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**TAKE-HOME  
POINTS FROM  
LECTURES BY  
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AND VISITING  
FACULTY**

## Short-term prognosis after a TIA: A simple score predicts risk

### ■ ABSTRACT

Transient ischemic attacks (TIAs) are ominous and call for acute interventions, including hospitalization. TIAs are defined by complete resolution of an acute neurologic deficit, but any amount of recovery is probably the most important defining feature and, paradoxically, is strongly predictive of a subsequent event. Most patients should be hospitalized after a TIA, to provide an opportunity to monitor, thoroughly evaluate, and treat conditions promptly if indicated.

### ■ KEY POINTS

The risk of stroke after a TIA is very high overall and can be quickly stratified with a simple score based on age, blood pressure, history of diabetes, and the duration and features of the TIA.

TIA patients should be evaluated with a history and physical examination, laboratory tests, electrocardiography, and head and neck imaging.

Hospitalization allows neurologic monitoring after a TIA so that tissue plasminogen activator (tPA) can be given promptly if a subsequent event occurs. Hospitalization also increases the likelihood that atrial fibrillation, carotid artery stenosis, and other conditions will be quickly evaluated and treated.

Carotid endarterectomy, if indicated, should be performed as soon as possible after a TIA.

**T**RANSIENT ISCHEMIC ATTACKS (TIAs) are common<sup>1</sup> and are often a harbinger of disabling strokes. But defining who is at risk for a subsequent event and what actions should be taken immediately remain important clinical issues. This article discusses the defining features of a TIA, a simple scoring system for determining the acute risk of stroke, and other aspects of the immediate evaluation and management of TIA.

### ■ TIAs ARE COMMON

Approximately 250,000 to 350,000 TIAs occur each year in the United States.<sup>2-4</sup> The median survival is more than 8 years,<sup>5</sup> and TIA survivors number approximately 2.4 million. A recent survey found that 1 in 15 people older than 65 years—equivalent to 2.3 million people in the United States—reported a history of TIA.<sup>6</sup> About 15% of patients who present with a stroke report having had a previous TIA.<sup>7</sup>

### ■ WHAT IS A TIA?

#### Traditional definition is symptom-based and problematic

A TIA is traditionally defined as a spell of neurologic impairment lasting less than 24 hours that is caused by focal ischemia in the brain or retina.

Although we have grown comfortable with this definition, it is problematic. Little agreement exists about which events are TIAs, even if they are independently evaluated by two neurologists.<sup>8,9</sup> In addition, 24 hours is a rather arbitrary time period and does not help to determine which events involve infarction; new infarction can occur within minutes and

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TABLE 1

### Predicting the risk of stroke after a transient ischemic attack: The California, ABCD, and ABCD<sup>2</sup> scores

CHARACTERISTIC	POINTS		
	CALIFORNIA	ABCD	ABCD <sup>2</sup>
Age ≥ 60 years	1	1	1
Blood pressure ≥ 140/90 mm Hg	—	1	1
Clinical features of transient ischemic attack			
Weakness <sup>a</sup>	1	2	2
Speech impairment <sup>b</sup>	1	1	1
Duration			
≥ 60 minutes	1	2	2
10–59 minutes	1	1	1
Diabetes	1	—	1
<b>Total score</b>	<b>0–5</b>	<b>0–6</b>	<b>0–7</b>

<sup>a</sup>Defined as any weakness (California score); unilateral weakness (ABCD and ABCD<sup>2</sup> scores)

<sup>b</sup>Regardless of weakness by the California score; in the absence of unilateral weakness by ABCD and ABCD<sup>2</sup> scores; the maximum possible score for clinical features of transient ischemic attack is thus 2 in all three scoring systems

ABCD = Age, Blood Pressure, Clinical Features, and Duration

ABCD<sup>2</sup> = Age, Blood Pressure, Clinical Features, Duration, and Diabetes

### TIAs carry a substantial short-term risk of stroke, cardiac events, and death

can often be documented after TIA.<sup>10</sup> And why should the diagnosis require that symptoms resolve completely, particularly when we know that in such circumstances, infarction is often present?

