TWO ACES
Transient Ischemic Attack Work-Up as Outpatient Assessment of Clinical Evaluation and Safety

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Background and Purpose—To evaluate a novel emergency department-based TIA triage system.

Methods—We developed an approach to TIA triage and management based on risk assessment using the ABCD² score in combination with early cervical and intracranial vessel imaging. It was anticipated that this triage system would avoid hospitalization for the majority of TIA patients and result in a low rate of recurrent stroke. We hypothesized that the subsequent stroke rate among consecutively encountered patients managed with this approach would be lower than predicted based on their ABCD² scores.

Results—From June 2007 to December 2009, 224 consecutive patients evaluated in the Stanford emergency department for a possible TIA were enrolled in the study. One hundred fifty-seven were discharged to complete their evaluation at the outpatient TIA clinic; 67 patients were hospitalized. One hundred sixteen patients had a final diagnosis of TIA/minor stroke or possible TIA. The stroke rates at 7, 30, and 90 days were 0.6% (0.1%–3.5%) for patients referred to the TIA clinic and 1.5% (0.3%–8.0%) for the hospitalized patients. Combining both groups, the overall stroke rate was 0.9% (0.3%–3.2%), which is significantly less than expected based on ABCD² scores (P=0.034 at 7 days and P=0.001 at 90 days).

Conclusions—This emergency department-based inpatient versus outpatient TIA triage system led to a low rate of hospitalization (30%). Recurrent stroke rates were low for both the hospitalized and outpatient subgroups. (Stroke. 2011;42:1839-1843.)

Key Words: transient ischemic attack triage

The annual incidence of TIA in the United States is estimated to be 240,000 patients per year.¹ The risk of stroke after TIA is estimated to be about 5% within the first 24 to 48 hours and up to 10% within the first few weeks.²,³ Therefore, the majority of TIA patients do not experience an early recurrent cerebrovascular event and it is unclear whether hospitalization is warranted for most TIA patients. Several factors have been identified that help clarify which patients are at the highest risk for early stroke after a TIA. These factors may be useful for optimizing triage decisions.

The ABCD² score is a 7-point scale based on clinical data available before neuroimaging, which can be used to estimate the risk of stroke after TIA.² In addition, meta-analyses have demonstrated that the presence of an infarction on brain imaging or symptomatic vessel stenosis was also associated with an increased risk of stroke.⁴,⁵ Studies have suggested that intracranial vessel occlusion or stenosis is associated with an increased risk of early stroke after TIA.⁶,⁷

Different strategies have been proposed to expedite the acute management of TIA patients as outpatients. In England, Rothwell et al⁸ developed a clinic where suspected TIA patients can be directly referred during business days by their primary care provider. Patients referred to the outpatient TIA clinic receive expedited evaluation and management of their TIA.⁹ In France, Amarenco et al⁹ developed a “24/7” intensive evaluation system to which TIA patients are directly admitted for a short period of time (4–6 hours) to have brain and vessel imaging performed and treatment initiated. Twenty-six percent of the patients were admitted to the stroke unit.⁹ In Canada, Wasserman et al¹⁰ initiated the stroke prevention treatment in the emergency department (ED). The urgency of specialized stroke clinic appointments was assigned based on ABCD² score. These outpatient-based approaches were all associated with a low rate 90-day stroke (2.1%, 1.2%, and 3.2%, respectively).⁸–¹⁰ At the Stanford Stroke Center, we developed a novel outpatient TIA clinic for triage and management of the patients seeking medical attention at the Stanford ED for a possible TIA or minor stroke. This approach was based on risk assessment using the ABCD² score in combination with early cervical and intra-
cranial vessel imaging. It was anticipated that this triage protocol system would avoid hospitalization for the majority of TIA patients. In addition, we hypothesized that the patients referred to the outpatient TIA clinic would have a rate of stroke recurrence (<2% at 1 week and <5% at 30 days) equivalent to previously published results, and that the stroke recurrence rate among both hospitalized and nonhospitalized patients would be lower than predicted based on their ABCD² scores.

Patients and Methods

Patients

Two hundred twenty-four patients evaluated at the Stanford ED for a possible TIA or minor stroke were included in the TIA Work-up as Outpatient Assessment of Clinical Evaluation and Safety (TWO ACES) study between June 2007 and December 2009. All patients signed an informed consent. The study was approved by the Stanford Administrative Panel on Human Subjects in Medical Research.

