Diagnostic Usefulness of the ABCD² Score to Distinguish Transient Ischemic Attack and Minor Ischemic Stroke From Noncerebrovascular Events

The North Dublin TIA Study

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Background and Purpose—Transient ischemic attack (TIA) diagnosis is frequently difficult in clinical practice. Noncerebrovascular symptoms are often misclassified as TIA by nonspecialist physicians. Clinical prediction rules such as ABCD² improve the identification of patients with TIA at high risk of early stroke. We hypothesized that the ABCD² score may partly improve risk stratification due to improved discrimination of true TIA and minor ischemic stroke (MIS) from noncerebrovascular events.

Methods—Consecutive patients with TIA were identified within a prospective population-based cohort study of stroke and TIA. The cohort was expanded by inclusion of patients with MIS and noncerebrovascular events referred to a daily TIA clinic serving the population. Diagnosis was assigned by a trained stroke physician independent of ABCD² score.

Results—Five hundred ninety-four patients were included (292 [49.2%] TIA, 45 [7.6%] MIS, and 257 [43.3%] noncerebrovascular). The mean ABCD² score showed a graded increase across diagnostic groups (MIS mean 4.8 [SD 1.4] versus TIA mean 3.9 [SD 1.5] versus noncerebrovascular mean 2.9 [SD 1.5]; P<0.00001). The ABCD² score discriminated well between noncerebrovascular and cerebrovascular events—TIA (c-statistic 0.68; 95% CI, 0.64 to 0.72), any vascular event (TIA+MIS; c-statistic 0.7; 95% CI, 0.66 to 0.74), and MIS (c-statistic 0.81; 95% CI, 0.75 to 0.87)—from noncerebrovascular events. Of ABCD² items, unilateral weakness (OR, 4.5; 95% CI, 3.1 to 6.6) and speech disturbance (OR, 2.5; 95% CI, 1.6, 4.1) were most likely overrepresented in TIA compared with noncerebrovascular groups.

Conclusion—The ABCD² score had significant diagnostic usefulness for discrimination of true TIA and MIS from noncerebrovascular events, which may contribute to its predictive usefulness. (Stroke. 2009;40:3449-3454.)

Key Words: ABCD² score ■ cerebrovascular disorders ■ diagnosis ■ transient ischemic attack

Transient ischemic attack (TIA) is common with 240 000 cases¹ in the United States and 70 000 cases² in the United Kingdom diagnosed annually. In population-based studies, almost one fifth of strokes are preceded by a TIA.³ The risk of early stroke after TIA may be high with rates of up to 35% observed in some high-risk subgroups.⁴ Accurate early diagnosis and initiation of intensive stroke prevention measures after TIA is associated with substantial reduction in early stroke rates.⁵

The diagnosis of TIA is frequently difficult in clinical practice, because objective findings have often resolved at the time of assessment, requiring the physician to elicit and interpret the details of the event as recalled and described by the patient. In studies of TIA diagnosis, nonstroke specialist physicians correctly classified only 10% to 49% of patients with true TIA and misclassified 31% to 55% of patients with noncerebrovascular transient symptoms as TIA.⁶-⁸ Only 50% of patients referred to a specialist TIA clinic for evaluation of transient neurological symptoms had confirmed TIA.⁴ Because patients with TIA are frequently initially assessed by physicians other than stroke specialists, methods to improve TIA diagnosis are needed.
The ABCD² score is an easily used clinical prediction instrument that combines vascular risk factors and features of the event to identify patients at high risk of early stroke after TIA. Although the predictive usefulness of the score has been validated, relatively few data exist on its potential diagnostic usefulness to differentiate true TIA from noncerebrovascular causes of transient neurological symptoms, which nonspecialist physicians may misclassify as TIA. We hypothesized that the ABCD² score may improve TIA diagnosis in addition to improving stroke risk prediction and investigated this hypothesis in a large population-based study.