#### New definition is tissue-based

A newer definition reclassifies TIA as an event with transient symptoms (typically lasting less than 1 hour) without evidence of acute brain infarction on imaging studies.<sup>10</sup> By the old definition, a patient with transient symptoms but an infarction evident by magnetic resonance imaging (MRI) had a TIA; by the new definition, this would be a stroke.

The new definition has some advantages for billing in that strokes are generally reimbursed more favorably than TIA. It is also conceptually simpler: infarction defines a stroke, and the reliance on time is reduced. But the definition also creates new problems. The likelihood of seeing evidence of infarction depends on the type of imaging study done: hospitals that routinely perform MRI diagnose fewer TIAs and more strokes.

About 30% to 50% of patients with clinically defined TIA have evidence of ischemic abnormalities on diffusion MRI, most of which become permanent infarcts.<sup>11</sup>

The new definition is not universally accepted: the traditional one is more familiar and is easier to use. No solution is perfect, but a broader acceptance of the spectrum of acute ischemic cerebrovascular syndromes might be a good first step: TIA and stroke are more similar than different.

#### DO PATIENTS WHO HAD A TIA REQUIRE ACUTE CARE?

TIA and stroke share common causes, risk factors, pathophysiology, and treatment.<sup>12</sup> But regardless of which definition is used, TIA does not involve a neurologic deficit at the time of diagnosis. This leaves important clinical questions that are generally irrelevant to stroke management: Is prompt intervention or hospitalization required? Should a patient who had a TIA the previous day be told to make an appointment or go immediately to the emergency department?

## Risk is high after a TIA

TIA carries a substantial short-term risk of stroke, hospitalization for cardiovascular events, and death. Most studies have found that the risk of stroke is more than 10% in the 90 days after a TIA,<sup>2,13–24</sup> with half of those strokes occurring within the first 2 days.<sup>2,13,18,21,23–25</sup> Studies in northern California and the United Kingdom found that the risk of stroke in the first 24 hours after a TIA is about 4%, which is about twice the risk of myocardial infarction or death in patients presenting with acute coronary syndromes.<sup>13,26,27</sup>

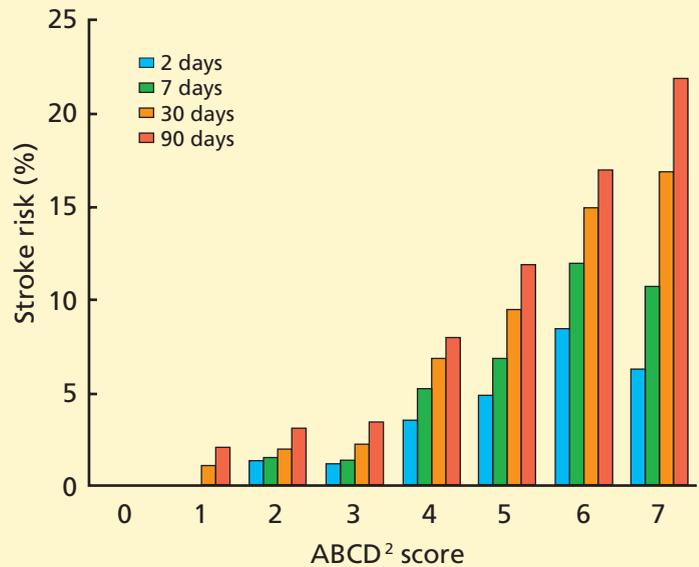
Paradoxically, the risk of a subsequent ischemic stroke may be less after a completed stroke than after a TIA, with reported 3-month risk generally ranging from 4% to 8%.<sup>19,20,22,28–41</sup> Thus, patients with TIA are actually more unstable in terms of new stroke than those presenting with an initial stroke.

The risk of cardiac events is also elevated after a TIA. Elkins et al<sup>42</sup> found that 2.6% of patients who were diagnosed with a TIA at an emergency department were hospitalized for a major cardiovascular event (myocardial infarction, unstable angina, or ventricular arrhythmia) within 90 days. Heyman et al<sup>43</sup> found that within 5 years after a TIA, the number of patients who had a myocardial infarction or sudden cardiac death nearly equaled the number who had a cerebral infarction.

