Poor Performance of Current Prognostic Scores for Early Risk of Recurrence After Minor Stroke

Arvind Chandratheva, MRCP; Olivia C. Geraghty, MRCP; Peter M. Rothwell, MD, PhD, FRCP, FMedSci

Background and Purpose—The ABCD² score predicts the early risk of stroke after transient ischemic attack. The early risk of recurrence after minor stroke is as high but the only validated prognostic scores for use in minor stroke predict long-term risk of recurrence: the Essen Stroke Risk Score and the Stroke Prognosis Instrument II.

Methods—We determined the prognostic value of the ABCD² score, Essen Stroke Risk Score, and Stroke Prognosis Instrument II in a prospective population-based study in Oxfordshire, UK, of all incident and recurrent stroke (Oxford Vascular Study). Minor stroke was defined as an National Institutes of Health Stroke Scale score ≤5 at the time of first assessment. The 90-day risks of recurrent stroke were determined in relation to each score. Areas under the receiver operator curves indicated predictive value.

Results—Of 1247 first events in the study period, 488 were transient ischemic attacks, 520 were minor strokes, and 239 were major strokes. The ABCD² score was modestly predictive (area under the receiver operator curve, 0.64; 0.53 to 0.74; P=0.03) of recurrence at 7 days after minor stroke and at 90 days (0.62; 0.54 to 0.70; P=0.004). Neither Essen Stroke Risk Score (0.50; 0.42 to 0.59; P=0.95) nor Stroke Prognosis Instrument II (0.48; 0.39 to 0.60; P=0.92) were predictive of 7-day or 90-day risk of recurrent stroke. Of the traditional vascular risk factors, etiologic classification (Trial of ORG 10172 in Acute Stroke Treatment) and variables in the ABCD² score, only blood pressure >140/90 mm Hg (hazard ratio, 2.75; 1.18 to 6.38; P=0.02) and large artery disease (hazard ratio, 2.21; 1.00 to 4.88; P=0.05) were predictive of 90-day risk.

Conclusions—The predictive power of the ABCD² score is modest in patients with minor stroke, and neither the Essen Stroke Risk Score nor the Stroke Prognosis Instrument II predicts early recurrence. More reliable early risk prediction after minor stroke is required. (Stroke. 2011;42:632-637.)

Key Words: minor stroke ■ prognosis ■ risk factors

At least 48 000 transient ischemic attacks (TIAs) and 43 000 minor strokes are managed as outpatients each year in England alone and approximately 150 000 suspected TIAs and minor strokes are referred to secondary care for assessment and investigation,1 with rates similar in the United States.2 Recent hospital- and population-based studies have shown high early risks of recurrent stroke after TIA.2–7 Similar risks have been observed after minor stroke.8–10 Clinical risk scores have been developed to stratify and select patients at highest risk of early recurrence after TIA. One such score, the ABCD score, is based on clinical characteristics detected at the time of first assessment. This score has been refined further to include diabetes (ABCD²)11 and more recently imaging (ABCD²-I) and has been incorporated into clinical guidelines to assist triaging and risk stratifying patients.12–14 The ABCD² score is now recommended for use in triaging patients with suspected TIA, but its role in minor stroke is yet to be determined.12–17 Other validated clinical risk prediction tools exist for long-term risk of recurrent stroke after TIA or stroke. These include the Essen Stroke Risk Score (ESRS), a 10-point scale used to predict 1-year risk of recurrent stroke derived from the data subset of 6433 cerebrovascular patients in the Clopidogrel versus Aspirin in patients at Risk of Ischemic events (CAPRIE) trial,18,19 and the Stroke Prognosis Instrument II (SPI-II) a 15-point score consisting of 7 factors used to predict 2-year risk of recurrent stroke validated in 4 test cohorts,20 but neither has been validated for 90-day risk of stroke recurrence. In addition, previous validations were based on data collected from trials in which patients were recruited weeks or months after the initial event, which would not therefore have included many early recurrences. The aim of our study was to determine whether the ABCD²,2 ESRS, and SPI-II scores were predictive of recurrence in the acute and subacute phases for patients presenting with minor stroke.
Severity of the recurrent event was based on clinical examination at presentation, with recurrent events were reassessed by a study physician and then adjudicated acutely by ongoing daily case reporting. Events were classified as minor stroke if there were focal neurological deficit lasting for >60 minutes. We restricted analysis to the risk of stroke after the first minor stroke (minor stroke or acute onset focal neurological deficit) and only presented after the recurrent stroke. In the analysis excluding patients who only sought medical attention after a recurrent stroke, 508 (98%) patients were prospectively assessed before the recurrent stroke, 508 (98%) patients were prospectively assessed before the recurrent stroke. Most of these patients had repeat assessment, with 79 (5%) patients having repeat assessment within 24 hours of the onset of symptoms. Event characteristics and risk factors were recorded and most patients underwent brain imaging (91%). All cases were subsequently reviewed by the study senior neurologist (P.M.R.) and classified using SDs. All patients were followed up formally face to face by a study nurse or physician. Recurrent symptoms, medications, and disability scores were recorded. Recurrent strokes that presented to medical attention would also be identified acutely by ongoing daily case ascertainment within OXVASC.