Methods

Patient Ascertainment

The North Dublin TIA Study is a substudy of the North Dublin Population Stroke Study, a population-based prospective cohort study of frequency and outcomes of stroke and TIA in 294529 inhabitants of the city of North Dublin. Multiple overlapping sources for hospital and community ascertainment were used to identify patients with new stroke and TIA using “hot” and “cold” pursuit methods according to recommended standards for rigorous epidemiological studies of stroke and TIA. Six general acute and 7 nonacute hospitals, 94% of general practitioners, and 95% of nursing homes in the city of North Dublin participated. A 5-day minor stroke/TIA clinic (Fast Assessment of Suspected Stroke and TIA Clinic) was established to facilitate referral and assessment of patients with suspected TIA from nonspecialist physicians (general practitioners and emergency department physicians) in North Dublin.

After completion of ascertainment for the stroke/TIA incidence study at the end of the first year, identification of patients with TIA continued with restriction of ascertainment sources to those that had proven most effective in the first year (daily review of emergency room referrals; acute hospital admissions; referrals to neurology, geriatric, medical, and vascular services; and general practitioner referrals to the 5-day minor stroke/TIA clinic).

Inclusion Criteria

Prespecified inclusion criteria were: (1) patients with suspected TIA referred by nonspecialist physicians (general practitioner or emergency department physicians) to the 5-day clinic or hospital in whom TIA was confirmed; (2) patients with suspected TIA referred to the 5-day clinic by nonspecialist physicians with a subsequent diagnosis of minor ischemic stroke; (3) patients with suspected TIA referred to the 5-day clinic by nonspecialist physicians with a subsequent diagnosis of noncerebrovascular transient neurological symptoms; (4) all consecutive patients during the first 2 years of the study period (December 1, 2005, to November 15, 2007) were included; and (5) verification of final diagnosis by a stroke specialist physician.

Assignment of Diagnosis

An in-person assessment by a trained stroke physician was performed on patients referred with suspected TIA. All new cases were reviewed at regular meetings of the research team. A second in-person evaluation by a stroke physician was performed when diagnostic ambiguity was present and the final diagnosis assigned by consensus. After assessment, all patients were assigned as confirmed TIA, minor ischemic stroke, or noncerebrovascular event (TIA mimic).

Definitions

TIA was defined according to the Oxfordshire Community Stroke Project (clinical) definition as an acute loss of focal cerebral or ocular function lasting <24 hours presumed, after investigation, to be due to embolic or thrombotic vascular disease. Patients fulfilling this clinical definition of TIA in whom brain imaging showed evidence of recent minor ischemic stroke were categorized as TIA rather than stroke. In cases in which multiple TIAs occurred during the study period, the first event was used for calculation of the ABCD² score. The World Health Organization definition of stroke was used. A noncerebrovascular event was defined as an episode of transient neurological symptoms prompting referral by a nonspecialist physician to the stroke specialist clinic for evaluation of suspected TIA but with an alternative diagnosis subsequently assigned (eg, migraine, focal seizures, hypoglycemia, mononeuropathy, somatoform symptoms, cerebral tumor). Confirmed TIA events were classified as carotid (anterior) territory or vertebralbasilar (posterior) territory using the National Institute of Neurological Disorders and Stroke diagnostic classification. An intermediate ABCD² score was defined as a score of 4 or 5 and a high score was defined as ≥6.

Clinical Management and ABCD² Score Assignment

Patients were referred and clinically managed independent of their ABCD² score. Patients with confirmed TIA and minor ischemic stroke (MIS) at the clinic were treated according to current guidelines with immediate initiation of an antplatelet agent, addition of an antihypertensive agent based on initial blood pressure, and early addition of a statin if indicated based on fasting lipid profile. Warfarin anticoagulation therapy was started after the detection of atrial fibrillation provided intracranial hemorrhage had been excluded by brain imaging and no other contraindication existed.

Patients who presented with a stroke but described a preceding TIA during the recruitment period, for which they had not sought medical attention, were deemed to have had a retrospective TIA and their ABCD² score calculated using the first blood pressure recorded after their TIA. All patients were followed up to 90 days.

Statistical Methods

Parametric and nonparametric comparisons of categorical and continuous variables were performed using the x² test, Student t test, and Mann-Whitney test as appropriate. Analysis of variance was performed for multiple group comparisons of means. ABCD² score discrimination among confirmed TIA, MIS, and noncerebrovascular transient neurological events was evaluated receiver-operating characteristic analysis. Statistical analysis was performed using Stata Version 9.0.

