# Addition of Brain Infarction to the ABCD$^2$ Score (ABCD$^2$I)

## A Collaborative Analysis of Unpublished Data on 4574 Patients

Matthew F. Giles, DPhil; Greg W. Albers, MD; Pierre Amarenco, MD; Murat M. Arsava, MD; Andrew Asimos, MD; Hakan Ay, MD; David Calvet, MD; Shelagh Coutts, MD; Brett L. Cucchiara, MD; Andrew M. Demchuk, MD; S. Claiborne Johnston, MD; Peter J. Kelly, MD; Anthony S. Kim, MD; Julien Labreuche, BS; Philippa C. Lavallee, MD; Jean-Louis Mas, MD; Aine Merwick, MB; Jean Marc Olivot, MD; Francisco Purroy; Wayne D. Rosamond, MD; Rossella Sciolla, MD; Peter M. Rothwell, PhD

***Background and Purpose***—The ABCD system was developed to predict early stroke risk after transient ischemic attack. Incorporation of brain imaging findings has been suggested, but reports have used inconsistent methods and been underpowered. We therefore performed an international, multicenter collaborative study of the prognostic performance of the ABCD$^2$ score and brain infarction on imaging to determine the optimal weighting of infarction in the score (ABCD$^2$I).

***Methods***—Twelve centers provided unpublished data on ABCD$^2$ scores, presence of brain infarction on either diffusion-weighted imaging or CT, and follow-up in cohorts of patients with transient ischemic attack diagnosed by World Health Organization criteria. Optimal weighting of infarction in the ABCD$^2$I score was determined using area under the receiver operating characteristic curve analyses and random effects meta-analysis.

***Results***—Among 4574 patients with TIA, acute infarction was present in 884 (27.6%) of 3206 imaged with diffusion-weighted imaging and new or old infarction was present in 327 (23.9%) of 1368 imaged with CT. ABCD$^2$ score and presence of infarction on diffusion-weighted imaging or CT were both independently predictive of stroke (n=145) at 7 days (after adjustment for ABCD$^2$ score, OR for infarction=6.2, 95% CI=4.2 to 9.0, overall; 14.9, 7.4 to 30.2, for diffusion-weighted imaging; 4.2, 2.6 to 6.9, for CT; all $P<0.001$). Incorporation of infarction in the ABCD$^2$I score improved predictive power with an optimal weighting of 3 points for infarction on CT or diffusion-weighted imaging. Pooled areas under the curve increased from 0.66 (0.53 to 0.78) for the ABCD$^2$ score to 0.78 (0.72 to 0.85) for the ABCD$^2$I score.

***Conclusions***—In secondary care, incorporation of brain infarction into the ABCD system (ABCD$^2$I score) improves prediction of stroke in the acute phase after transient ischemic attack. **(*Stroke*. 2010;41:1907-1913.)**

**Key Words:** ABCD$^2$ score ■ ABCD$^2$I score ■ infarction ■ prediction ■ risk ■ TIA



Transient ischemic attack (TIA) carries a high early risk of stroke[1] and the presence of acute brain infarction may be associated with a particularly high risk.[2–6] The ABCD system (ABCD and subsequent ABCD$^2$ score)[7,8] is a prognostic tool developed to predict stroke risk in the acute phase after TIA. The system was designed to be used in primary and emergency care settings by identifying high-risk individuals to facilitate triage to specialist care and target secondary prevention. It is based on clinical features identifiable at the time of initial assessment, before specialist evaluation, and deliberately does not include the results of brain imaging.

Since publication, the use of the system has been recommended by national guidelines in North America, Europe, and Australasia[9–12] and validation studies have found it to be

Received February 1, 2010; accepted April 15, 2010.

From the Stroke Prevention Research Unit (M.F.G., P.M.R.), National Institute for Health Research Biomedical Research Centre, Oxford, UK; Seaman Family Centre (A.M.D., S.C.), Departments of Clinical Neurosciences and Radiology, University of Calgary, Calgary, Canada; the Department of Neurology and Neurological Sciences (G.W.A., J.M.O.), Stanford Stroke Center, Stanford, Calif; the Department of Neurology and Stroke Centre (P.A., J.L., P.C.L.), Bichat–Claude Bernard University Hospital, Paris, France; the Department of Neurology (F.P.), University of Lleida, Lleida, Spain; the Department of Neurology (D.C., J.-L.M.), Centre Hospitalier Sainte-Anne, Paris, France; the Department of Neurology (S.C.J., A.S.K.), University of California, San Francisco, San Francisco, Calif; the Department of Neurology (B.L.C.), University of Pennsylvania Medical Center, Philadelphia, Pa; the Departments of Neurology and Radiology (H.A., M.M.A.), Massachusetts General Hospital, Boston, Mass; the Neurology Department (R.S.), University of Turin, Turin, Italy; the Neurovascular Clinical Science Unit (P.J.K., A.M.), Mater University Hospital, Dublin, UK; the Department of Emergency Medicine (A.A.), Carolinas Medical Center, Charlotte, NC; and the Department of Epidemiology (W.D.R.), University of North Carolina School of Public Health, Chapel Hill, NC.

All 12 collaborating centers received ethics committee approval for the study.