Baseline characteristics were recorded in all patients and assessments were made for severity of event (using National Institutes of Health Stroke Scale24), territory, and clinical features. All patients with recurrent events were reassessed by a study physician and then case-reviewed by P.M.R. with most receiving repeat brain imaging. Severity of the recurrent event was based on clinical examination at the time of assessment by the study physician.

Analysis
We restricted analysis to the risk of stroke after the first minor stroke in the study period. Events were classified as minor stroke if there was a focal neurological deficit lasting >24 hours and a National Institutes of Health Stroke Scale score ≥5 at the time of assessment by a study physician. A cutoff of National Institutes of Health Stroke Scale score ≥5 was chosen because this included the majority (97%) of strokes seen in the outpatient setting. The study denominator was all events ascertained from April 1, 2002, to March 31, 2007. The study methods have been described elsewhere.21,22

To not miss patients who presented late or had events out of the area, patients who were referred to other services, or patients who were not referred to secondary care, we also performed monthly computerized searches of family doctor diagnostic coding, hospital discharge codes, and all cranial and carotid imaging studies performed in local hospitals. All patients were consented and seen by study physicians as soon as possible after their initial presentation. Overall, 70% were seen within 24 hours of the onset of symptoms. Event characteristics and risk factors were recorded and most patients underwent brain imaging (91%). All cases were subsequently reviewed by the study senior neurologist (P.M.R.) and classified using SDs.21,22

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Table 1 shows the baseline characteristics of all cases of minor stroke. Data were missing on blood pressure at first assessment in 6 patients to complete calculation of the ABCD² score leaving 514 of 520 patients with minor stroke (99%). Table 2 shows the 90-day risk of recurrent stroke after minor stroke stratified by ABCD² score. The score was calculated as a measure of predictive ability with ideal prediction producing a value of 1.00, whereas no better than chance prediction is represented by 0.50. Probability values that we quote are based on the difference between the observed predictive value (AUROC) and chance (ie, no predictive value).

Results
Of 1247 first events in the study period, 488 were TIsAs, 520 were minor strokes, and 239 were major strokes. The mean age at first event was 73 years (range, 24 to 98 years). Forty-seven percent of patients were female. There were 142 recurrent strokes within 90 days (81, 111, and 142 within 7, 30, and 90 days, respectively).

Of the 1247 first events within 90 days of a first event, 72 (51%) were preceded by a TIA, 61 (43%) by a minor stroke, and 9 (6%) by major strokes. The 90-day risks of stroke after TIA, minor stroke, and major stroke were 14.8% (95% CI, 11.7 to 17.9), 11.7% (9.0 to 14.4), and 3.8% (1.4 to 6.2), respectively.

