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Journal Club: Early stroke risk and ABCD2 score performance in tissue vs time-defined TIA

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In this journal club article, we evaluate a study by Giles and colleagues[1] that reports stroke risk in patients with classically defined TIA subcategorized by presence or absence of radiologic brain infarction.

The concept of a TIA is evolving in parallel with better understanding of brain ischemia and insights gained from neuroimaging studies. TIAs were classically defined as a sudden focal neurologic deficit resulting from brain or retinal ischemia lasting less than 24 hours.[2,3] The time threshold of 24 hours was arbitrarily chosen, and given that there is no evidence to support any single time criterion associated with infarction, this has appropriately been questioned.

A newer and well-received definition of TIA is "a transient episode of neurologic dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction."[4] This definition communicates the important concept that transient symptoms can nonetheless be associated with permanent brain injury, encourages the use of neuroimaging studies, and may promote rapid interventions for acute brain ischemia.

The ABCD2 score, a risk-stratifying score for patients with TIA, is derived from the patient's age, blood pressure, clinical features, TIA duration, and history of diabetes. This simple, validated score identifies patients at highest risk of early stroke after TIA.[5] Scores are commonly divided into low risk (0–3), intermediate risk (4–5), and high risk.[6,7]

The clinical ABCD2 scale is integrated in this study with results from acute brain imaging to assess how the new tissue-based definition of TIA further assists with risk stratification of patients with transient neurologic symptoms.

HYPOTHESIS AND DESIGN In this analysis of data pooled from 12 medical centers which included 4,574 patients, Giles and colleagues subcategorized TIA as "tissue positive" or "tissue negative," depending on the presence or absence of radiographic brain infarction seen on MRI or CT scans.[1] They set out to determine the added value of brain imaging to the risk stratification of patients with TIA and hypothesized that the ABCD2 score retains its prognostic value within these groups.

These questions are undoubtedly relevant to today's clinical practice in which imaging studies are increasingly obtained and criteria for admission to the hospital are becoming stricter. Having objective, accurate means of identifying the patients at highest risk for stroke after TIA could facilitate rapid interventions and hopefully lead to better clinical outcomes.

METHODS The authors performed a systematic review of the literature in 2009 and identified 12 research centers that had sufficient prospective data of interest available. To be included, the center needed to have a cohort of patients with TIA (traditional time-based definition), ABCD2 scores, brain imaging, and clinical follow-up until at least 7 days after the TIA. Five studies were based in emergency departments, 5 in specialized neurovascular units, and 2 were population-based. ABCD2 scores were calculated by local investigators and the presence of brain infarction could be determined by a routine report from individual centers. For patients who had MRI with diffusion-weighted imaging (DWI), any acute infarct was counted as tissue-positive (whether or not the location corresponded to clinical symptoms) and for patients with CT, any infarct, regardless of age, was also considered positive. Because CT is less sensitive than MRI for the detection of acute ischemia, combining results from these different imaging modalities could potentially jeopardize the internal validity of the study results. However, this also allows the results to be generalized to a greater extent, given that CT scans are still used as the primary imaging modality for TIA evaluations at some centers.

The statistical method used to determine the predictive power of the ABCD2 score was the area under the receiver operating characteristic curve (AUC). The receiver operating characteristic curve is a graph of sensitivity against 1 − specificity[6] (figure).

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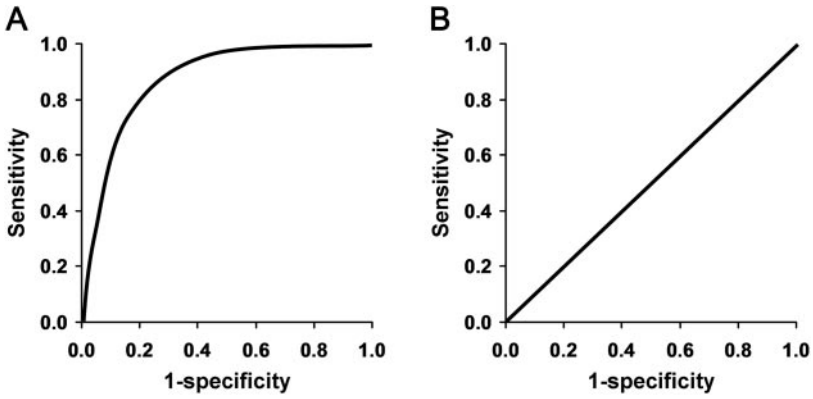
Disclosure: Author disclosures are provided at the end of the article.

Figure Area under the receiver operating characteristic curve (AUC)



(A) An AUC close to 1 indicates an accurate test with sensitivity and specificity both approaching 1. The line starts at the origin (0,0), goes up to the y-axis to (0,1), and then horizontally across to (1,1). (B) If a variable has no diagnostic capability, the AUC is 0.5, which is as good as a random guess. A test based on this variable would be equally likely to produce a false positive or a true positive. This appears as a straight line from the bottom left corner (0,0) diagonally across to the top right corner (1,1).

The closer the AUC is to 1, the better the test's sensitivity and specificity. An AUC of 0.5, which appears as a straight diagonal line, indicates that the variable has no diagnostic capability.