The ED evaluation for all patients included a noncontrast CT, routine laboratory studies, EKG, and a consult from a neurology resident that included a consultation, typically by telephone, with a vascular neurology fellow or attending vascular neurologist who made the triage decision. Physicians who evaluated TIA patients in the Stanford ED were educated about the protocol multiple times during the course of the study and were encouraged to follow the protocol; however, they had the option to deviate from the suggested triage recommendations based on their clinical judgment.

Triage Protocol

Patients with an ABCD² score of 0 to 3 were eligible to be discharged directly from ED to the TIA clinic. Efforts were made to evaluate the patient in the TIA clinic within 1 to 2 business days and to obtain an MRI and MRA (cervical and intracranial) before the clinic visit (if there were MRI contraindications, then the patients would undergo a head CT with CTA or carotid ultrasound or both). For patients with an ABCD² score of 4 to 5, the protocol recommended obtaining cervical and intracranial vessel imaging (typically with CTA) in the ED. If a symptomatic cervical or intracranial stenosis (>50% narrowing) were identified, then the protocol recommended hospital admission. If vessel imaging did not reveal a significant symptomatic lesion, then referral to the TIA clinic was recommended as described. For patients with ABCD² scores >5, hospitalization was recommended.

Assessments, Follow-Up, and Outcome Events

Patients were routinely started, or continued, on antithrombotic therapy (typically antiplatelet agents) at ED discharge. Anticoagulants for nonanticoagulated patients with atrial fibrillation were typically initiated in the TIA clinic or during the hospitalization. Previous statin and antihypertensive agents were adjusted during hospitalization or at the TIA clinic visit. The specific management of blood pressure and lipids was not specified in the protocol (treatment decisions were left to the discretion of the attending neurologist); however, the recommendations of the American Heart Association for secondary stroke prevention recommendations were followed as a general policy.11,12 All the patients who were referred to the TIA clinic were evaluated by a TIA clinic nurse practitioner and a physician with subspecialty training in vascular neurology. Hospitalized patients were admitted to the Stanford stroke service and evaluated by an attending stroke neurologist.

The attending stroke neurologist who evaluated the patient determined the final diagnosis after the evaluation was complete. The final diagnosis was categorized as TIA/minor stroke, possible TIA, and not a cerebrovascular event. The definition of TIA versus minor stroke was based on symptom duration (<24 versus >24 hours), independent of diffusion-weighted imaging (DWI) positivity.

We evaluated the rate of stroke, MI, and vascular death at 7, 30, and 90 days. These evaluations were primarily performed by telephone, unless a routine return visit to the clinic occurred at 1 of the prespecified time points. The final adjudication of whether an end point had occurred was based on review of all available medical records and was consensually validated by 2 neurologists (J.M.O. and G.W.A.). All the MRI, MRA, and CTA obtained during the course of the study were reviewed by a neuroradiologist and 2 stroke neurologists.

Statistical Analysis

The risks of stroke, as well as the combined end point of stroke, MI, and vascular death were calculated at 7, 30, and 90 days. Patients who died from causes other than stroke or vascular disease were censored. The number of expected stroke events was calculated by the product of the risk for each ABCD² score category (low, moderate, and high) measured in the pivotal publication of Johnston et al13 by the number of patients in each category. The stroke rate was then obtained by the sum of expected events divided by the total number of patients.

The proportions were compared using χ² or Fisher exact tests. Continuous data were compared using Student t test, whereas ABCD² scores were compared using Mann-Whitney U test. Logistic regression analysis was performed to identify independent risk factors for hospitalization. Statistical tests were 2-tailed. Significance was defined at α<0.05. Statistical analyses were performed using PASW Statistics 18 (SPSS).

Results

Patient Characteristics

From June 2007 to December 2009, 224 consecutive patients evaluated at the Stanford ED for suspicion of TIA were enrolled in the study. One hundred fifty-seven (70%) patients were discharged to the TIA clinic, whereas 67 (30%) were hospitalized. The general characteristics of the study population are presented in Table 1. Two hundred six patients (92%) were seen within 24 hours after symptom onset. Median delay from symptom onset to the evaluation at the ED was 0 days (interquartile range [IQR], 0–0). Two hundred nine patients (93%) had vascular imaging; among these, 127 (61%) had the imaging performed in the ED. The final diagnosis from the attending stroke neurologist was TIA in 86 patients, minor stroke in 7, and possible TIA in 23 patients. One hundred eight (48%) had a final diagnosis of a noncerebrovascular event. Among these patients with nonvascular diagnoses, the final diagnoses were: migraine, 30%; toxic/metabolic, 8%; benign paroxysmal positional vertigo (BPPV); 6%, seizure, 4%; transient global amnesia, 3%; recurrence of previous stroke symptoms, 3%; syncope, 2%; tumor, 1%; and peripheral neuropathy, 1%. No definite alternate diagnosis was reached in 42%.

