Guidelines For The Evaluation And Management Of Acute Cerebrovascular Syndrome Part I: Diagnosis And Evaluation Of Transient Ischemic Attack

This is the first of a 2-part series for EM Practice Guidelines Update looking at guidelines on the evaluation and management of acute cerebrovascular syndrome. Transient ischemic attack (TIA) has traditionally been defined as the sudden onset of focal neurological dysfunction of presumed vascular origin that resolves within 24 hours. The American Heart Association/American Stroke Association (AHA/ASA) revised its definition, however, to reflect a “tissue-based” diagnosis. This guideline reviews the definition and evaluation of TIAs.

Practice Guideline Impact

- The AHA/ASA has redefined TIA as the absence of infarction on neuroimaging rather than resolution of symptoms by an arbitrary time point (eg, within 24 hours).
- Neuroimaging should be performed urgently in patients with suspected TIA. Diffusion-weighted magnetic resonance imaging (MRI) is the imaging test of choice, but if MRI is not available, computed tomography (CT) should be performed.
- Noninvasive imaging of the cervicocephalic vessels should be performed as part of the standard evaluation of patients with suspected TIA.
- An electrocardiogram (ECG) should be performed as soon as possible to identify atrial fibrillation, evidence of a ventricular aneurysm, or myocardial ischemia.
- The ABCD² rule has been proposed to risk stratify patients for short-term risk of stroke; however, since the publication of this statement, studies have not supported the utility of this scoring system.
Introduction To The Guideline: Transient Ischemic Attack

This issue of *EM Practice Guidelines Update* reviews 1 guideline on transient ischemic attack:


This scientific statement, published by the American Heart Association/American Stroke Association Stroke Council, published in 2009, presents a still-useful discussion of the definition, diagnosis, and evaluation of TIAs. The document was not called a formal “guideline” because of the paucity of clinical trials in this area. Next month’s *EM Practice Guidelines Update* issue (August 2013) will discuss 2 recently published guidelines from the AHA/ASA and the American College of Emergency Physicians that cover the management of acute ischemic stroke.

The clinical relevance of identifying a TIA is that many of these patients are at high short-term risk of stroke. The AHA/ASA supported using the ABCD² prediction rule to stratify short-term risk of stroke, but recommendations about who may be safe for outpatient workup were based on a very low level of evidence, and more-recent studies have cast further doubt on the accuracy of this tool. The purpose of the rapid evaluation is to identify cardiac or vascular pathology that can be treated to prevent stroke.

This issue presents an opening comment from Guest Editor, Jonathan A. Edlow, MD as well as relevant excerpts of the guideline with editorial comments.

Comment From Guest Editor, Jonathan A. Edlow, MD

The approach to the TIA patient continues to evolve, and over the last decade, the evolution has been at a fast pace. Even the definition has changed. The traditional definition of TIA, adopted in the mid-1970s, was abrupt onset of a focal neurological deficit thought to be cerebrovascular and lasting less than 24 hours. Even then, however, physicians knew that most TIA patients’ symptoms lasted less than 1 hour. In that era—one without MRI, without tPA treatment for acute ischemic stroke, without the knowledge of the high short-term risk of stroke after TIA, and without the convincing data that emergent treatment of TIA greatly reduces the risk of an acute stroke outcome—the traditional definition worked. Nevertheless, all 4 of these advances have rendered the traditional definition irrelevant (at best) and dangerous (at worst). Stepping back from these concerns, which are nicely summarized in this issue, there are 2 overarching concepts that are critically important for emergency physicians managing TIA.

The first critically important concept is that TIA is a neurological emergency. The asymptomatic patient in front of you may not look like an emergency, but 1 in 20 of those patients will have a stroke within 48 hours. Many of these strokes are major events with significant morbidity and mortality.

The second critically important concept is that secondary stroke prevention is a laudable goal. Although emergency physicians are not typically in the business of prevention, preventing a stroke is an incredibly valuable action. The emotional and financial impact to patients, to their families, and to society is huge. With these 2 concepts in mind, the following are a few thoughts about the current state of the art in terms of the emergency response to TIA.