Correspondence to Matthew F. Giles, DPhil, Stroke Prevention Research Unit, NIHR Biomedical Research Centre, Oxford University Department of Clinical Neurology, Level 6, West Wing, John Radcliffe Hospital, Oxford OX3 9DU, UK. E-mail matthew.giles@clneuro.ox.ac.uk



*Stroke* **is available at http://stroke.ahajournals.org** **DOI: 10.1161/STROKEAHA.110.578971**

**Table 1. Summary of Study Methodology**

| Study | Study Period | Country | Study Setting | Diagnosis by | Imaging Modality | Imaging Adjudication | Delay to Evaluation |
|---|---|---|---|---|---|---|---|
| California[4] | 1997–1998 | USA | ED | ED physician | CT | Abstracted from radiology reports | <2 days |
| OXVASC[7] | 2002–2004 | UK | Population-based | Neurologist | CT | Single study neuroradiologist | Median 1 day (IQR 0–2) |
| Cucchiara[19] | 2002–2007 | USA | Neurovascular unit | Neurologist | DWI and CT | Study neuroradiologist | <2 days |
| Lavallee[20] | 2003–2007 | France | Neurovascular unit | Neurologist | DWI and CT | Study neuroradiologist | Median 1 day (IQR 0–5) |
| SINPAC[5] | 2006 | Italy | ED | Neurologist | CT | Abstracted from radiology reports | <24 hours |
| Calgary[5] | 2003–2006 | Canada | ED | Neurologist | DWI | Single study neuroradiologist | <12 hours |
| Calvet[2] | 2003–2007 | France | Neurovascular unit | Neurologist | DWI | Single study neuroradiologist | Median 11 hours (IQR 5–23) |
| Ay[6] | 2000–2006 | USA | Neurovascular unit | Neurologist | DWI | Single study neuroradiologist | <24 hours |
| Purroy[21] | 2006–2008 | Spain | ED | Neurologist | DWI | Study neurologist | Median 1 day |
| Stanford[22] | 2001–2005 | USA | Neurovascular unit | Neurologist | DWI | Study neurologist | <2 days |
| NDSS[23] | 2005–2007 | Ireland | Population-based | Neurologist | DWI and CT | Study neuroradiologist | Median 1 day |
| Asimos[24] | 2005–2008 | USA | ED | ED physician | DWI and CT | Abstracted from radiology reports | <24 hours |

OXVASC indicates Oxford Vascular Study; SINPAC, Società Inter-regionale Piemonte-Aosta Cerebrovasculopatie; NDSS, North Dublin Stroke Study; IQR, interquartile range.

predictive in a large number patients with TIA diagnosed according to World Health Organization, time-based criteria[13,14] recruited from a range of clinical settings.[15]

Although developed for use in cohorts of patients before investigation, the possibility has been raised that prognostication might be improved after evaluation in secondary care by the incorporation of information from investigations, particularly the presence of brain infarction on imaging.[3,6] However, patients with high $ABCD^2$ scores are more likely to have brain infarction on diffusion-weighted imaging (DWI)[16] and so the additional predictive value of a composite score is uncertain. Studies published thus far have been too small to address this issue reliably, far too small to determine appropriate weighting for any imaging features, and meta-analysis of published data is undermined by inconsistent definitions of abnormality on imaging.

We therefore performed an appropriately powered international, multicenter collaborative study to determine the extent to which the predictive value of the $ABCD^2$ score is improved by incorporation of brain infarction on imaging and the optimal weighting of infarction in the score ($ABCD^2I$ score).

## Methods

This is a multicenter collaborative study. Independent research centers that collected sufficiently detailed information on prognosis, $ABCD^2$ score, and brain infarction in cohorts of patients with TIA were identified from a systematic review[15] and were invited to submit unpublished data. Patients were eligible if they had a diagnosis of TIA made according to the World Health Organization, time-based definition,[13,14] brain imaging by either MRI or CT, and follow-up to at least 7 days. Those with stroke according to the World Health Organization criteria[13,14] or alternative, non-neurovascular diagnoses were excluded.

We also searched for other studies of the ABCD system, stroke risk, and brain imaging in TIA not included in the systematic review.[15] PubMed, Ovid Medline, and EMBASE (2000 to July 2009) were searched by use of both the medical subject heading terms and text words: [transient isch(a)emic attack OR TIA OR amaurosis fugax] AND [prognosis OR outcome OR predict OR risk OR ABCD OR $ABCD^2$] AND [brain infarction OR brain ischa(e)mia]. The final search was done on July 11, 2009. We also hand-searched relevant reference lists, the contents pages of the 3 journals in which most eligible studies were published, and abstract booklets of recent international stroke conferences. Abstracts of all relevant articles were reviewed and, where appropriate, full texts were read.

The following data were requested from authors or extracted from reports: (1) study method—country, dates, clinical setting, methods of ascertainment, inception diagnosis and by whom it was made, delay to evaluation, methods of follow-up, and adjudication of outcomes; (2) brain imaging—modality and adjudication of the presence of brain infarction; (3) application of $ABCD^2$ scores—method of extraction of data and calculation of score; and (4) results—numbers of subjects and outcomes stratified by $ABCD^2$ score and presence or absence of brain infarction as defined subsequently.

To investigate the incorporation of brain infarction into the ABCD system, an infarction component was derived as follows: (1) on DWI, any acute infarction, irrespective of whether it was appropriate to the presenting symptoms; and (2) on CT imaging, any infarction (given the unreliability of distinction between acute and old infarction).

To assess the optimal weighting of infarction for incorporation into the ABCD system to yield maximal discrimination, the infarction component was allocated an "I score" of increasing integer value in separate analyses. Patients without infarction on brain imaging were allocated an I score of zero. For each cohort, the clinical component ($ABCD^2$ score, total 0 to 7) and infarction component (I score of 0 to x, depending on weighting) were then added to calculate a unified $ABCD^2I$ score. The discriminatory power of the $ABCD^2$ and differently weighted $ABCD^2I$ scores were then calculated for each cohort separately. Random-effects meta-analysis was used to calculate pooled estimates.