## ■ ESTIMATING RISK OF STROKE AFTER TIA

Several studies have identified risk factors for stroke after TIA, and these risk factors may help guide initial management. Three similar formal prediction rules have been developed and cross-validated in California and the United Kingdom (TABLE 1). The scores are based on five factors. The California score predicts the risk of stroke within 90 days; the Age, Blood Pressure, Clinical Features, and Duration (ABCD) score predicts the risk at 7 days and at 90 days. The newer Age, Blood Pressure, Clinical Features, Duration, and Diabetes (ABCD<sup>2</sup>) score, which was meant to replace the other two scores, incorporates elements from those scores and predicts the risk at 90, 30, 7, and 2 days (FIGURE 1).

## The ABCD<sup>2</sup> score predicts risk of stroke after a transient ischemic attack



**FIGURE 1.** Stroke risk after TIA by Age, Blood Pressure, Clinical Features, Duration, and Diabetes (ABCD<sup>2</sup>) score at 2 days, 7 days, 30 days, and 90 days after TIA in 4,809 patients treated in California and the United Kingdom.

JOHNSTON SC, ROTHWELL PM, NGUYEN-HUYNH MN, ET AL. VALIDATION AND REFINEMENT OF SCORES TO PREDICT VERY EARLY STROKE RISK AFTER TRANSIENT ISCHAEMIC ATTACK. LANCET 2007; 369:283–292. COPYRIGHT 1977, WITH PERMISSION FROM ELSEVIER

In a study of nearly 3,000 patients presenting with a TIA to clinics and emergency departments in the United Kingdom and the United States, using the ABCD<sup>2</sup> score, 21% of patients were classified as being at very high risk (score 6 or 7; 2-day risk of stroke 8.1%), 45% at moderate risk (score 4 or 5; risk 4.1%), and 34% at low risk (score 0–3; risk 1%).<sup>44</sup>

The scores do not account for imaging findings, which also have prognostic value. A new infarct seen on brain imaging (which is consistent with the traditional definition of TIA but would now lead to a diagnosis of stroke) is associated with a twofold to 15-fold increase in subsequent short-term risk of stroke.<sup>18,22,45–48</sup> Evidence of vessel occlusion on acute brain magnetic resonance angiography is also associated with a fourfold increased short-term risk of stroke.<sup>48</sup> MRI changes are associated with the clinical factors identified in prior prediction rules,<sup>49</sup> so it is unclear how much predictive power they would add to the scores.

### Degree of acute recovery predicts stroke risk

Patients who have only partially recovered from an acute neurologic deficit after 24 hours are considered by both the traditional and new definitions to have had a stroke rather than a TIA, but partial recovery may actually indicate that they are at high risk of a subsequent event. Studies show that the greater the degree of acute recovery after a neurologic ischemic event, the greater the chance of neurologic deterioration over the subsequent 3 months.<sup>50-54</sup>

It is not clear why a patient who promptly and largely recovers from a major ischemic event is at such high risk of early and permanently disabling recurrence. The pathophysiology of TIA may be similar to that of acute coronary syndromes (eg, unstable angina and non-Q-wave myocardial infarction), in which thrombosis and thrombolysis are acutely active and protracted. Similarly, cerebral ischemia that rapidly resolves may be a marker for ongoing thrombosis and thrombolysis.

In contrast, major ischemia that persists may be a result of largely completed thrombosis that is not amenable to acute antithrombotic therapy. Aggressive, early antithrombotic therapy with combinations of new, potent agents is highly effective in acute coronary syndromes,<sup>55-58</sup> and such an approach should be tested in patients after a TIA.

### 'Benign recurrent' TIA may be migraine

Many patients who present in the emergency department or clinic have only sensory symptoms lasting less than 10 minutes. These patients are far less likely than other TIA patients to develop a stroke and are more likely to have recurrent episodes that completely resolve.<sup>59</sup> I believe these are not TIAs but are related to migraines. Treatment with calcium channel blockers can be effective.

### EVALUATING TIA PATIENTS

A history and physical examination are essential to diagnosing a TIA.

Recommended laboratory tests—some of which can help identify conditions that mimic a TIA—include a complete blood cell count; blood levels of electrolytes, blood urea nitro-

gen, glucose, and calcium; the erythrocyte sedimentation rate; and a rapid plasma reagin test.

