

Transient Ischemic Attack: An Evidence-Based Update

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Abstract

Transient ischemic attack represents a medical emergency and warns of an impending stroke in roughly one-third of patients who experience it. The risk of stroke is highest in the first 48 hours following a transient ischemic attack, and the initial evaluation in the emergency department is the best opportunity to identify those at highest risk of stroke recurrence. The focus should be on differentiating transient ischemic attack from stroke and common mimics. Accurate diagnosis is achieved by obtaining a history of abrupt onset of negative symptoms of ischemic origin fitting a vascular territory, accompanied by a normal examination and the absence of neuroimaging evidence of infarction. Transient ischemic attacks rarely last longer than 1 hour, and the classic 24-hour time-based definition is no longer relevant. Once the diagnosis has been made, clinical risk criteria may augment imaging findings to identify patients at highest and lowest risk of early recurrence. Early etiologic evaluation, including neurovascular and cardiac investigations, allows for catered secondary prevention strategies. Specialized transient ischemic attack clinics and emergency department observation units are safe and efficient alternatives to hospital admission for many transient ischemic attack patients.

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CME Objectives

Upon completion of this article, you should be able to:

1. Cite recent studies on TIA diagnosis and management and practice their indications.
2. Using available resources, incorporate imaging-enhanced risk stratification tools in the early evaluation of TIA in the ED.

Prior to beginning this activity, see the back page for faculty disclosures and CME accreditation information.

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Case Presentations

A 59-year-old obese woman presents to your community hospital ED after experiencing a distinct episode in which her left hand felt “clumsy,” along with a left facial droop and left-sided numbness. She denies experiencing frank weakness and states that the symptoms resolved in less than 10 minutes. She mentions a similar episode 2 weeks ago and is concerned because both her parents and an older sibling experienced significantly disabling ischemic strokes. Her vital signs and point-of-care glucose were within normal limits, and her ECG showed sinus rhythm. Her physical exam, including a detailed neurologic exam, was largely unrevealing, with no facial asymmetry, unilateral weakness, sensory loss, or dysmetria appreciated. A noncontrast cranial CT scan of the brain was remarkable only for nonspecific subcortical and periventricular white matter changes without evidence of acute or old infarction, mass, or hemorrhage. Although she was relieved to learn that she has not had a stroke, she is concerned that this may be a precursor of a more serious event. She does not have a primary care physician and states that she has not seen a physician in several years. She asks whether this was a “mini stroke” and, if yes, what the chances are that she will have a stroke in the future.

An 80-year-old man with a history of diabetes, carotid stenosis status post right carotid endarterectomy, and pacemaker-dependent cardiomyopathy presents after multiple brief episodes of garbled speech over the past week. He states that each episode resolved completely before recurring and that he is presently symptom-free. While in the ED, he experiences a 5-minute episode of right hemiparesis and then, once again, normalizes. His vital signs remain stable, and your physical exam is notable for a high-pitched carotid bruit on the right and a stroke scale of zero. A noncontrast CT scan of the brain shows no evidence of infarction. You have no inhouse neurology, and your carotid duplex lab has closed for the evening. How do you proceed?

A 72-year-old woman with a history of hypertension, diabetes, coronary artery disease, and chronic kidney disease presents shortly after experiencing a 20-minute episode of slurred speech and right facial droop. She denies experiencing similar events in the past, but she does endorse a transient episode of vision loss a week ago, intermittent vertigo, and left-sided weakness last month. On exam, her blood pressure is 178/100 mm Hg, her heart rate is 80 beats per minute and regular, and the ECG shows a sinus rhythm. Her stroke scale is zero, and noncontrast cranial CT scan shows an old small cerebellar infarct. It is Friday evening, and you have no inhouse neurology and no MRI capabilities overnight. The patient attributes her symptoms to stress and states that she has experienced anxiety and palpitations recently. She asks if it is necessary for her to be admitted or whether she can seek follow-up with her primary care physician next week.