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Table 4 shows the associations between the individual components of the ABCD² score and 90-day risk of recurrent stroke. Only blood pressure ≥140/90 mm Hg significantly predicted 7-day risk (hazard ratio, 8.14; 95% CI, 1.11 to
By comparison in patients presenting with TIA, the ABCD² score was predictive of stroke recurrence within 7 days (AUROC, 0.71; 0.63 to 0.79; P<0.001) and moderately predictive at 90 days (AUROC, 0.64; 0.56 to 0.71; P<0.001). Neither ESRS (7-day AUROC, 0.51; 0.44 to 0.59; P=0.74; 90-day AUROC, 0.47; 0.36 to 0.59; P=0.60) nor SPI-II (7-day AUROC, 0.50; 0.42 to 0.58; P=0.96; 90-day AUROC, 0.49; 0.38 to 0.60; P=0.84) was predictive at 7 or 90 days, respectively.

Table 2. Seven- and 90-Day Risk of Stroke Stratified According to ABCD² Score at First Assessment in Patients Presenting With Minor Stroke

<table>
<thead>
<tr>
<th>ABCD²</th>
<th>Patients (%)</th>
<th>Strokes (%)</th>
<th>Percent Risk (95% CI)</th>
<th>Strokes (%)</th>
<th>Percent Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>2</td>
<td>5 (1%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>3</td>
<td>65 (13%)</td>
<td>1 (5%)</td>
<td>1.5 (0.4–4.6)</td>
<td>2 (4%)</td>
<td>3.1 (0.6–7.4)</td>
</tr>
<tr>
<td>4</td>
<td>95 (18%)</td>
<td>2 (9%)</td>
<td>2.1 (0.5–5.0)</td>
<td>7 (14%)</td>
<td>7.4 (2.1–12.7)</td>
</tr>
<tr>
<td>5</td>
<td>135 (26%)</td>
<td>5 (23%)</td>
<td>3.7 (0.6–6.8)</td>
<td>11 (22%)</td>
<td>8.1 (3.4–12.8)</td>
</tr>
<tr>
<td>6</td>
<td>196 (38%)</td>
<td>13 (59%)</td>
<td>6.6 (3.1–10.1)</td>
<td>26 (53%)</td>
<td>13.3 (8.6–18.0)</td>
</tr>
<tr>
<td>7</td>
<td>18 (4%)</td>
<td>1 (5%)</td>
<td>5.6 (0–16.2)</td>
<td>3 (6%)</td>
<td>16.7 (3.4–34.3)</td>
</tr>
<tr>
<td>Total</td>
<td>514 (100%)</td>
<td>22 (100%)</td>
<td>4.2 (2.4–6.0)</td>
<td>49 (100%)</td>
<td>9.4 (6.9–11.9)</td>
</tr>
</tbody>
</table>

P value for trend 0.030 0.004

AUROC 0.64 (0.53–0.74) 0.62 (0.54–0.70)

Total no. of minor strokes was 520. Complete data required for completion of ABCD² score unavailable for 6 cases.
Table 3. Risk of Recurrent Stroke After Minor Stroke at 90 Days Stratified by ESRS and SPI-II Scores*