### Statistical Analysis

For each study, the percentage risk of stroke and the corresponding sensitivity and specificity were calculated for all reported cut points of the scores over the time interval(s) reported. Discriminatory power was calculated from the area under the receiver operator characteristic curve (AUC) with 95% CIs using standard methods. Ideal discrimination produces an AUC of 1.0, whereas discrimination that is no better than chance produces an AUC of 0.5. Pooled AUCs were obtained by random-effects meta-analysis.[17,18] Statistical analyses were done with SPSS Version 15.0 (SPSS Inc, Chicago, Ill).

## Results

The systematic review of the ABCD system[15] included 20 studies, of which 12 studies had sufficiently detailed clinical and imaging data to calculate $ABCD^2$ scores and characterize brain infarction.

**Table 2. Total Numbers of Participants and Numbers With Infarction on Brain Scanning and Stroke Outcomes at 7 and 90 Days**

| Study | Imaging Modality | No. | Infarction | Strokes 7 Days | Strokes 90 Days |
|---|---|---|---|---|---|
| California[4] | CT | 322 | 80 | 19 | 35 |
| OXVASC[7] | CT | 227 | 79 | 28 | 45 |
| Cucchiara[19] | DWI and CT | DWI 96; CT 71 | DWI 22; CT 30 | 4 | 5 |
| Lavallee[20] | DWI and CT | DWI 880; CT 204 | DWI 134; CT 33 | 5 | 17 |
| SINPAC[5] | CT | 274 | 53 | 10 | 15* |
| Calgary[5] | DWI | 111 | 41 | 4 | 6 |
| Calvet[2] | DWI | 339 | 136 | 5 | 10 |
| Ay[6] | DWI | 586 | 200 | 28 | N/A |
| Purroy[21] | DWI | 204 | 95 | 3 | 9 |
| Stanford[22] | DWI | 99 | 15 | 1 | 1† |
| NDSS[23] | DWI and CT | DWI 125; CT 88 | DWI 30; CT 37 | 2 | 10 |
| Asimos[24] | DWI and CT | DWI 766; CT 182 | DWI 211; CT 15 | 36 | 38 |

*Follow-up available only to 30 days.

†Follow-up to 90 days available in 85.

OXVASC indicates Oxford Vascular Study; SINPAC, Società Inter-regionale Piemonte-Aosta Cerebrovasculopatie; NDSS, North Dublin Stroke Study; N/A, not available.

The additional search of electronic databases yielded 2297 publications. After screening, 156 reports were identified for full-text review. Five further reports were identified by searching relevant reference lists and abstract books from recent conferences. No further studies were identified by hand searches of the 3 journals from which most eligible studies were identified electronically (*Lancet, Stroke, Cerebrovascular Diseases*). All publications were in English. The literature search identified all 12 studies already included in the systematic review but found no other relevant reports.

Twelve independent studies were therefore included in the collaboration.[2–7,19–24] Authors from all centers provided unpublished data. Study methods are summarized in Table 1. All studies included patients with World Health Organization-defined TIA who received brain imaging and excluded those with stroke and non-cerebrovascular diagnoses. Two studies were population-based,[7,23] recruiting consecutive patients from predefined populations, 5 were from emergency departments (EDs),[3–5,21,24] and 5 were from specialist neurovascular units.[2,6,19,20,22] In 10, the diagnosis of

**Table 3. AUCs for Prediction of the Presence of Infarction by the ABCD$^2$ Score and Prediction of 7-day and 90-day Stroke Risks by the Presence of Infarction**

| Cohort | Imaging | ABCD$^2$ Score Versus Infarction | Infarction Versus 7-Day Stroke Risk | Infarction Versus 90-Day Stroke Risk |
|---|---|---|---|---|
| California[4] | CT | 0.58 (0.51–0.65) | 0.59 (0.45–0.73) | 0.6 (0.50–0.70) |
| OXVASC[7] | CT | 0.61 (0.53–0.68) | 0.61 (0.49–0.72) | 0.67 (0.58–0.76) |
| Cucchiara DWI[19] | DWI | 0.51 (0.37–0.65) | 0.89 (0.75–1.00) | 0.89 (0.75–1.00) |
| Cucchiara CT[19] | CT | 0.64 (0.51–0.77) | 0.63 (0.31–0.95) | 0.67 (0.41–0.93) |
| Lavallee DWI[20] | DWI | 0.67 (0.60–0.70) | 0.42 (0.00–0.90) | 0.56 (0.38–0.074) |
| Lavallee CT[20] | CT | 0.53 (0.42–0.64) | 0.80 (0.55–1.00) | 0.67 (0.43–0.92) |
| SINPAC[3]* | CT | 0.56 (0.48–0.65)* | 0.66 (0.47–0.85) | 0.61 (0.45–0.77)† |
| Calgary[5] | DWI | 0.62 (0.51–0.72) | 0.83 (0.71–0.94) | 0.75 (0.56–0.93) |
| Calvet[2] | DWI | 0.61 (0.55–0.67) | 0.80 (0.70–0.91) | 0.76 (0.63–0.88) |
| Ay[6] | DWI | 0.58 (0.53–0.63) | 0.75 (0.67–0.84) | N/A |
| Purroy[21] | DWI | 0.58 (0.5–0.66) | 0.77 (0.61–0.93) | 0.61 (0.42–0.79) |
| Stanford[22] | DWI | 0.86 (0.77–0.96) | 0.93 (0.83–1.00) | 0.92 (0.81–1.00) |
| NDSS DWI[23] | DWI | 0.60 (0.49–0.71) | 0.38 (0.06–0.81) | 0.51 (0.21–0.80) |
| NDSS CT[23] | CT | 0.44 (0.32–0.57) | 0.79 (0.55–1.04) | 0.72 (0.53–0.91) |
| Asimos DWI[24] | DWI | 0.61 (0.56–0.65) | 0.84 (0.78–0.90) | 0.83 (0.76–0.89) |
| Asimos CT[24] | CT | 0.63 (0.50–0.76) | 0.98 (0.96–1.00) | 0.98 (0.96–0.99) |

*ABCD score substituted for ABCD$^2$ score.