[continued]
Importance Of History And Physical Examination: This scientific statement focuses heavily on high-tech diagnostic testing; however, to paraphrase Mark Twain, reports of the death of the history and physical examination are greatly exaggerated. Patients with TIA are usually neurologically normal on arrival to the emergency department (ED). Physicians should take a careful history to establish what symptoms occurred, their onset, and their offset. Over the last 2 years, it has become increasingly clear that many nonspecific symptoms of posterior circulation ischemia, such as dizziness (which, according to the traditional definition of TIA, did not count as TIA), in fact, do represent brain ischemia. With regard to symptom offset (resolution), performing a careful neurological examination is important. One needs to know that the examination is normal to establish that the patient is having a TIA and not a minor stroke.

Although MRI with diffusion-weighted imaging will establish which patients have had a stroke by imaging criteria, documenting a normal examination and a National Institutes of Health (NIH) Stroke Scale score of zero provides the context in which to interpret the imaging findings. Before imaging the carotid arteries and the brain with CT scans and MRIs, do a careful history and physical examination. (The NIH Stroke Scale worksheet is available at: http://www.ninds.nih.gov/doctors/NIH_Stroke_Scale.pdf.)

Risk Stratification: The application of risk stratification has gone haywire. At the time of the publication of the AHA/ASA scientific statement in 2009, the National Stroke Association ABCD² Score was the most cutting-edge risk stratification tool in use. (The ABCD² Score worksheet is available at: http://www.stroke.org/site/DocServer/NSA_ABCD2_tool.pdf). Since then, ABCD² has become ABCD²I (I = imaging), which has evolved into ABCD²I plus cerebrovascular imaging. Any purely clinical risk stratification score misses a significant proportion of patients with treatable lesions because they are “mechanism blind.” Risk stratification scores that include advanced brain and cerebrovascular imaging render the concept of risk stratification meaningless; the "stratification" is actually simply performing the entire workup. Given clear evidence that 5% of TIA patients have a stroke within 48 hours, performing this diagnostic testing to identify treatable lesions makes perfect sense, but it is not risk stratification.

Because the ABCD² rule (which is still the dominant rule in use) does not identify patients with intervenable pathology (mostly carotid stenosis or cardiac embolism) with acceptable sensitivity and specificity, and because all patients with TIA need a workup at some point, it makes sense to simply do the workup as soon as feasible, when the risk of stroke is the highest and the opportunity to prevent a stroke is the highest.

Systems Of Care: Large studies have clearly documented an approximately 80% reduction in the acute outcome of stroke and TIA patients who were worked up and treated emergently. This has traditionally been done in the hospital setting; however, it can be done more efficiently and more cheaply in an ED observation unit. This scientific statement only discusses the role of hospitalization, and it does not address this alternative approach. Emergency physicians are in a unique position in the chain of care of patients with acute cerebrovascular conditions to make a real impact. It is, therefore, important that physicians acquire the knowledge about TIA and its evaluation and that they work with colleagues from other specialties to set up systems of care so that we can deliver the highest-quality care. Treating a TIA patient provides us with the chance to prevent a stroke – and, although it’s not as exciting as intubating a trauma patient, the impact is enormous.

Prevent a stroke today. ■

–Jonathan A. Edlow, MD
Assessment Of The Guideline Methodology

Although not formally called a “guideline,” the scientific statement development councils used the same approach that they use for guidelines, including providing classes of recommendations and grading levels of evidence. (See Table 1.) Overall, this document has clearly defined methods, recommendations, and discussion. The weakness of the methodology, in our opinion, is the lack of explicit discussion of how a low level of evidence can yield a Class I recommendation. They note, “A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Even though randomized trials are not available, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.” While the latter statement is often true, the guideline writers do not always provide a clear explanation of how they arrived at their consensus recommendation, a process that likely includes value judgments about traditional standards of care, costs, and resource use, among other factors.