At initial evaluation in the ED, 157 were discharged to TIA clinic. The median times between the ED encounter and TIA clinic were 3 days (IQR, 2–5) and 4 days (IQR, 2–6) from symptom onset; 1 patient was seen the same day as the ED visit, 47 were seen within 1 to 3 days, and 104 were seen >3 days after the ED visit.

Before their TIA clinic visit, 119 patients (76%) had an MRI performed; the median delay between symptoms onset and MRI was 3 days (IQR, 2–4). Eleven (9%) patients had an acute DWI lesion. One hundred forty-four (92%) had vascular imaging performed before the clinic visit (91 of these imaging procedures were performed in the ED). Five patients had symptomatic vessel occlusions or a significant stenosis (1 cervical internal carotid and 4 involving intracra-
The symptomatic internal carotid artery stenosis was detected by outpatient imaging, but this patient was not thought to be a candidate for endarterectomy.

Of the 157 patients discharged to TIA clinic, 51 (32%) had a final diagnosis of a cerebrovascular event (46 TIA and 5 minor strokes). An additional 19 patients had a possible TIA (45% had either TIA/stroke or possible TIA). Among the 71 patients with an ABCD² score of ≥4, 38 (54%) had a final diagnosis of TIA/stroke or possible TIA. Two patients were discharged from the ED with an ABCD² score of 6, but neither of these had a final diagnosis of a cerebrovascular event.

Five patients (3%) who were discharged from the ED and instructed to follow-up in the TIA clinic were never seen in the TIA clinic: 1 patient had a stroke and was hospitalized before the expected clinic visit and 4 patients declined the TIA clinic visit but received follow-up with their primary care provider or outside neurologist.

Among the 67 patients who were seen in the ED and then admitted, 61 (91%) were seen in the ED within 24 hours of symptom onset. During hospitalization, 54 of these patients (81%) had an MRI performed; the median delay between symptom onset and MRI was 1 day (IQR, 1–2; P<0.001 compared to patients referred to TIA clinic). Fifteen (27%) patients had an acute DWI lesion. Sixty-five patients had vascular imaging; 14 patients had symptomatic vessel occlusions or high-grade stenosis (7 cervical and 7 intracranial). Four patients underwent an endarterectomy and all were symptomatic cervical or intracranial stenoses detected in the ED. Twelve patients had an ABCD² score >5. A final diagnosis of a cerebrovascular event was reached in 8 (42%) patients with an ABCD² score <4, 28 (78%) patients with an ABCD² score of 4 to 5, and 10 (83%) patients with an ABCD² score of >5 (P=0.017).

### Factors Associated With Hospitalization

Compared to the patients referred to the TIA clinic, hospitalized patients had a strong trend for being older (mean age 71 (SD±15) versus 67 (SD±16); P=0.052), had higher median ABCD² scores (median 4 and IQR 3–5 versus median 3 and IQR 3–4; P<0.001), and had a trend for hospitalization as the predominant determinant of hospitalization. After adjustment for sex, binary logistic regression analysis demonstrated that previous MI (P=0.022; OR, 4.7; CI, 1.2–17) and atrial fibrillation (P=0.029; OR, 2.2; CI, 1.1–4.4) were independently associated with the hospitalization.