†Outcomes available to 30 days only.

OXVASC indicates Oxford Vascular Study; SINPAC, Società Inter-regionale Piemonte-Aosta Cerebrovasculopatie; NDSS, North Dublin Stroke Study; N/A, not available.

**Table 4. AUCs for Prediction of Stroke at 7 Days Calculated for $ABCD^2$ and $ABCD^2I$ (Allocating 1 to 3 Points for Infarction) Scores for Individual Cohorts and Pooled AUCs Across Cohorts Using Either DWI or CT**

| | | | $ABCD^2I$ | No. of Points Allocated to I Score | |
|---|---|---|---|---|---|
| Cohort | Imaging | $ABCD^2$ | 1 | 2 | 3 |
| California[4] | CT | 0.64 (0.55–0.73) | 0.67 (0.57–0.77) | 0.67 (0.56–0.78) | 0.67 (0.55–0.78) |
| OXVASC[7] | CT | 0.78 (0.69–0.86) | 0.79 (0.71–0.87) | 0.77 (0.69–0.86) | 0.76 (0.68–0.84) |
| Cucchiara DWI[19] | DWI | 0.99 (0.97–1.00) | 1.00 (1.00–1.00) | 1.00 (1.00–1.00) | 1.00 (1.00–1.00) |
| Cucchiara CT[19] | CT | 0.62 (0.24–0.99) | 0.64 (0.23–1.00) | 0.65 (0.23–1.00) | 0.65 (0.22–1.00) |
| Lavallee DWI[20] | DWI | 0.49 (0.36–0.63) | 0.47 (0.33–0.59) | 0.45 (0.33–0.57) | 0.45 (0.33–0.56) |
| Lavallee CT[20] | CT | 0.77 (0.58–0.95) | 0.85 (0.72–0.98) | 0.89 (0.80–0.99) | 0.91 (0.82–1.00) |
| SINPAC[3]* | CT | 0.75 (0.63–0.88) | 0.78 (0.64–0.92) | 0.77 (0.62–0.92) | 0.76 (0.61–0.92) |
| Calgary[5] | DWI | 0.75 (0.56–0.94) | 0.85 (0.72–0.98) | 0.89 (0.80–0.99) | 0.90 (0.81–0.98) |
| Calvet[2] | DWI | 0.80 (0.62–0.98) | 0.87 (0.75–0.99) | 0.9 (0.81–0.99) | 0.90 (0.82–0.98) |
| Ay[6] | DWI | 0.65 (0.56–0.74) | 0.73 (0.64–0.81) | 0.77 (0.69–0.85) | 0.79 (0.71–0.86) |
| Purroy[21] | DWI | 0.51 (0.21–0.80) | 0.62 (0.34–0.91) | 0.70 (0.49–0.92) | 0.74 (0.58–0.9) |
| Stanford[22] | DWI | 0.62 (0.43–0.82) | 0.81 (0.71–0.91) | 0.86 (0.79–0.93) | 0.87 (0.80–0.94) |
| NDSS DWI[23] | DWI | 0.48 (0.32–0.64) | 0.44 (0.27–0.60) | 0.40 (0.26–0.55) | 0.40 (0.26–0.53) |
| NDSS CT[23] | CT | 0.24 (0.11–0.36) | 0.31 (0.17–0.45) | 0.45 (0.26–0.64) | 0.60 (0.44–0.75) |
| Asimos DWI[24] | DWI | 0.69 (0.61–0.77) | 0.81 (0.75–0.87) | 0.86 (0.82–0.91) | 0.88 (0.84–0.92) |
| Asimos CT[24] | CT | 0.68 (0.54–0.83) | 0.86 (0.76–0.95) | 0.95 (0.91–1.00) | 0.98 (0.96–1.00) |
| Pooled | All | 0.66 (0.53–0.78) | 0.73 (0.63–0.83) | 0.77 (0.69–0.84) | 0.78 (0.72–0.85) |
| | DWI | 0.67 (0.51–0.84) | 0.74 (0.61–0.87) | 0.77 (0.66–0.88) | 0.78 (0.68–0.88) |
| | CT | 0.64 (0.49–0.79) | 0.71 (0.57–0.84) | 0.76 (0.63–0.88) | 0.78 (0.64–0.91) |

*ABCD score substituted for $ABCD^2$ score.

OXVASC indicates Oxford Vascular Study; SINPAC, Società Inter-regionale Piemonte-Aosta Cerebrovasculopatie; NDSS, North Dublin Stroke Study.



TIA was made by a stroke physician or neurologist, whereas in 2,[4,24] the diagnosis was made by an ED physician. Nine studies excluded patients who presented after prespecified intervals after symptom onset.[2–6,19,21,22,24] Five studies used DWI only,[2,5,6,21,22] 3 studies used CT imaging only,[3,4,7] and 4 used a combination of the 2 modalities.[19,20,23,24] These latter 4 studies[19,20,23,24] each contributed 2 cohorts, 1 imaged with DWI and the other with CT; to avoid double-counting of patients, only DWI results were counted in patients who had been imaged with both DWI and CT. Sixteen cohorts in total were therefore included from the 12 studies; 9 were DWI-imaged and 7 were CT-imaged. CT tended to be used in the ED and population-based studies and DWI was used in neurovascular unit studies. $ABCD^2$ scores were recorded in 15 of the cohorts but 1 recorded only the ABCD score, values of which were substituted for the $ABCD^2$ score.[3] All outcome stroke events were based on patient evaluation, review of clinical notes, and brain imaging.