Of note, the authors did not state the statistical test used for the comparison of the tissue-positive and tissue-negative groups, though based on the nonoverlapping confidence intervals and the *p* values reported, the comparisons are statistically significant.

RESULTS The authors confirmed that radiographic evidence of brain infarction in patients with TIA is a predictor of higher risk of early stroke. There was a remarkable 18-fold increase in the rate of stroke at 7 days, from 0.4% in those with negative DWI to 7% in those with positive DWI. For those with infarcts on CT scans, the 7-day risk was 3% in those with negative CT and 13% with a positive CT. The overall risk of stroke at 90 days was 2.2% in the tissue-negative group and 12% in the tissue-positive group.

However, the value of brain imaging in addition to ABCD2 score seemed to be less clear when looking at the longer-term outcome of stroke within 90 days, specifically for low-risk patients as stratified by ABCD2 score. Of patients with ABCD2 score ≤3, only 21 patients (2%) had a stroke within 90 days, but over half of these (n = 12, 57%) had tissue-negative imaging.

Nevertheless, the ABCD2 score was predictive of recurrent stroke at 7 days within both the tissue-positive and tissue-negative groups. Of 1,665 patients with ABCD2 ≤3, 10 patients (0.6%) had a recurrent stroke in 7 days, of which 7 were in the tissue-positive group. Of 2,909 patients with ABCD2 ≥4, 135 patients, or 4.6%, had recurrent stroke at 7 days. Ninety-eight of these (73%) had evidence of brain infarction on either MRI or CT.

The AUC for prediction of stroke by ABCD2 at 90 days was 0.66 for tissue-positive and 0.69 for tissue-negative patients. AUC for the prediction of stroke at 7 days was 0.68 for tissue-positive vs 0.73 for tissue-negative. Thus the ABCD2 score meaningfully stratifies risk among both the tissue-positive and tissue-negative groups.

INTERPRETATION In their large, international multicenter study, Giles and colleagues show that the ABCD2 score retains its prognostic value for refining the risk of stroke in both tissue-positive and tissue-negative groups. They also confirm that brain imaging adds value to the ABCD2 score by identifying patients at a higher risk within a given ABCD2 score category. Because the ABCD2 score meaningfully stratifies risk within both tissue-positive and tissue-negative groups, it indicates that the score does more than simply separate "real TIAs" from TIA mimickers. These findings add to the growing body of literature suggesting that early brain imaging (particularly DWI) enhances prediction of early stroke risk in patients with TIA.[7–10]

In order to implement the author's findings into clinical practice, routine imaging in TIA evaluation protocols would be necessary. This would best be achieved with the use of MRI, rather than CT. Based on the author's results that patients with tissue-positive imaging after TIA had 7.5% more risk of having a stroke within the following week, one would need to image 14 (95% confidence interval 11–17.1) patients to identify one additional patient at high risk of early stroke. When extended out to assess the risk of stroke within 90 days, this number decreases to 11 (95% confidence interval 8.4–13.1). The authors appropriately conclude that the information provided by acute imaging is clinically relevant and should influence management and triage decisions.

The results of the study are valid, though there are some inevitable limitations. The data, pooled from 12 studies, were collected over 11 years from various medical centers with assessments by clinicians with different degrees of cerebrovascular experience and using different imaging techniques. This variation in study methods threatens validity to an extent, but also reflects the reality of clinical practice more accurately. Mixing results from CT scan and MRI appears most problematic, not only because of the higher sensitivity of MRI but also because DWI can demonstrate acute lesions while this is impossible with CT scans. Still, the overall rates of stroke at 90 days were similar in this study to those found in a

prospective study that used only MRI (current study had 2.2% vs 4.3% for tissue-negative and 12% vs 10.8% for tissue-positive).[10]

Overall, these findings provide further support for the evolving concept of a tissue-based rather than the traditional time-based definition of TIA. The results make a compelling argument for the use of prompt brain imaging (specifically MRI with DWI sequences) to optimize the triage of patients with transient neurologic symptoms ascribed to focal cerebral ischemia. One specific interpretation of the data, when applying it to an emergency room situation, might be that patients with low risk ABCD2 scores (<3) with negative DWI could be discharged, while those with positive DWI should be admitted, despite the low ABCD2 score, given the substantial increased risk of stroke within the next 7 days.

Within the past few decades there have been tremendous advances in the diagnosis and treatment of cerebrovascular disorders. The results of this study support that our definitions and scoring systems should be correspondingly modified to maximize clinician decision-making with the aim of positively impacting on patient outcomes.

AUTHOR CONTRIBUTIONS

Dr. Fugate: drafting and revising the manuscript, interpretation of data. Dr. Rabinstein: revising the manuscript, interpretation of data, study supervision.

DISCLOSURE

Dr. Fugate is a member of the editorial team for the *Neurology*® Resident & Fellow Section. Dr. Rabinstein has a research grant from CardioNet and receives royalties for books published with Elsevier.

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Neurology 2012;78;e77-e79
DOI 10.1212/WNL.0b013e31824c4706