Introduction

A transient ischemic attack (TIA) may not seem significant to patients and providers, but it should always be considered a true medical emergency. Caused by temporary focal central nervous system hypoperfusion, a TIA is often a warning of an impending stroke. Patients presenting to the emergency department (ED) with TIA are at highest risk of stroke within the next 48 hours,¹ and thus, it is critically important for the emergency clinician to recognize this opportunity to initiate primary stroke prevention strategies. Since the 2008 issue of *Emergency Medicine Practice* on TIA was published, there have been numerous studies focusing on improving risk stratification and early management strategies in TIA. This update will provide the best available evidence on diagnosing and managing TIAs.

For more information on current strategies for management of stroke, refer to the July 2012 issue of *Emergency Medicine Practice*, “Four Evolving Strategies In The Emergent Treatment Of Acute Ischemic Stroke,” the April 2012 issue of *Emergency Medicine Practice*, “Carotid And Vertebral Arterial Dissections In The Emergency Department,” and the May 2012 issue of *EM Practice Guidelines Update*, “Current Guidelines On Atrial Fibrillation In The Emergency Department.”

Critical Appraisal Of The Literature

The American Heart Association / American Stroke Association (AHA / ASA) released its current recommendations for the evaluation of TIA in a Scientific Statement published in the journal, *Stroke*, in 2009² and released guidelines for the prevention of stroke following TIA in 2011,³ also in *Stroke*. The current recommendations are supported by an increasingly robust body of clinical research. The AHA / ASA classification of recommendations and level of evidence are shown in **Table 1**.

A literature search was performed in September 2012 using PubMed, The National Guidelines Clearinghouse (www.guidelines.gov), and the Cochrane Library. The search was limited to human studies and reviews published in the English language since 2008 using the MeSH term TIA. The search yielded more than a thousand publications, of which hundreds were reviewed. Most were excluded based on reviewing the title, and those most relevant to emergency medicine were included. Preference was given to studies focusing on the diagnostic evaluation, risk stratification, and management of TIA. Additional articles were included if they were judged to be needed for completeness or historical reference.

There exists heterogeneity in the primary outcome measures in the current body of TIA literature. Most studies focus on recurrent events or

disabling stroke, but the timeframe is often variable, with 2, 7, 30, and 90 days being the most commonly reported. Although studies with each of the time points are included in this review, emphasis is placed on 2 and 7 days, as they are most relevant to emergency medicine.

History And Definition

Although our understanding of TIA continues to evolve, the concept is not new. Descriptions of fleeting events preceding stroke date back to the writings of Sir Thomas Willis, MD, credited for (among other things) coining the term “neurology” and describing the vascular circle at the base of the brain that bears his name.⁴ The clinical phenomenon of TIA remained unnamed until the fourth Princeton Cerebrovascular Disease Conference in 1965, when the term TIA emerged, thanks in part to the effort of C. Miller Fisher, MD.⁵ The classic time-based definition of TIA as “focal cerebral dysfunction of an ischemic nature lasting no longer than 24 hours with a tendency to recur” was agreed to in 1975 and persisted despite early knowledge that most TIAs, in fact, last < 1 hour. With the emergence of advanced imaging modalities such as diffusion-weighted imaging (DWI) using magnetic resonance imaging (MRI) technology and time-selective use of intravenous thrombolytics, a plea for a revised, tissue-based definition was submitted in 2002⁶ and endorsed by the AHA / ASA in 2009.² The AHA / ASA endorsed the current definition of TIA as “a transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction.”

The new definition of TIA completely eliminates the element of time and emphasizes neuroimaging instead. Additionally, inherent in the new definition is the creation of a new, clinically distinct entity: the radiographic infarction without lingering symptoms. Classically, patients with these symptoms would have been considered to have TIAs if the clinical deficits had completely resolved within 24 hours. The revised definition presents a diagnostic dilemma. It has been proposed that this cohort represents a clinically distinct group with a unique risk of subsequent stroke and should be referred to as transient symptoms with infarction (TSI).⁷ Collectively, TIA, TSI, and ischemic stroke represent a spectrum of disease along the continuum of acute cerebrovascular syndrome, and they are akin to angina and acute myocardial infarction with acute coronary syndromes.