### Table 1. Definition Of Classes And Levels Of Evidence Used In American Heart Association Recommendations

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<th>Level of Evidence</th>
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<tr>
<td>A</td>
<td>Data derived from multiple sources</td>
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<tr>
<td>B</td>
<td>Data derived from a single randomized trial or nonrandomized studies</td>
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<tr>
<td>C</td>
<td>Consensus opinion of experts</td>
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<tr>
<th>Classes of Recommendation</th>
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<tr>
<td>Class I</td>
<td>Conditions for which there is conflicting evidence for and/or general agreement that the procedure or treatment is useful and effective</td>
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<tr>
<td>Class II</td>
<td>Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment</td>
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<tr>
<td>Class IIa</td>
<td>The weight of evidence or opinion is in favor of the procedure or treatment</td>
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<tr>
<td>Class IIb</td>
<td>Usefulness/efficacy is less well established by evidence or opinion</td>
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<tr>
<td>Class III</td>
<td>Conditions for which there is evidence and/or general agreement that the procedure or treatment is not useful/effective and in some cases may be harmful</td>
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The recommendations excerpted here are presented as they originally appeared in the scientific statement, including the strength of recommendation and the level of evidence. (See Table 1.)

**Scientific Statement Recommendations: Defining Transient Ischemic Attacks**

- A 24-hour duration of symptoms does not accurately demarcate patients with and without tissue infarction (Class III, Level of Evidence A).
- Defining TIA with a 24-hour maximum duration has the potential to delay the initiation of effective stroke therapies (Class I, Level of Evidence C).
- The frequency distribution of durations of transiently symptomatic cerebral ischemic events shows no special relationship to the 24-hour time point (Class III, Level of Evidence A).
- A tissue-based definition of TIA will harmonize cerebrovascular nosology with other ischemic conditions and appropriately direct diagnostic attention to identifying the cause of ischemia and whether brain injury occurred (Class IIa, Level of Evidence C).
- Imaging studies currently play a central role in both determining the origin of and classifying acute cerebrovascular syndromes (Class I, Level of Evidence A).
- The new definition will modestly alter stroke and TIA prevalence and incidence rates, but these changes are to be encouraged, not discouraged, because they reflect increasing accuracy of diagnosis (Class IIa, Level of Evidence C). To facilitate comparison with prior studies, symptom duration is an important data element to collect in epidemiological studies (Class IIa, Level of Evidence C).
- It would be reasonable to adopt a term such as "acute neurovascular syndrome"... that can be used until the diagnostic evaluation is completed or if a diagnostic evaluation is not performed (Class IIa, Level of Evidence C).

- It is reasonable to use terms like "cerebral infarction with transient signs" without a fixed time criterion (Class IIa, Level of Evidence A). We do not support linking any of these terms to a 24-hour time criterion because all cerebral infarction definitions with specific time limitations are capricious (Class III, Level of Evidence A). We prefer to emphasize that all episodes of acute brain ischemia should be urgently assessed, including events not associated with underlying tissue infarction, events associated with minor degrees of infarction, and events associated with major infarction.
- It is impossible to define a specific time cutoff that can distinguish whether a symptomatic ischemic event will result in brain injury with high sensitivity and specificity (Class III, Level of Evidence A).

**Editorial Comment, Sigrid Hahn, MD**

As laid out in these recommendations, the AHA/ASA guideline critiques the traditional definition of a TIA ("sudden focal neurological deficit of presumed vascular origin lasting for < 24 hours") in light of studies using high-resolution neuroimaging that show infarctions in approximately a third of patients despite resolution of symptoms within this timeframe.¹ They further argue against the use of any arbitrary time cutoff in the definition. The AHA/ASA has formally endorsed the following definition: “A transient episode of neurologic dysfunction caused by focal brain, spinal cord, or retina ischemia, without acute infarction.” Given that this new definition of TIA relies upon imaging for confirmation, the scientific statement development councils suggest using an ambiguous term such as “acute neurovascular syndrome” while the workup is ongoing. They draw parallels to the term “acute coronary syndromes,” where patients may not be diagnosed with a myocardial infarction until biomarkers are completed.
Scientific Statement Recommendations: Use Of Risk Stratification To Guide The Evaluation Of Transient Ischemic Attacks

It is reasonable to hospitalize patients with TIA if they present within 72 hours of the event and any of the following criteria are present:

a. ABCD² score of ≥ 3 (Class IIa, Level of Evidence C).

b. ABCD² score of 0 to 2 and uncertainty that diagnostic workup can be completed within 2 days as an outpatient (Class IIa, Level of Evidence C).

c. ABCD² score of 0 to 2 and other evidence that indicates the patient's event was caused by focal ischemia (Class IIa, Level of Evidence C).