Ethics committee approval was obtained from all collaborating institutions and participants provided informed consent for inclusion in the study.

Results

Clinical Characteristics

Five hundred ninety-four patients were included, 292 (49.2%) confirmed TIA, 45 (7.6%) MIS, and 257 (43.3%) noncerebrovascular transient neurological events (Table 1). Ninety-seven percent of patients (575 of 594) were evaluated in person by a study stroke physician with medical record review in the remainder. The median time from symptom onset to assessment by either a general or emergency department physician was 1 day (interquartile range, 0 to 5) for patients with confirmed TIA, 3 days (interquartile range, 1 to 7) for patients with MIS, and 4 days (interquartile range, 1 to 9.5) for patients with noncerebrovascular events.

Compared with patients with noncerebrovascular events, patients with TIA were older (P<0.00001) and more likely to have had a previous TIA (P<0.0001), prior hypertension (P=0.008), coronary artery disease (P=0.001), atrial fibrillation (P<0.0001), and carotid stenosis (P=0.04).

Two hundred sixty-four of 292 (90.4%) patients with confirmed TIA, 42 of 45 (93.3%) patients with MIS, and 127 of 256 (49.6%) of patients with noncerebrovascular events...
had carotid imaging. Two hundred sixty-three of 292 (90.1%) of patients with confirmed TIA, 43 of 45 (95.6%) patients with MIS, and 81 of 257 (31.5%) of patients with noncerebrovascular events had brain imaging.

Twenty-eight patients with TIA (9.6%) and one patient with MIS (2.2%) had a recurrent stroke by 90 days. No patient with a noncerebrovascular event had a stroke at 90-day assessment.

Distribution of Individual ABCD² Characteristics in TIA and Noncerebrovascular Events

Compared with those with noncerebrovascular events, patients with TIA were more likely to be aged ≥60 years (81.8% versus 70.8%; OR, 1.9; 95% CI, 1.2 to 2.8; P=0.008) and had a greater frequency of blood pressure ≥140/90 mm Hg at initial recording (62.3% versus 54.1%; OR, 1.4; 95% CI, 1.0 to 2.0; P=0.04; Table 2). The greatest differences between those with TIA and noncerebrovascular events were observed in the frequency of unilateral weakness (52.7% versus 19.8%; OR, 4.5; 95% CI, 3.1 to 6.6; P<0.0001) and isolated speech disturbance (23.6 versus 10.9; OR, 2.5; 95% CI, 1.6, 4.1; P<0.0001). No difference in the duration of symptoms or prevalence of diabetes mellitus was observed between groups (Figure 1; Table 2).

Distribution of ABCD² Scores in TIA, MIS, and Noncerebrovascular Events

The ABCD² score distributions showed a graded relationship across each diagnostic group with highest scores observed in patients with MIS, intermediate scores in those with confirmed TIA, and lowest scores in those with noncerebrovascular events (MIS mean, 4.8 [SD 1.4] versus TIA mean, 3.9