Table 2 summarizes rates of infarction and stroke outcomes for each cohort. The $ABCD^2$ score was used in 3206 patients imaged with DWI from 9 cohorts.[2,5,6,19–24] Acute infarction was present in 884 (27.6%). Follow-up was complete to 7 days, when 72 patients had a stroke; 2606 patients were followed up to 90 days when a further 72 had a stroke. ABCD or $ABCD^2$ scores were used in 1368 patients imaged with CT from 7 cohorts.[3,4,7,19,20,23,24] Acute or old infarction was present in 327 (23.9%). Seventy-three of 1368 CT-imaged patients had a stroke within 7 days of TIA; 1094 were followed up to 90 days when 104 patients had a stroke. For patients imaged with DWI, the rate of stroke at 7 days was 63 of 884 (7.1%, 5.5 to 9.1) for those with infarction compared with 9 of 2322 (0.4%, 0.2 to 0.7) without. Corresponding stroke rates for those imaged with CT were 42 of 327 (12.8%, 9.3 to 17.4) for those with acute or old infarction compared with 31 of 1041 (3.0%, 2.0 to 4.2) for those without.

Table 3 reports the discriminatory power as measured by the AUC of the $ABCD^2$ score and the presence of infarction for stroke at 7 and 90 days. The presence of infarction on DWI tended to be a more powerful predictor of stroke than on CT. The pooled AUC for the prediction of the presence of infarction by the $ABCD^2$ score was 0.60 (0.57 to 0.64) across all cohorts combined and 0.62 (0.57 to 0.58) and 0.57 (0.53 to 0.61) for cohorts imaged with DWI and CT, respectively (all $P<0.0001$). The OR for stroke at 7 days in the presence of brain infarction was 7.9 (5.4 to 11.4) overall and 19.7 (9.8 to 39.8) for DWI and 4.8 (3.0 to 7.8) for CT (all $P<0.001$). Corresponding OR after adjustment for $ABCD^2$ scores were 6.2 (4.2 to 9.0) overall and 14.9 (7.4 to 30.2) for DWI and 4.2 (2.6 to 6.9) for CT (all $P<0.001$).

For each cohort, those with brain infarction were allocated an integer I score and those without were allocated an I score of zero. Unified scores ($ABCD^2I$) were calculated by adding the I score to the $ABCD^2$ score, and corresponding discriminatory power for prediction of stroke was determined using receiver operator characteristic analyses. Table 4 gives the AUCs for prediction of stroke at 7 days for individual cohorts

**Table 5. AUCs for Prediction of Stroke at 90 Days Calculated by ABCD$^2$ and ABCD$^2$I (Allocating 1 to 3 Points for Infarction) for Individual Cohorts and Pooled AUCs for All Cohorts Using DWI or CT**

| Cohort | Imaging | ABCD$^2$ | ABCD$^2$I Score | Points Allocated for I Score | |
|---|---|---|---|---|---|
| | | | 1 | 2 | 3 |
| California[4] | CT | 0.70 (0.62–0.78) | 0.72 (0.64–0.80) | 0.72 (0.64–0.80) | 0.72 (0.63–0.80) |
| OXVASC[7] | CT | 0.67 (0.58–0.76) | 0.71 (0.63–0.8) | 0.73 (0.65–0.81) | 0.74 (0.66–0.82) |
| Cucchiara DWI[19] | DWI | 0.99 (0.97–1.00) | 1.0 (1.0–1.0) | 1.0 (1.0–1.0) | 1.0 (1.0–1.0) |
| Cucchiara CT[19] | CT | 0.57 (0.27–0.87) | 0.64 (0.32–0.95) | 0.66 (0.34–0.98) | 0.67 (0.35–0.99) |
| Lavallee DWI[20] | DWI | 0.73 (0.63–0.84) | 0.73 (0.62–0.85) | 0.72 (0.61–0.84) | 0.71 (0.60–0.83) |
| Lavallee CT[20] | CT | 0.60 (0.36–0.84) | 0.65 (0.39–0.91) | 0.67 (0.41–0.94) | 0.68 (0.41–0.95) |
| SINPAC[3]* | CT | 0.76 (0.66–0.86) | 0.76 (0.65–0.88) | 0.75 (0.63–0.87) | 0.74 (0.61–0.86) |
| Calgary[5] | DWI | 0.77 (0.61–0.93) | 0.82 (0.66–0.98) | 0.83 (0.67–1.0) | 0.84 (0.67–1.00) |
| Calvet[2] | DWI | 0.75 (0.61–0.89) | 0.81 (0.67–0.95) | 0.83 (0.70–0.97) | 0.84 (0.70–0.97) |
| Ay[6] | DWI | N/A | N/A | N/A | N/A |
| Purroy[21] | DWI | 0.56 (0.38–0.73) | 0.61 (0.44–0.78) | 0.63 (0.46–0.79) | 0.63 (0.47–0.79) |
| Stanford[22] | DWI | 0.60 (0.38–0.81) | 0.79 (0.69–0.90) | 0.84 (0.76–0.92) | 0.85 (0.77–0.93) |
| NDSS DWI[23] | DWI | 0.36 (0.15–0.57) | 0.38 (0.15–0.62) | 0.40 (0.13–0.68) | 0.41 (0.12–0.71) |
| NDSS CT[23] | CT | 0.61 (0.38–0.85) | 0.70 (0.50–0.90) | 0.78 (0.62–0.93) | 0.82 (0.7–0.93) |
| Asimos DWI[24] | DWI | 0.70 (0.62–0.78) | 0.81 (0.74–0.87) | 0.86 (0.81–0.91) | 0.87 (0.83–0.92) |
| Asimos CT[24] | CT | 0.68 (0.54–0.83) | 0.86 (0.76–0.95) | 0.95 (0.91–1.00) | 0.98 (0.96–1.00) |
| Pooled | All | 0.68 (0.57–0.79) | 0.75 (0.66–0.84) | 0.78 (0.71–0.86) | 0.80 (0.74–0.86) |
| | DWI | 0.69 (0.54–0.85) | 0.76 (0.64–0.88) | 0.79 (0.68–0.90) | 0.80 (0.71–0.90) |
| | CT | 0.69 (0.65–0.74) | 0.75 (0.70–0.80) | 0.77 (0.66–0.88) | 0.78 (0.65–0.91) |