Editorial Comment, Sigrid Hahn, MD

The importance of diagnosing TIAs is to identify and address treatable risk factors in order to mitigate the high short-term risk of stroke, which is approximately 10% within 90 days.¹ Risk is particularly high in the first few days after TIA. Not every patient has the same risk of stroke, however, and prediction rules have been developed to attempt to stratify patients. Risk stratification could allow for better resource utilization, potentially allowing emergency clinicians to safely discharge patients for timely outpatient workup as part of a “low-risk algorithm.” Very-high-risk patients, on the other hand, might be admitted to a higher level of inpatient care.

The ABCD² rule is still the most commonly studied and discussed rule. ABCD² assigns points for each of the following factors: age ≥ 60 years (1 point); blood pressure ≥ 140/90 mm Hg on first evaluation (1 point); clinical symptoms of focal weakness with the spell (2 points) or speech impairment without weakness (1 point); duration ≥ 60 minutes (2 points) or 10 to 59 minutes (1 point); and diabetes (1 point). Since the writing of this scientific statement, there have been multiple further studies and meta-analyses of ABCD² that have been published.²⁻⁴ Unfortunately, there is still no consensus about the predictive utility of this tool, regardless of where the line is drawn between low risk and high risk. One meta-analysis with over 16,000 patients found suboptimal performance for the predictive value of stroke at 2 days for “low-risk” patients (score 0-3). The positive likelihood ratio was 1.4 (95% confidence interval [CI], 1.3-1.5) and the negative likelihood ratio was 0.4 (95% CI, 0.3-0.6).³

As an emergency physician deciding whether to discharge or admit a patient with suspected TIA, be aware that discharging is supported by a weak recommendation in this scientific statement, based on a low level of evidence. The ABCD² score should not drive this decision. There are promising, potentially cost-effective alternatives to hospitalization. For example, ED-based observation units are becoming more common. Multiple prospective trials of ED-based observation unit-based TIA care have determined this strategy to be feasible, time- and cost-saving, and not associated with higher rates of short-term stroke compared to hospital admission.⁵⁻⁶ The key, regardless of where the patient goes, is ensuring that the workup occurs as quickly as feasible.
Scientific Statement Recommendations: Evaluation Of Patients With Transient Ischemic Attack

- Patients with TIA should preferably undergo neuroimaging evaluation within 24 hours of symptom onset. MRI, including diffusion-weighted imaging, is the preferred brain diagnostic imaging modality. If MRI is not available, head CT should be performed (Class I, Level of Evidence B).
- Noninvasive imaging of the cervicocephalic vessels should be performed routinely as part of the evaluation of patients with suspected TIA (Class I, Level of Evidence A).
- Noninvasive testing of the intracranial vasculature reliably excludes the presence of intracranial stenosis (Class I, Level of Evidence A) and is reasonable to obtain when knowledge of intracranial steno-occlusive disease will alter management. Reliable diagnosis of the presence and degree of intracranial stenosis requires the performance of catheter angiography to confirm abnormalities detected with noninvasive testing.
- Patients with suspected TIA should be evaluated as soon as possible after an event (Class I, Level of Evidence B).
- Initial assessment of the extracranial vasculature may involve any of the following: carotid ultrasound, transcranial Doppler, magnetic resonance angiography, or CT angiography, depending on local availability and expertise and characteristics of the patient (Class IIa, Level of Evidence B).
- ECG should occur as soon as possible after TIA (Class I, Level of Evidence B). Prolonged cardiac monitoring (inpatient telemetry or Holter monitor) is useful in patients with an unclear origin after initial brain imaging and ECG (Class IIa, Level of Evidence B).
- Echocardiography (at least transesophageal echocardiogram [TEE]) is reasonable in the evaluation of patients with suspected TIA, especially in patients in whom no cause has been identified by other elements of the workup (Class IIa, Level of Evidence B). TEE is useful in identifying patent foramen ovale, aortic arch atherosclerosis, and valvular disease and is reasonable when identification of these conditions will alter management (Class IIa, Level of Evidence B).
- Routine blood tests (complete blood count, chemistry panel, prothrombin time and partial thromboplastin time, and fasting lipid panel) are reasonable in the evaluation of patients with suspected TIA (Class IIa, Level of Evidence B).