<table>
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<tr>
<th>Table 1. Clinical Characteristics</th>
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<tr>
<td>Noncerebrovascular Event (n=257)</td>
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<tr>
<td>Female, n (%)</td>
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<tr>
<td>Age, years, mean (SD)</td>
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<td>Hypertension, n (%)</td>
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<td>Hypercholesterolemia, n (%)</td>
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<td>Current smoker, n (%)</td>
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<td>Coronary artery disease, n (%)</td>
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<td>Atrial fibrillation, n (%)</td>
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<td>Carotid stenosis ≥50%, n (%)</td>
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<th>Table 2. ABCD² Characteristics</th>
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<td>Noncerebrovascular Event (n=257)</td>
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<tr>
<td>Age ≥60 years, n (%)</td>
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<td>Systolic blood pressure, mm Hg, mean (SD)</td>
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<td>Diastolic blood pressure, mm Hg, mean (SD)</td>
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<td>Hypertension per ABCD, n (%)</td>
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<td>Unilateral weakness, n (%)</td>
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<td>Speech disturbance, n (%)</td>
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<td>Duration of symptoms</td>
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<td>&lt;10 minutes, n (%)</td>
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<td>10–59 minutes, n (%)</td>
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<tr>
<td>≥60 minutes, n (%)</td>
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<td>Diabetes mellitus, n (%)</td>
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NS indicates nonsignificant.
Similarly, the proportion of patients with ABCD² scores of \( \geq 4 \) (intermediate or high ABCD²) and \( \geq 6 \) (high ABCD²) showed a graded relationship across diagnostic categories (Figure 2). An ABCD² score of \( \geq 4 \) was observed in 82.2% of MIS, 60.3% of TIA, and 35.4% of patients with noncerebrovascular events \((P<0.00001\) for trend). Similarly, an ABCD² score of \( \geq 6 \) was observed in 35.6% of MIS, 16.8% of TIA, and 6.2% of patients with noncerebrovascular events \((P<0.00001\) for trend; Figure 2). An ABCD² score of \( \geq 4 \) increased the likelihood of a final diagnosis of confirmed TIA (OR, 2.8; 95% CI, 2.0 to 3.9) and MIS (OR, 8.4; 95% CI, 3.8 to 18.9) when compared with patients with noncerebrovascular events. A score of \( \geq 6 \) increased the likelihood of a final diagnosis of confirmed TIA (OR, 3.0; 95% CI, 1.7 to 5.5) and MIS (OR, 8.3; 95% CI, 3.8 to 18.4).

**Usefulness of ABCD² Score to Identify Confirmed TIA, Any Cerebrovascular (TIA + MIS), and Noncerebrovascular Events**

On receiver-operator characteristic analysis, the ABCD² score displayed good performance in distinguishing confirmed TIA from noncerebrovascular events (c-statistic 0.68; 95% CI, 0.64 to 0.72; Figure 3A). An ABCD² score (\( \geq 4 \)) had 60.3% sensitivity and 64.6% specificity for discriminating TIA from noncerebrovascular events. A score \( \geq 6 \) had 16.8% sensitivity and 93.8% specificity to discriminate TIA from noncerebrovascular events.

The performance of the score improved for identification of any cerebrovascular event (TIA + MIS; c-statistic 0.7; 95% CI, 0.66 to 0.74) with some improvement in sensitivity (63.2%) and specificity (64.6%) of an ABCD² threshold of 4 to identify any cerebrovascular event. A score \( \geq 6 \) had 19.3% sensitivity and 93.8% specificity to discriminate any cerebrovascular event from noncerebrovascular events.

The score performance was maximal for discrimination between MIS and noncerebrovascular events (c-statistic 0.81; 95% CI, 0.75 to 0.87; Figure 3B). An ABCD² threshold of 4 had 82.2% sensitivity and 64.6% specificity, whereas a threshold of 6 had 35.6% sensitivity and 93.8% specificity to identify MIS. The positive predictive value for identification of noncerebrovascular events was 42.4% for ABCD² \( 0 \) to 2 and 18.7% for ABCD² \( \leq 1 \).
ABCD² Score and Vascular Territory
Two hundred sixty-three of 292 (90.1%) TIAIs were classified as anterior circulation and 29 of 292 (9.9%) were posterior circulation territory events. No difference in ABCD² score was observed in anterior circulation compared with posterior circulation events (mean, 4.0 [SD 1.5] versus 3.7 [SD 1.4]; \( P = 0.3 \)).

Discussion
In a large population-based study, we found that the ABCD² score contained significant diagnostic information to distinguish ambulatory patients with TIA and MIS from those with noncerebrovascular events. In our study, patients with cerebrovascular events confirmed by a stroke specialist had higher ABCD² scores compared with noncerebrovascular events. The score distributions exhibited a graded relationship across diagnostic groups with lowest scores observed in patients with noncerebrovascular events, intermediate scores in those with TIA, and highest scores in those with minor stroke. On receiver-operating characteristic analysis, the score demonstrated good performance to discriminate between TIA and noncerebrovascular diagnoses with an area under the curve (c-statistic) of 0.68. In our cohort, it exhibited better performance to distinguish ambulatory patients with minor stroke from those with noncerebrovascular events (c-statistic 0.8).

