帮助证明或反驳我们的发现。第二,部分之前有 TIA 的大卒中患者由于失语、意识障碍或无意识不能获得其确切 TIAs 病史而被我们排除,因此也许低估了发生严重卒中的风险。第三,对于 ABCD² 评分和卒中复发严重程度之间关系的机制仍然不清楚。今后的工作应对 ABCD² 评分、复发严重程度和根本病因机制进行分层分析来了解复发事件的风险,但这三个分层需要更大的合作研究。

总体严格来说,ABCD² 评分似乎能预测复发事件的严重程度而不是任何复发事件的风险。高 ABCD² 评分和严重卒中复发之间的强烈关联,使有 ABCD² 高分患者能得到最佳的预防治疗,出现复发时也能得到早期溶栓治疗。低 ABCD² 评分患者应该有所警惕,因有明显的 TIA 复发风险,但卒中风险仍然很低。