*ABCD score substituted for ABCD$^2$ score.

OXVASC indicates Oxford Vascular Study; SINPAC, Società Inter-regionale Piemonte-Aosta Cerebrovasculopatie; NDSS, North Dublin Stroke Study; N/A, not available.



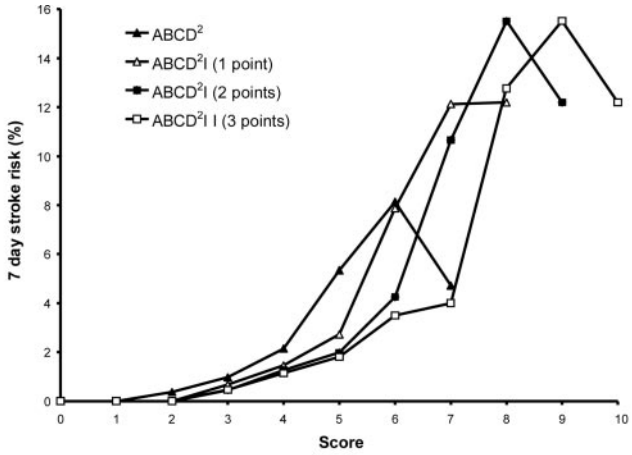
and pooled estimates for the ABCD$^2$ and ABCD$^2$I scores with different weightings of the infarction component. Table 5 gives corresponding results for prediction of stroke risk at 90 days. For all cohorts except 2, and in all pooled analyses, the predictive power of the unified ABCD$^2$I scores was better than the ABCD$^2$ score alone. The greatest improvement in predictive power was observed when the infarction component was weighted more heavily with the allocation of 3 points, making the ABCD$^2$I score out of a total of 10. Sensitivity analyses were performed by allocating weightings to the infarction component of $>3$ points, but these did not yield improvements in predictive performance.

The Figure shows the percentage risk of stroke at 7 days plotted against the cut points of ABCD$^2$ and differently weighted ABCD$^2$I scores.

## Discussion

Our results show that in 4574 patients with TIA from 12 independent centers, diagnosed according to the World Health Organization, time-based definition,[13,14] with 145 stroke outcomes at 7 days, the incorporation of infarction into the ABCD$^2$ score (ABCD$^2$I) improves discriminatory power for prediction of early recurrent stroke. Discrimination, measured by pooled AUCs, is greatest when the infarction component is heavily weighted (3 points) in comparison to other elements of the ABCD$^2$ score, giving an ABCD$^2$I score out of a total of 10 points. Acute infarction on DWI and new or old infarction identified on CT improve discrimination measured by AUC to a similar extent. Our results support the use of a staged approach to risk prediction in patients with TIA, first with clinical data available at initial patient assessment and then with brain imaging data, available after evaluation in specialist care.

Infarction, particularly on DWI, is associated with high early stroke risk after TIA,[2,5,6] and the incorporation of brain infarction into a risk prediction tool is therefore sensible. However, several studies have shown that the presence of brain infarction on DWI is associated with individual elements of the ABCD system.[16,25] In a meta-analysis of published and unpublished data from 19 studies, Redgrave and colleagues found that symptom duration over 60 minutes, dysphasia, dysarthria, and motor weakness were all independently associated with the presence of acute infarction on DWI, although diabetes, increasing age, and hypertension were not.[16] In a separate analysis of individual patient data in 808 patients with TIA from 9 studies, Shah and colleagues also found motor weakness and longer duration of symptoms to be associated with DWI positivity.[25] Corresponding studies of the association between determinants of stroke risk after TIA and findings on CT are lacking. Such associations between the elements of the ABCD system and DWI positivity may be expected to partially confound the predictive value of the unified ABCD$^2$I score. However, our results indicate that brain infarction provides additional prognostic information and incorporation of an infarction component into the system is justified.