The appropriate cardiac evaluation is still being determined, but evidence supports performing electrocardiography (ECG) on all patients presenting with a TIA. ECG frequently reveals unexpected atrial fibrillation or a myocardial infarction or suggests a left ventricular aneurysm, all of which are important causes of cardiogenic emboli and have a high risk of recurrence. In addition, ECG abnormalities are independently associated with the risk of cardiac events in the 3 months after a TIA.<sup>42</sup> Most patients also would benefit from 2-day cardiac monitoring, which can identify patients with paroxysmal atrial fibrillation. Echocardiography is warranted in some patients, although transesophageal echocardiography is not used as often as it once was in patients with a TIA because of new evidence that correcting a patent foramen ovale does not help prevent strokes.

Head imaging should be done on all TIA patients, usually with computed tomography (CT). Hemorrhage, tumor, and multiple sclerosis, all of which could mimic a TIA, may be seen.

Neck imaging to look for carotid artery stenosis can be done by CT angiography, ultrasonography, or magnetic resonance angiography. We use CT angiography with perfusion, which is the fastest way to get all the information needed, entails a low risk from exposure to contrast agents, and often helps to determine treatment.

### HOSPITALIZATION IS USUALLY INDICATED

The short-term prognosis after a TIA justifies a sense of urgency if interventions exist that can alter the outcome. Hospitalization may reduce the risk of stroke or other adverse events by hastening the workup and targeted therapy. Proven therapies are available for several important causes of TIA, and identifying and treating them should be a high priority.

The National Stroke Association guidelines for managing TIAs recommend hospitalizing patients at high risk of stroke or if a special treatment is needed (eg, for carotid stenosis or atrial fibrillation).<sup>60</sup> The guidelines came out before the ABCD<sup>2</sup> score was devel-

**Head imaging should be done on all TIA patients**

oped, so no specific thresholds of risk were advised. In the United States, a patient with an ABCD<sup>2</sup> score of 6 or 7 should definitely be hospitalized, and those with a score of 4 or 5 should probably be hospitalized, although thresholds differ in other countries and even differ between similar hospitals within the United States.

### **Prompt tPA therapy if stroke occurs**

If a patient is hospitalized after a TIA, he or she can be observed carefully to increase the likelihood of receiving tissue plasminogen activator (tPA, alteplase, Activase) promptly should ischemic symptoms recur, and this is probably enough to justify the costs of hospitalization. tPA can have a profound impact on a patient's outcome, and because the long-term costs associated with having a stroke are so high, averting even a small proportion of strokes makes hospitalization cost-effective.

Nguyen-Huynh et al<sup>61</sup> analyzed the cost-utility of 24-hour hospitalization at the University of California, San Francisco, for patients diagnosed with a recent TIA who were candidates for tPA if a stroke occurred. The overall cost-effectiveness ratio was \$55,044 per quality-adjusted life-year (a value considered to be borderline cost-effective), and less for patients at higher risk of stroke.

This kind of analysis is highly affected by several variables: the degree of risk of stroke (as calculated by the ABCD<sup>2</sup> score), the costs of hospitalization, and the ability to identify whether a patient is having a stroke during hospitalization. Monitoring neurologic status requires frequent examination; in most hospitals, such monitoring is not currently up to the standard of cardiac monitoring.

### **Detecting atrial fibrillation and starting treatment for it**

Although data are sparse about the stroke risk early after a TIA, specifically in patients with atrial fibrillation, case series suggest that the risk is higher than in the general population: probably 10% to 15% in the first month after a TIA. In our study,<sup>6</sup> the 90-day risk was 13%, but many patients were already receiving anticoagulation, making this a conservative estimate.

EKG is necessary to confirm the diagnosis

of atrial fibrillation, and cardiac monitoring may identify additional cases. CT of the head is necessary to rule out a hemorrhage, and echocardiography may demonstrate a clot but may not alter one's choice of therapy.