### Outcome Events

One hospitalized patient discharged with a diagnosis of migraine was lost to follow-up. Among the patients referred

| Table 1. Baseline Characteristics According to Triage Destination |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
|                                | Total Population (n=224) | Referred to TIA Clinic (n=157) | Hospitalization (n=67) | P (Hospitalization vs TIA Clinic) |
| Mean age (SD), y               | 68 (16)                | 67 (16)            | 71 (15)               | 0.052                           |
| Female, n (%)                  | 102 (46%)             | 70 (45%)          | 32 (48%)             | 0.662                           |
| ABCD² median (IQR)            | 4 (3–5)               | 3 (3–4)           | 4 (3–5)              | <0.001                          |
| Hypertension, n (%)           | 126 (56%)             | 77 (49%)         | 49 (73%)             | 0.001                           |
| Diabetes, n (%)               | 27 (12%)              | 17 (11%)         | 10 (15%)             | 0.388                           |
| Hypercholesterolemia, n (%)   | 112 (50%)             | 80 (51%)         | 32 (48%)             | 0.662                           |
| Current smoker, n (%)         | 10 (5%)               | 9 (6%)           | 1 (2%)               | 0.288                           |
| History of stroke, n (%)      | 36 (16%)              | 24 (15%)        | 12 (18%)             | 0.624                           |
| History of MI, n (%)          | 10 (5%)               | 4 (3%)           | 6 (9%)               | 0.069                           |
| Atrial fibrillation, n (%)    | 43 (19%)              | 25 (16%)        | 18 (27%)             | 0.057                           |
| MRI performed, n (%)          | 173 (77%)             | 119 (76%)       | 54 (81%)             | 0.300                           |
| Positive DWI, n (%)           | 26 (15%)              | 11 (9%)         | 15 (28%)             | 0.002                           |
| Cervical vessel imaging, n (%)| 209 (93%)             | 144 (92%)       | 65 (97%)             | 0.241                           |
| Cervical vessel stenosis, n (%)| 8 (4%)               | 1 (0.7%)       | 7 (11%)              | 0.001                           |

DWI indicates diffusion-weighted imaging; IQR, interquartile range; MI, myocardial infarction; MRI, magnetic resonance imaging; SD, standard deviation; TIA, transient ischemic attack.
to the TIA clinic, one patient experienced a stroke during follow-up. This patient presented with an ABCD² score of 4 and had a negative CTA in the ED. The stroke occurred 2 days after the TIA (before the TIA clinic visit) and was minor in severity (NIHSS score=2). This patient had a good recovery with a modified Rankin scale score of 1 at 90 days. The rate of vascular outcome events for the 157 patients who were referred to the TIA clinic was 0.6% (IQR, 0.1–3.5) at 7 days. No additional outcome events occurred between 7 and 90 days in these patients.

Among the patients who were hospitalized, one patient experienced a stroke and an MI within 7 days. This patient presented with an ABCD² score of 6 and a 90% symptomatic internal carotid artery stenosis. A mild stroke (NIHSS score=1) occurred during the first hours after hospital admission. The patient had an endarterectomy the next day and experienced a postoperative MI. This patient had a complete recovery at 30 days. The median rate of vascular outcome events for the 67 patients who were hospitalized was 1.5% (IQR, 0.3–8.0). No additional outcome events occurred between 7 and 90 days in these patients.

The observed stroke rate at 7 and 90 days for the total population was lower (P<0.001) than the expected rate based on data from the validation of ABCD² publication (Table 2).² The stroke rate was also lower than the expected rates for the subgroup of patients with a final diagnosis stroke/TIA or possible TIA at 90 days (P=0.028; Table 2).

### Discussion

Our results demonstrate that the management of suspected TIA in patients using a specialized outpatient clinic with triage from the ED based on ABCD² and vascular imaging avoided hospitalization for the majority of patients. In addition, the rate of recurrent stroke was in keeping with previous studies evaluating expedited specialized outpatient management (1.24% in the SOS TIA study and 2.1% in the phase 2 of the EXPRESS study).⁸,⁹ Previous studies have attributed the lower than expected event rates to early administration of stroke prevention therapies.¹³

Our ABCD² score/vessel imaging-based triage system was designed to reserve hospital admission for the TIA patients at highest risk. Although the early stroke rate was only slightly higher for our hospitalized patients compared with the TIA clinic group, hospitalized patients were considerably more likely to have an acute DWI lesion, a symptomatic vessel stenosis, and a final diagnosis of a cerebrovascular event. These findings suggest that our protocol led to early outpatient triage of patients who were less likely to have had a true cerebral ischemic event.