We found a good balance between sensitivity and specificity for TIA diagnosis when an ABCD² threshold of ≥4 was applied. We observed that when the threshold was increased from 4 to 6, the sensitivity for discrimination between TIA and noncerebrovascular events decreased, whereas the specificity increased. This is to be expected because, with each progressive increase of a threshold for discrimination, a greater number of patients with TIA will have ABCD² scores below the threshold (leading to progressive reduction in sensitivity), whereas a relatively higher proportion of patients above the threshold will have true TIA (leading to higher specificity).

Our analysis may give some insights into the underlying reasons for these diagnostic properties. Although patients with cerebrovascular disease were older and more often hypertensive than those with noncerebrovascular diagnoses, the overall differences were small and did not discriminate well between the groups. Similarly, the duration of transient symptoms caused by confirmed TIA was similar to those caused by noncerebrovascular events and conveyed little discriminatory information in our cohort. In contrast, focal clinical symptoms were substantially more common among patients with cerebrovascular events with unilateral limb weakness almost 3 times more frequent and speech disturbance twice as frequent compared with those with noncerebrovascular events. By definition also, all patients with minor stroke had a syndrome lasting at least 24 hours. Because the ABCD² score weights motor weakness and prolonged symptom duration items with scores of 2, these features likely contribute in large part to the observed stepwise increase in score distributions across noncerebrovascular, TIA, and MIS groups. Our findings are further supported by MRI studies reporting associations among individual ABCD² items, higher ABCD² scores, and diffusion-weighted imaging evidence of minor ischemic injury in patients with symptoms fulfilling the clinical definition of TIA.²²,²³

The diagnosis of TIA may prove difficult in practice for several reasons. Older patients may have difficulty recalling or describing resolved symptoms, particularly if a prolonged delay to medical assessment occurs. Physicians may have difficulty eliciting and interpreting the information provided, particularly those without specific training in stroke medicine. Several studies have demonstrated high rates of misdiagnosis of stroke specialist-assigned TIA and misclassification of symptoms due to noncerebrovascular disorders as TIA by nonspecialist physicians.⁴,⁶–⁹ Audits of TIA clinics have reported that up to 50% of referred patients have noncerebrovascular diagnoses. In our cohort, all patients with cerebrovascular events were referred by nonspecialist physicians for assessment of suspected TIA. Although rates of some vascular risk factors were statistically lower in this group, overall rates were high in both patients with cerebrovascular events and those with noncerebrovascular events and did not clearly identify a “low-risk” group at referral.

Our findings are consistent with recent studies that reported that the ABCD² score may have some diagnostic usefulness.¹²,¹³ Although providing useful information, these were limited by retrospective design and did not analyze TIA and minor stroke separately. This study has several advantages of prospective design, in-person stroke specialist confirmation of diagnosis, and detailed analysis by cerebrovascular event (TIA and minor stroke), individual ABCD² score items, and TIA vascular territory. We acknowledge that our study may have some limitations, including relatively small samples of patients with MIS and posterior territory events and lack of in-person stroke specialist assessment in a small proportion (3%) of patients. Brain imaging was unavailable in 2 patients with minor stroke and 29 patients with TIA and although unlikely, intracranial pathology such as tumors cannot be completely excluded in these patients.

Our data contribute to an improved understanding that the ability of ABCD² score to predict early recurrent stroke after TIA is likely explained in part by improved TIA diagnosis. The inclusion of common clinical TIA syndromes in the score may substantially contribute to this diagnostic property. In our study, 75% of patients with TIA had either focal limb weakness or speech disturbance, almost identical rates to those described in the Oxfordshire Community Stroke Project. However, we emphasize that an important subgroup of patients with TIA may have other symptoms (eg, amaurosis fugax) equally requiring urgent investigation. We also emphasize that significant proportions of patients with confirmed cerebrovascular events had low ABCD² scores, whereas 35% of those with noncerebrovascular events had an intermediate or high score (≥4) in our study, indicating that further refinement of the score is needed.

In practice, we believe that the score may function as a useful aid for diagnosis and triage of patients with transient neurological symptoms, particularly for nonspecialist physicians who may be the first to assess such patients. However, we caution that it should be used in tandem with improved clinician education and not be used as the sole basis for
clinical decision-making for patients with focal neurological symptoms of sudden onset.

Disclosures

None.

References


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