<table>
<thead>
<tr>
<th>Clinical Score</th>
<th>Patients (%)</th>
<th>Strokes (%)</th>
<th>Percent Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESRS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;3</td>
<td>236 (45%)</td>
<td>21 (43%)</td>
<td>8.9 (5.2–12.6)</td>
</tr>
<tr>
<td>≥3</td>
<td>284 (55%)</td>
<td>28 (57%)</td>
<td>9.9 (6.4–13.4)</td>
</tr>
<tr>
<td>1</td>
<td>25 (5%)</td>
<td>1 (2%)</td>
<td>4.0 (0–11.6)</td>
</tr>
<tr>
<td>2</td>
<td>87 (17%)</td>
<td>10 (20%)</td>
<td>11.5 (4.6–18.4)</td>
</tr>
<tr>
<td>3</td>
<td>124 (24%)</td>
<td>20 (20%)</td>
<td>8.1 (3.2–13.0)</td>
</tr>
<tr>
<td>4</td>
<td>138 (27%)</td>
<td>15 (31%)</td>
<td>10.9 (6.6–16.2)</td>
</tr>
<tr>
<td>5</td>
<td>80 (15%)</td>
<td>6 (12%)</td>
<td>7.5 (1.6–13.4)</td>
</tr>
<tr>
<td>6</td>
<td>49 (9%)</td>
<td>5 (10%)</td>
<td>10.2 (1.8–18.6)</td>
</tr>
<tr>
<td>7</td>
<td>13 (3%)</td>
<td>2 (4%)</td>
<td>15.4 (0–35.0)</td>
</tr>
<tr>
<td>8</td>
<td>3 (0.6%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>1 (0.2%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>520 (100%)</td>
<td>49 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

P value for trend: 0.84
AUROC: 0.51 (0.42–0.59)

SPI-II

- I: 314 (61%), 31 (63%); 9.9 (6.6–13.2)
- II: 172 (33%), 15 (31%); 8.7 (4.4–13.0)
- III: 28 (5%), 3 (6%); 10.7 (0–22.1)

P value for trend: 0.89
AUROC: 0.48 (0.39–0.60)

*Total no. of minor strokes was 520. Complete data required for completion of SPI-II score unavailable for 6 cases.

Discussion

Minor strokes account for a significant proportion of patients with acute cerebrovascular events and the early risk of recurrence is similar to that after TIA. Although the ABCD² score has been shown to be effective in prediction of recurrent stroke after TIA in the acute phase, our study has shown that it is a relatively poor predictor of recurrent stroke after minor stroke up to 90 days and that neither the ESRS nor the SPI-II was predictive.

Previous studies of clinical risk scoring in minor stroke have varied in methodology with most excluding the acute phase and also those patients who may have had a preceding event for which they did not seek medical attention before hospital admission. They also vary in population size, follow-up, and completeness of case ascertainment within the defined population. We performed the first prospective population-based study of risk scoring in patients with minor stroke.

Although the ABCD² score was modestly predictive after minor stroke, 1 argument is that the score may act as a diagnostic tool to identify patients more likely to have a true TIA or minor stroke because diagnosis is not completely reliable and some patients with seizure or migraine are indistinguishable from those due to brain or retinal ischemia. However, diagnostic accuracy is likely to be greater in patients with minor stroke compared with those with transient symptoms. Moreover, previous work has shown that in analysis limited to neurologist-confirmed TIA, the ABCD² score remains predictive. Also, in a recent multicenter international collaborative analysis of patients with diffusion-weighted imaging-positive TIA, the ABCD² score was still predictive of early recurrent stroke.

In a univariate analysis of the individual components of the ABCD² score, vascular risk factors, and Trial of ORG 10172 in Acute Stroke Treatment criteria, only hypertension and large artery disease were predictive of recurrent stroke with a nonsignificant trend for a combination of motor and speech symptoms, diabetes, and anterior circulation of event. In a recent prospective hospital series by Ois et al, recurrence after minor stroke was associated with the presence of weakness, speech disturbance, high alcohol intake, previous TIA, and severe symptomatic extra- or intracranial arterial disease.

Cerebral and vascular imaging studies could enhance prediction of stroke after minor stroke. The presence of new ischemic lesions on MRI or CT has been associated with an increased short-term risk of stroke as has severe symptomatic arterial disease. Our study did not look at the role of MRI in improving risk stratification in patients with minor stroke. However, MRI as the first and immediate assessment tool is not yet commonplace in daily clinical practice. One benefit of purely clinical scoring systems with simple, easily obtainable information is that they can be used at the point of first presentation to facilitate rapid triage by first-line health-care professionals. Further research is required to determine whether newer technologies such as biomarkers of cerebral ischemia or thrombosis can add prognostically useful information in patients presenting with minor stroke.