Percentage of total patients (& cumulative percentage of strokes at seven days in brackets) for ABCD$^2$ score and ABCD$^2$I scores allocated 1-3 points

| Score | I score allocation | Cut point 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ABCD$^2$ | | 1.7 (0.0) | 4.8 (0.0) | 11.8 (1.4) | 18 (6.9) | 25.5 (24.1) | 22.1 (61.4) | 13.7 (96.6) | 2.3 (100) | | | |
| ABCD$^2$I | 1 | 1.6 (0.0) | 4.5 (0.0) | 10.2 (0.0) | 16.2 (3.4) | 22.6 (13.8) | 21.7 (32.4) | 15.8 (71.7) | 6.5 (96.6) | 0.9 (100) | | |
| ABCD$^2$I | 2 | 1.6 (0.0) | 4.4 (0.0) | 9.9 (0.0) | 14.6 (2.1) | 20.8 (10.3) | 18.8 (22.1) | 15.4 (42.8) | 8.6 (71.7) | 5.1 (96.6) | 0.9 (100) | |
| ABCD$^2$I | 3 | 1.6 (0.0) | 4.4 (0.0) | 9.8 (0.0) | 14.3 (2.1) | 19.2 (9.0) | 17 (18.6) | 12.5 (32.4) | 8.2 (42.8) | 7.2 (71.7) | 5.1 (96.6) | 0.9 (100) |

**Figure.** Graph of 7-day stroke risk (%) plotted against cut points for the ABCD$^2$ and ABCD$^2$I (given different weights for the infarction component) pooled across all cohorts.

Our results show that the prognostic yield of the combination of acute or old infarction on CT is similar to that of acute infarction on DWI. Our study did not identify chronic infarction on MRI, and this may have reduced the yield of MRI, but this would probably have led to the inclusion of nonspecific findings in a large number of cases. In comparison to MRI, CT scanning is quick, inexpensive, and widely available, especially in emergency care settings, and remains the predominant neuroimaging modality available for TIA in many centers. In a countrywide survey of ED attenders with TIA in the United States from the National Hospital Ambulatory Medical Care Survey (NHAMCS) up to 2001, 56% of patients received CT imaging and <5% received MRI, although rates of MRI will have increased subsequently.[26] However, despite its availability, CT has the disadvantages of reduced sensitivity for early infarction and radiation exposure and MRI with DWI remains the imaging modality of choice in TIA.[9,10]

The use of the ABCD$^2$ score for identifying either high- or low-risk groups currently differs between healthcare systems. For instance, in the United Kingdom, guidelines recommend that patients with scores >3 are triaged to urgent assessment within 24 hours,[10] whereas in the United States, some centers use the score to triage patients in the ED between hospital admission and outpatient assessment.[9] The Figure summarizes observed stroke risks and percentages of patients for different ABCD$^2$ score cut points and demonstrate that low-, intermediate-, and high-risk groups can be identified. Importantly, of the 9 cohorts imaged with DWI, 5 were based in specialist neurovascular units,[2,6,19,20,22] providing urgent and intensive treatment, in which low rates of subsequent stroke are frequently observed, whereas in the 7 cohorts using CT, 5[3,4,7,23,24] were based in either EDs or population-based studies in which higher rates of subsequent stroke are observed.[1] It is likely that the use of a staged approach to risk stratification will vary between healthcare systems, according to the delays to patients' presentation to emergency and specialist care, relative availability of different imaging modalities, and the preferred setting(s) for specialist assessment.

In addition to its usefulness in routine clinical practice, a unified ABCD$^2$I score could also be beneficial in selecting patients for clinical trials in research. The Figure shows that recruiting subjects into a trial with an ABCD$^2$I cut point of ≥5 would enroll 50% of patients and capture 90% of outcome strokes in contrast to a cut point of 4 for the ABCD2 score, which would capture a similar proportion of outcome strokes but enroll approximately 60% of patients.

Although we believe our findings are valid, our study does have some shortcomings. We have combined results from 12 studies, ascertained over an 11-year period, treated in different healthcare settings in different countries and using different imaging modalities. Rates of outcomes also differed. Although such variation in study methods may jeopardize the validity of a prognostic scoring system, we feel that this approach is justified because it reflects routine clinical practice in which the system is designed to be used. The consistent improvement in predictive power observed with the incorporation of infarction into the ABCD$^2$I score supports the generalizability of our findings.

In summary, we have found that incorporation of brain infarction into the ABCD$^2$ score (ABCD$^2$I) improves prediction of stroke in the early phase after TIA defined by World Health Organization, time-based criteria. Our findings support a staged approach to the evaluation of patients with transient neurological symptoms caused by brain ischemia in

which clinical and then imaging data characterize diagnosis and risk. However, other potential determinants of stroke risk after TIA have been identified in addition to clinical features and infarction, including large artery disease, although this may depend on delay to carotid intervention. Further refinement of the ABCD system is likely, but large studies using consistent methodology and individual patient data are necessary to determine the exact weighting of markers of vascular instability for optimal risk prediction.

## Source of Funding

M.F.G. receives funding from the National Institute for Health Research, Biomedical Research Centre, Oxford, UK.

## Disclosures

None.