Multiple randomized trials have found that anticoagulation reduces the risk of stroke. The Heparin in Acute Embolic Stroke Trial<sup>62</sup> did not find low-molecular-weight heparin to be beneficial in patients with atrial fibrillation and acute stroke, but the trial was small. The risk of bleeding at the site of an ischemic stroke is likely to be much smaller after a TIA than after a stroke, and it is logical to anticipate that starting effective therapy earlier would reduce the risk of cardioembolic events sooner. Guidelines from the National Stroke Association and American Stroke Association recommend starting oral anticoagulation.

### **Prompt endarterectomy for carotid artery stenosis**

Carotid artery atherosclerosis accounts for about 11% of TIAs. The risk of stroke in patients with carotid artery stenosis was as high as 20% at 90 days in one study.<sup>18</sup> Traditional teaching was that patients should wait 4 to 6 weeks after any neurologic event before undergoing endarterectomy or stenting, but new data strongly contradict this.

The North American Symptomatic Carotid Endarterectomy Trial<sup>63</sup> found that in patients with medically treated high-grade internal carotid artery stenosis, 43.5% of those presenting with hemispheric TIA had a stroke within 2 years. Half the strokes occurred within the first month, suggesting that the danger is greatest acutely after a TIA. Patients were enrolled in the study up to 4 months after the initial TIA, so the immediate post-TIA period, during which the risk of stroke may have been even higher, was not studied.

Carotid endarterectomy, if indicated, should be performed as soon as possible after a TIA, and hospitalizing a patient after an event may help ensure that it is done promptly. Randomized trials have shown that carotid endarterectomy is beneficial for patients with TIAs in the distribution of a carotid stenosis of more than 60% to 70%.<sup>64</sup> Rothwell et al<sup>65</sup> analyzed pooled data from the European Carotid Surgery Trial and North American

**Hospitalization may reduce the risk of stroke by hastening workup, triage, and targeted therapy**

Symptomatic Carotid Endarterectomy Trial and found that the benefit from surgery was greatest if it was performed within 2 weeks after the last ischemic event and fell rapidly with increasing delay: the absolute risk reduction at 5 years for stroke or operative death was 20% for patients with at least 50% stenosis if endarterectomy was done less than 2 weeks after the ischemic event, and was only 0.8% if done later.

Carotid ultrasonography, CT angiography, or magnetic resonance angiography should be performed in all patients with TIAs in the anterior circulation. Many experts think this should be performed within 24 hours of presentation because the early risk of stroke is so high.

National Stroke Association guidelines<sup>66</sup> recommend that endarterectomy be performed as soon as possible—preferably within 2 weeks—for those with 70% to 90% stenosis that is symptomatic, as well as for those with 50% to 69% stenosis who can be treated with a less than 6% risk of perioperative stroke or death.

### Evaluating other problems

Other causes of TIA include small-vessel (lacunar) ischemia, intracranial atherosclerosis, aortic arch atheroma, and paradoxical emboli. These account for about 80% of all TIAs, so risks determined by larger studies are also applicable to these patients.

Evaluation should be individualized on the basis of history and comorbidities and may include transesophageal echocardiography,

intracranial magnetic resonance angiography, catheter angiography, and laboratory tests for hypercoagulable states. Before subjecting patients to testing, one should take into account whether or not the findings would influence the choice of treatment.

### OTHER TREATMENT CONSIDERATIONS

The National Stroke Association recently published updated guidelines for managing TIAs.<sup>60</sup> The American Stroke Association also recently published guidelines for secondary prevention that include TIA as well as ischemic strokes.<sup>67</sup>

These guidelines extensively review the evidence and opinion supporting other aspects of treatment that cannot be covered in detail in this short review highlighting the new aspects of TIA treatment distinct from stroke. Of course, all patients with non-cardioembolic stroke should receive an antiplatelet agent, and guidelines have implied that combined dipyridamole and aspirin is the best first choice, based on the European Stroke Prevention Study 2 and the European/Australasian Stroke Prevention in Reversible Ischaemia Trial,<sup>68,69</sup> with aspirin and clopidogrel as alternatives.<sup>70</sup> A high-dose, high-potency statin is also indicated for the vast majority of patients, and other risk factors for stroke, such as hypertension and diabetes, should be controlled. Clinical trials are still needed to help determine appropriate acute therapies for TIA. No single large-scale trial has been performed that treated TIA as an acute condition. ■

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