Our study had some potential limitations. First, we cannot be completely precise about the risk of stroke in the acute phase because an unknown proportion of patients with minor stroke will never seek medical attention. Second, we might have underestimated the early risk of stroke slightly because some patients with major stroke with a preceding minor stroke may not have been identified because we excluded those in whom it was impossible to obtain a definite history of TIA or minor stroke because they were aphasic, confused,
or unconscious. Third, our validation of the clinical scores for recurrences in the acute phase was based on relatively small numbers of outcomes and so further studies would help to confirm or refute our findings. Fourth, our study included some patients recruited into the Effect of urgent treatment of transient ischemic attack and minor stroke on early recurrent stroke (EXPRESS) study,9 Phase 2, which involved more urgent investigation and treatment and which will have reduced the absolute risk of events and possibly influenced the association with particular risk factors.

In summary, although the ABCD2 score is highly predictive of recurrent stroke after TIA in the acute phase, it is less predictive after minor stroke, and neither the ESRS nor the SPI-II predict 90-day recurrence. More reliable early prediction after minor stroke is required.

Acknowledgments
We thank all primary care practices and physicians who collaborate with the Oxford Vascular Study, the details of which have been published previously.19,20

Table 4. Ninety-Day Risk of Stroke and HR (95% CI) for Minor Stroke in Relation to Potential Risk Factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>7-Day Risk HR (95% CI)</th>
<th>90-Day Risk HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.77 (0.30–2.03)</td>
<td>1.07 (0.51–2.25)</td>
<td>0.86</td>
</tr>
<tr>
<td>Blood pressure &gt;140/90 mm Hg</td>
<td>1.14 (0.33–3.69)</td>
<td>1.93 (0.61–5.89)</td>
<td>0.04</td>
</tr>
<tr>
<td>Motor symptoms</td>
<td>1.25 (0.52–3.00)</td>
<td>2.12 (0.85–5.09)</td>
<td>0.14</td>
</tr>
<tr>
<td>Speech symptoms</td>
<td>1.04 (0.33–2.69)</td>
<td>1.20 (0.62–2.31)</td>
<td>0.34</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.94 (0.53–1.62)</td>
<td>1.26 (0.74–2.13)</td>
<td>0.53</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>0.36 (0.05–2.64)</td>
<td>0.50 (0.16–1.61)</td>
<td>0.25</td>
</tr>
<tr>
<td>TIA</td>
<td>0.83 (0.29–2.37)</td>
<td>0.89 (0.44–1.81)</td>
<td>0.76</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>0.39 (0.05–2.58)</td>
<td>0.76 (0.28–2.10)</td>
<td>0.60</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.88 (0.42–1.82)</td>
<td>0.96 (0.58–1.59)</td>
<td>0.87</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>0.56 (0.17–1.84)</td>
<td>0.52 (0.22–1.21)</td>
<td>0.13</td>
</tr>
<tr>
<td>Prior antiplatelet</td>
<td>0.74 (0.33–166)</td>
<td>0.80 (0.46–1.39)</td>
<td>0.43</td>
</tr>
<tr>
<td>Prior statin</td>
<td>0.50 (0.15–1.66)</td>
<td>0.65 (0.31–1.37)</td>
<td>0.26</td>
</tr>
<tr>
<td>Prior antihypertensive</td>
<td>1.12 (0.54–2.34)</td>
<td>1.00 (0.61–1.66)</td>
<td>0.99</td>
</tr>
<tr>
<td>Vascular territory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior circulation</td>
<td>1.51 (0.64–3.57)</td>
<td>1.45 (0.80–2.62)</td>
<td>0.22</td>
</tr>
<tr>
<td>Posterior circulation</td>
<td>0.79 (0.32–1.95)</td>
<td>0.83 (0.45–1.55)</td>
<td>0.56</td>
</tr>
</tbody>
</table>

HR indicates hazard ratio; TOAST, Trial of Org 10172 in Acute Stroke Treatment.

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Disclosures
None.

References


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