Editorial Comment, Sigrid Hahn, MD

In their document, the AHA/ASA outline the goals of the evaluation of the patient who had a TIA: (1) to obtain evidence of a vascular origin for the symptoms either directly (evidence of hypoperfusion and/or acute infarction) or indirectly (identification of a presumptive source such as a large-vessel stenosis); (2) to exclude an alternative nonischemic origin; (3) to ascertain the underlying vascular mechanism of the event (eg, large-vessel atherothrombotic, cardioembolic, small-vessel lacunar), which, in turn, allows selection of the optimal therapy; and (4) to identify prognostic outcome categories. Currently, only 50% to 70% of patients who present to the ED with symptoms of a TIA have a CT performed, and far fewer have MRIs. The major message of these recommendations is that patients should have imaging and that MRI (with diffusion-weighted imaging) is preferred to CT (if available, and if not, a CT should be done).

The AHA/ASA document gives the highest recommendation, based on the highest level of evidence, for routine noninvasive testing of the cervicocephalic vessels. The emergency physician will likely choose the testing modality in conjunction with a consultant and in line with usual practice at the institution, depending on resources and expertise. Cardiac evaluation is important in patients with TIA because approximately 20% of strokes have a cardioembolic etiology. An ECG can identify atrial fibrillation, left ventricular aneurysm, or recent myocardial infarction. Approximately 2% of patients with TIA will have new-onset atrial fibrillation. Prolonged telemetry monitoring is useful in patients with an unclear TIA cause after neuroimaging and ECG, as it can identify paroxysmal atrial fibrillation in approximately 14% of patients. Echocardiography should be considered when no other cause has been found, although it is given the relatively weak recommendation of IIb. Echocardiography is useful in detecting large valvular lesions, intracardiac thrombus, and foci for thrombi (with TEE even more than with transthoracic echocardiogram [TTE]). However, only 3% of TTEs in patients with stroke or TIA reveal a cardioembolic source in patients lacking other signs of heart disease.
References


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1. A "transient ischemic attack" is defined as:
   a. A sudden onset focal neurological deficit that resolves within 1 hour
   b. A sudden onset focal neurological deficit that resolves within 24 hours
   c. A transient episode of neurologic dysfunction without acute infarction
   d. A transient episode of neurologic dysfunction without residual deficit

2. Use of the ABCD² score to risk stratify the TIA patient:
   a. Is endorsed as a reliable tool by the AHA/ASA to differentiate between low risk and high risk
   b. Has been demonstrated, in multiple studies, to accurately assign risk
   c. Should be used to identify patients at low enough risk to allow ED discharge

3. The evaluation of TIA should include which of the following:
   a. MRI within 1 week of symptoms
   b. Either MRI or CT within 24 hours of symptoms
   c. Brain imaging is not required if the patient has no deficits
   d. Noninvasive imaging of the cervicocephalic vessels is indicated only when symptoms are suggestive of a posterior circulation issue
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**Goals:** Upon completion of this article, you should be able to: (1) demonstrate medical decision-making based on the strongest clinical evidence, (2) cost-effectively diagnose and treat the most critical ED presentations, and (3) describe the most common medicolegal pitfalls for each topic covered.

**Objectives:** Upon completion of this article, you should be able to: (1) describe how TIA has been redefined and the implications this new definition has on evaluation and diagnosis; (2) describe the key diagnostic tests that should be performed on every patient with suspected TIA; and (3) discuss the controversies of using the ABCD² risk stratification tool in TIA patients.

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