## References

1. Giles MF, Rothwell PM. Risk of stroke early after transient ischaemic attack: a systematic review and meta-analysis. *Lancet Neurol*. 2007;6: 1063–1072.
2. Calvet D, Touze E, Oppenheim C, Turc G, Meder J-F, Mas J-L. DWI lesions and TIA etiology improve the prediction of stroke after TIA. *Stroke*. 2009;40:187–192.
3. Sciolla R, Melis F. SINPAC Group. Rapid identification of high-risk transient ischemic attacks: prospective validation of the ABCD score. *Stroke*. 2008;39:297–302.
4. Douglas VC, Johnston CM, Elkins J, Sidney S, Gress DR, Johnston SC. Head computed tomography findings predict short-term stroke risk after transient ischemic attack. *Stroke*. 2003;34:2894–2898.
5. Coutts SB, Eliasziw M, Hill MD, Scott JN, Subramaniam S, Buchan AM, Demchuk AM. VISION Study Group. An improved scoring system for identifying patients at high early risk of stroke and functional impairment after an acute transient ischemic attack or minor stroke. *Int J Stroke*. 2008;3:3–10.
6. Ay H, Arsava EM, Johnston SC, Vangel M, Schwamm LH, Furie KL, Koroshetz WJ, Sorensen AG. Clinical- and imaging-based prediction of stroke risk after transient ischemic attack. The CIP model. *Stroke*. 2009; 40:181–186.
7. Rothwell PM, Giles MF, Flossmann E, Lovelock CE, Redgrave JN, Warlow CP, Mehta Z. A simple score (ABCD) to identify individuals at high early risk of stroke after transient ischaemic attack. *Lancet*. 2005; 366:29–36.
8. Johnston SC, Rothwell PM, Nguyen-Huynh MN, Giles MF, Elkins JS, Bernstein AL, Sidney S. Validation and refinement of scores to predict very early stroke risk after transient ischaemic attack. *Lancet*. 2007;369: 283–292.
9. Easton JD, Saver JL, Albers GW, Alberts MJ, Chaturvedi S, Feldmann E, Hatsukami TS, Higashida RT, Johnston SC, Kidwell CS, Lutsep HL, Miller E, Sacco RL. Definition and evaluation of transient ischemic attack: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association Stroke Council; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; and the Interdisciplinary Council on Peripheral Vascular Disease. The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists. *Stroke*. 2009;40: 2276–2293.
10. Department of Health. *National Stroke Strategy*. London: Crown; 2007.
11. National Stroke Foundation. Clinical Guidelines for Acute Stroke Management. Melbourne: NSF; 2007. Available at: www.strokefoundation.com.au/. Accessed 14 September 2009.
12. Stroke Foundation of New Zealand. New Zealand Guideline for the Assessment and Management of Transient Ischaemic Attack. Wellington. Available at: www.stroke.org.nz. Accessed 14 September 2009.
13. Hatano S. Experience from a multicentre stroke register: a preliminary report. *Bull World Health Organ*. 1976;54:541–553.
14. Advisory Council for the National Institute of Neurological and Communicative Disorders and Stroke. A classification and outline of cerebrovascular diseases. *Stroke*. 1975;6:564–616.
15. Giles MF, Rothwell PM. Systematic review and pooled analysis of published and unpublished validations of the ABCD and ABCD2 TIA risk scores. *Stroke*. 2010;41:667–673.
16. Redgrave JN, Coutts SB, Schulz UG, Briley D, Rothwell PM. Systematic review of associations between the presence of acute ischemic lesions on diffusion-weighted imaging and clinical predictors of early stroke risk after transient ischemic attack. *Stroke*. 2007;38:1482–1488.
17. Kester AD, Buntinx F. Meta-analysis of ROC curves. *Med Decis Making*. 2000;20:430–439.
18. Lipsey MW, Wilson D. Practical Meta-Analysis. Los Angles, CA; 2001. Sage Publishing. Available at: http://mason.gmu.edu/~dwilsonb/ma.html. Accessed 14 September 2009.
19. Cucchiara B, Messe S, MacKenzie L, Sansing LH, Taylor RA, Pacelli J, Shah QA, Pollak E, Kasner SE. D-dimer, MRI DWI, and ABCD2 score for TIA risk stratification. *J Stroke Cerebrovasc Dis*. 2009;18:367–373.
20. Lavallee PC, Meseguer E, Abboud H, Cabrejo L, Olivot JM, Simon O, Mazighi M, Nifle C, Niclot P, Lapergue B, Klein IF, Brochet E, Steg PG, Leseche G, Labreuche J, Touboul PJ, Amarenco P. A TIA clinic with round-the-clock access (SOS-TIA): feasibility and effects. *Lancet Neurol*. 2007;6:953–960.
21. Purroy F, Begué R, Quílez A, Piñol-Ripoll G, Sanahuja J, Brieva L, Setó E, Gil MI. The California, ABCD, and unified ABCD2 risk scores and the presence of acute ischemic lesions on DWI in TIA patients. *Stroke*. 2009;40:2229–2232.
22. Mlynash M, Olivot JM, Tong DC, Lansberg MG, Eyngorn I, Kemp S, Moseley ME, Albers GW. Yield of combined perfusion and diffusion MR imaging in hemispheric TIA. *Neurology*. 2009;72:1127–1133.
23. Sheehan OC, Merwick A, Kelly LA, Hannon N, Marnane M, Kyne L, McCormack PM, Duggan J, Moore A, Moroney J, Daly L, Harris D, Horgan G, Kelly PJ. Diagnostic usefulness of ABCD2 score to distinguish TIA and minor ischemic stroke from non-cerebrovascular events: the North Dublin TIA Study. *Stroke*. 2009;40:3449–3454.
24. Asimos AW, Johnson AM, Rosamond WD, Price MF, Rose KM, Catellier D, Murphy CV, Singh S, Tegeler CH, Felix A. A multicenter evaluation of the ABCD(2) score's accuracy for predicting early ischemic stroke in admitted patients with transient ischemic attack. *Ann Emerg Med*. 2010;55:201–210.e5.
25. Shah SH, Saver JL, Kidwell CS, Albers GW, Rothwell PM, Ay H, Koroshetz WJ, Inatomi Y, Uchino M, Demchuk AM, Coutts SB, Purroy F, Alvarez-Sabin JS, Sander D, Sander K, Restrepo L, Wityk RJ, Marx JJ, Easton JD. A multicenter pooled, patient-level data analysis of diffusion-weighted MRI in TIA patients. *Stroke*. 2007;38:463.
26. Edlow JA, Kim S, Pelletier AJ, Camargo CA Jr. National study on emergency department visits for transient ischemic attack, 1992–2001. *Acad Emerg Med*. 2006;13:666–672.