Epidemiology

The spectrum of cerebrovascular disease, collectively, represents the second most common cause of death, accounting for 5.7 million deaths, or roughly 10%, worldwide each year.⁸ In the United States,

cerebrovascular disease recently declined from the third to the fourth most common cause of death, but it remains a leading cause of long-term disability.⁹ Stroke accounts for a significant proportion of total healthcare expenditure, with an estimated cost of nearly \$74 billion in the United States in 2010.⁹

TIAs occur in 12% to 30% of patients who experience a stroke.^{10,11} They account for approximately 0.3% of ED visits annually, with a nationwide incidence between 200,000 and 500,000.^{12,13} A nationwide survey conducted in 1999 estimated the prevalence of physician-diagnosed TIA to be 2.3%, or 4.9 million people.¹⁴ This is likely an underestimate, as an additional 3.2% of surveyed individuals reported symptoms of TIA but did not seek medical attention. Although strokes occur more commonly in women, TIAs have been shown to be more common in men.¹⁵ The prevalence increases with age and varies by ethnicity, with the risk being greater among blacks and Hispanics compared to their non-Hispanic and white counterparts.^{15,16} Additionally, TIAs have been observed more commonly among individuals of lower socioeconomic status and in those with fewer years of education.¹⁴

The risk of stroke is highest within the first 24 hours after a TIA, with roughly half of the strokes that occur within 7 days occurring within the first 24 hours.¹⁷ The overall risk of stroke has been reported to be between 5% and 10% within the first 2 days and between 11% and 17% at 90 days.^{1,18-20} Within 1 year of a TIA, roughly 12% of patients will die; at 10 years, 43% will have experienced a stroke, myocardial infarction, or vascular death.^{15,21} Individual stroke risk is dependent on clinical risk factors, imaging findings, and the underlying pathology that caused the TIA. Hemispheric TIA from tight internal carotid artery stenosis confers the highest risk compared to

Table 1. American Heart Association Classification Of Levels And Classes Of Evidence

Levels of Evidence	
Level A	Multiple populations evaluated. Data derived from multiple randomized controlled trials or meta-analyses.
Level B	Limited populations evaluated. Data derived from a single randomized trial or nonrandomized studies.
Level C	Very limited populations evaluated; only consensus opinion of experts, case studies, or standard of care.
Classes of Recommendation	
Class I	Benefit >>> Risk; procedure SHOULD be performed/administered.
Class IIa	Benefit >> Risk; IT IS REASONABLE to perform procedure/administer treatment.
Class IIb	Benefit ≥ Risk; procedure/treatment MAY BE CONSIDERED.
Class III	No proven benefit/harmful to patients.

other causes (such as intracranial small-vessel disease or cardioembolism).²² Early identification and definitive management has been shown to improve outcomes and reduce the proportion of patients experiencing a disabling stroke after TIA.²³⁻²⁷

Etiology And Pathophysiology

Both TIA and ischemic stroke share the same causes and pathophysiology that lead to focal hypoperfusion, oligemia, and eventual impairment of cerebral oxygen and glucose metabolism. It appears that an individual's ability to tolerate short periods of cerebral hypoperfusion is variable and dependant upon multiple factors, including collateral flow and oxygen delivery capacity. The phenomenon of ischemic preconditioning appears to provide some degree of protection to certain individuals and is being explored as a novel preventative treatment strategy.²⁸ On the other hand, those with extensive periventricular and subcortical white matter disease, known as leukoaraiosis, appear to have an impaired capacity to compensate for cerebral injury.²⁹