Despite the low event rates observed, some limitations to our triage strategy are noteworthy. Four patients who were discharged from the ED declined the TIA clinic appointment, whereas 1 patient experienced a stroke before the clinic visit. In addition, although efforts were made to offer patients TIA clinic appointments and MRI within 1 to 2 business days of their ED evaluation, many patients were not able or willing to return for these early appointments. Therefore, our median delay to MRI/MRA was longer in the TIA clinic group than the hospitalized patients and longer than currently recommended by the American Heart Association guidelines.¹⁴

The physicians who evaluated the patients in the ED did not always follow the protocol closely. They were allowed to deviate from protocol based on their clinical judgment. Nineteen patients with ABCD² scores that qualified for TIA clinic evaluation were admitted to the hospital and 3 were discharged from the ED despite the detection of a symptomatic intracranial stenosis in the ED. Eleven patients with an ABCD² score of 4 to 5 and a final diagnosis of a cerebrovascular event were discharged from the ED without vascular imaging. Only 52% of the patients considered to have experienced a possible TIA at the conclusion of their ED visit had a final diagnosis of a possible or definite cerebrovascular event after completion of their full evaluation. As previously described, this finding outlines the difficulty of making a clinical diagnosis of TIA in the ED.¹⁵

By definition, our population was limited to patients referred to the Stanford ED for presumed TIA. The expected event rates used for comparison were derived from a more heterogeneous population of TIA patients. Our patients may have higher socioeconomic status than the comparison populations and might be more likely to follow secondary stroke prevention recommendations than patients in other regions. These issues may have contributed to the lower than expected rate of stroke observed.

Other limitations include the fact that we did not systematically collect data on how many patients in the hospitalized and TIA clinic groups actually received and complied with stroke prevention therapies. In addition, the number of patients with a definitive diagnosis of TIA or stroke in our study is modest. Therefore, our results require confirmation in a larger dataset, preferably involving multiple centers.

Other options to consider that could improve TIA triage include a short admission to an ED-based observation unit where MRI and MRA would be obtained rapidly. Recent

### Table 2. Observed Versus Expected 7-Day and 90-Day Risks of Stroke

<table>
<thead>
<tr>
<th></th>
<th>% Risk of Stroke at 7 d and 90 d</th>
<th>% Expected Risk at 7 d⁸</th>
<th>P</th>
<th>% Expected Risk at 90 d⁹</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients† (n=223)</td>
<td>0.9 (0.3–3.2)</td>
<td>4.0</td>
<td>0.034</td>
<td>7.1</td>
<td>0.001</td>
</tr>
<tr>
<td>TIA/stroke+possible TIA (n=116)</td>
<td>1.7 (0.5–6.1)</td>
<td>4.6</td>
<td>0.446</td>
<td>7.9</td>
<td>0.028</td>
</tr>
</tbody>
</table>

†One patient was lost to follow-up.

*Estimated from ABCD² score.

### Notes

1. The stroke rate was also lower than the expected rates for the TIA/stroke+possible TIA population was lower (P=0.001) than the expected rate based on data from the validation of ABCD² publication (Table 2).²

2. The rate of vascular outcome events for the 157 patients who were referred to the TIA clinic was 0.6% (IQR, 0.1–3.5) at 7 days. No additional outcome events occurred between 7 and 90 days in these patients.

3. The observed stroke rate at 7 and 90 days for the total population was lower (P<0.001) than the expected rate based on data from the validation of ABCD² publication (Table 2).²

4. The stroke rate was also lower than the expected rates for the subgroup of patients with a final diagnosis stroke/TIA or possible TIA at 90 days (P=0.028; Table 2).

5. Our ABCD² score/vessel imaging-based triage system was designed to reserve hospital admission for the TIA patients at highest risk. Although the early stroke rate was only slightly higher for our hospitalized patients compared with the TIA clinic group, hospitalized patients were considerably more likely to have an acute DWI lesion, a symptomatic vessel stenosis, and a final diagnosis of a cerebrovascular event. These findings suggest that our protocol led to early outpatient triage of patients who were less likely to have had a true cerebral ischemic event.

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10. Other options to consider that could improve TIA triage include a short admission to an ED-based observation unit where MRI and MRA would be obtained rapidly. Recent
studies have shown that addition of DWI and vessel imaging to the ABCD² score improves the ability to discriminate between high and low stroke risk in TIA patients.⁴⁵ There are also data to suggest that the combination of DWI and perfusion-weighted imaging can improve the yield for detecting ischemic lesions among patients experiencing a possible TIA.⁴⁶ Having both MRI and vascular imaging findings available before making the decision to hospitalize TIA patients has the potential to result in more accurate triage of patients at high risk for hospitalization, whereas patients at low risk can be more confidently discharged to complete their evaluation in an outpatient setting.

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Disclosures
None.

References
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