When a definitive cause of TIA or ischemic stroke can be identified, there appears to be a fairly even distribution of large-artery atherosclerosis, small-vessel disease, and cardioembolism. Nonetheless, in all classification schemes, the proportion of undifferentiated or cryptogenic causes remains as high as 25% to 50%.³⁰ An additional 5% of cases are caused from rare vascular processes (eg, vasculopathy, vasospasm, or arterial dissection) or from an underlying hypercoagulable state or inherited thrombophilia. (See Table 2.) Various tools have been used to standardize stroke subtyping, including the Trial of ORG 10172 in Acute Stroke (TOAST) criteria and the Causative Classification System (CCS), which vary slightly in their reporting of the distribution of causes of ischemic stroke and TIA.³¹⁻³³ Regardless of the subtype, if an etiology can be found, these patients have a higher incidence of recurrent stroke as compared to cryptogenic cases.³⁴

Atheromatous disease of large- to medium-sized arteries is a multifocal process that is often caused by—and results from—sustained hypertension. It usually forms at branch points or in tortuous vessels where endothelial damage can progress to smooth muscle proliferation and fibrolipid plaque formation over time. The most common sites of plaque formation are the aortic arch, proximal subclavian arteries, carotid bifurcation, and vertebral artery origins.³⁵ An ulcerated plaque is at risk of embolization to distal sites, or it can directly propagate and obstruct flow to a branching vessel or cause stenosis to the point of reducing flow to susceptible tissue or to the point of complete occlusion. Individuals with large-artery atherosclerosis are at risk of morbidity from often-widespread vas-

cular disease, and they have been shown to have a higher all-cause mortality at 2 years.³⁶

Small-vessel disease refers to hyaline arteriosclerosis (which is pathologically distinct from extracranial atherothromboembolic disease) that forms in small penetrating arteries (< 0.5 mm in thickness) within the brain. It causes small-volume and lacunar strokes, with common culprits being the lenticulostriate branches of the middle cerebral artery and perforating vessels of the anterior and posterior cerebral arteries. Intracranial vessels are less elastic than their extracranial parent vessels, and they are more prone to narrowing from collagen deposition that occurs with aging. Cortical lacunar strokes and TIAs may present with minor deficits or may be clinically silent.

Cardioembolism accounts for between 10% and 30% of TIAs and ischemic strokes, has been associated with severely debilitating strokes, and, most recently, has been identified as an independent predictor of mortality.³⁷⁻³⁹ Atrial fibrillation is the most common cause of cardioembolism, as the average risk of first-time stroke in patients (who are not anticoagulated) with nonrheumatic atrial fibrillation is roughly 4% per year, and it is higher in those with rheumatic atrial fibrillation.³⁵ Recent myocardial infarction (particularly anterior wall) as well as infective endocarditis, valvular disease, mechanical valvular prostheses, patent foramen ovale, septal aneurysm, myxomas, and dilated cardiomyopathies are other causes of cardiac embolism.

Differential Diagnosis

Differentiating true TIAs from the numerous alternative diagnoses that can mimic focal ischemic symptoms can be challenging and time-consuming. Common mimics include complicated migraine, seizure with or without Todd paralysis, hypoglycemia, central nervous system mass lesion, neuropathy, acute vestibular syndrome, vasculitis, and psychogenic causes. (See Table 3.) One ED cohort found

Table 2. Etiologic Subtypes Of Transient Ischemic Attack

Mechanism	Examples
Large-artery atherosclerosis	Carotid stenosis, vertebrobasilar disease, aortic atherosclerosis
Cardioaortic embolism	Atrial fibrillation, left ventricle thrombus, valvular disease
Small-artery occlusion	Intracranial small-vessel disease from longstanding hypertension, increased age, intracranial atherosclerosis
Other defined mechanisms	Arterial dissection, hypercoagulable states, inherited thrombophilias, etc.
Cryptogenic	Unidentified causes

that epileptic seizures and migraine headaches accounted for 44% and 24% of mimics, respectively.⁴⁰ In this study, unilateral paresis was found to be positively correlated with true TIA, whereas speech and sensory disturbance was not.

Prehospital Care

Efficient prehospital care in TIA depends, foremost, on patient awareness of the diagnosis followed by the appropriate level of urgency in seeking care. Lay-person recognition of the signs and symptoms of TIA has traditionally been considered to be very poor. One nationwide telephone survey found that only 8.6% of respondents correctly identified a symptom consistent with TIA.¹⁴ In this study, it was found that, of the participants who reported having been diagnosed with a TIA by a physician, only 64% endorsed seeking medical care within 24 hours of the event. Since the symptoms are nearly always painless and most often resolve within minutes, it is understandable why many do not commit to immediate ED evaluation. Emergency medical services (EMS) utilization among TIA patients has been reported to be < 40%,⁴¹ but when utilized, time-to-treatment rates are lower. Multiple prehospital screening tools have been developed, which utilize easily identifiable clinical deficits (such as facial droop and arm weakness) to help trigger prehospital notification and preferential triage to comprehensive stroke centers. EMS protocols typically include checking a finger-stick glucose and investigating whether the patient has a history of seizure disorder.^{42,43}

Thanks to the aggressive “Get With The Guidelines” program in acute ischemic stroke, public awareness of the importance of time-to-treatment has increased, and from 2005 to 2009, the proportion of patients treated with thrombolytics doubled.⁴⁴ Unfortunately, the same is not true for TIA, as

Table 3. Differential Diagnosis Of Transient Ischemic Attack

- Stroke
- Hypoglycemia / hyperglycemia
- Seizure with Todd paralysis
- Complicated migraine
- Structural brain lesion (tumor, hemorrhage, aneurysm)
- Demyelinating disease (multiple sclerosis)
- Central nervous system infection (encephalitis, cerebritis, abscess)
- Acute vestibular syndrome (labyrinthine disorders)
- Recrudescence of old stroke
- Syncope (of any etiology)
- Metabolic disarray (hyponatremia, hypokalemia, etc.)
- Peripheral nervous system lesion (radiculopathy, neuropathy, plexopathy)
- Psychogenic (conversion disorder, somatization)
- Delirium

many patients and providers remain unaware of the heightened risk of stroke immediately following TIA, which can be largely abated with early initiation of secondary preventative strategies. Thus, regardless of the transience or severity of the acute focal neurologic deficit, the initial response to a suspected TIA should be indistinct from that of acute ischemic stroke. Patients should be transported to the ED without delay. Depending on regional availability, destination protocols are becoming more common for EMS to preferentially seek primary or comprehensive stroke centers for patients with suspected acute TIA, in the event that symptoms recur.

Emergency Department Evaluation

History And Physical Examination

A detailed history is paramount to the accurate diagnosis of TIA. In 1 study, misdiagnosis among emergency physicians was reported to be as high as 60%.⁴⁵ Moreover, discordance rates among neurologists in the diagnosis of TIA, by history, ranges between 42% and 86%, and 1 study found that agreement was low even among stroke-trained neurologists.⁴⁶⁻⁴⁸ Patients may also find it difficult to identify and accurately describe focal neurologic dysfunction, making the diagnosis that much more challenging. Since a TIA is a focal process, the history should be comprehensive in characterizing focal neurologic symptoms. Nonfocal symptoms such as loss of consciousness, confusion, lightheadedness, generalized weakness, or incontinence are less often caused by TIAs and tend not to be predictive of future stroke.⁴⁹ Furthermore, headache, involuntary movements, and dizziness have been shown to be symptoms most associated with emergency physician and neurologist discordance in the diagnosis of TIAs, whereas tingling was associated with concordance.⁵⁰ Typically, the symptoms experienced in a TIA are predominantly “negative;” that is to say, they are associated with a loss of a function such as strength, speech, or sensation. “Positive” symptoms (with the exception of tingling) usually suggest an alternative diagnosis. Dizziness is a positive symptom characteristic of—but not specific to—posterior circulation ischemia. It has been associated with TIA or stroke in only 3.2% of patients reporting the symptom and in 0.7% of patients with isolated dizziness.⁵¹ The history should also ascertain the abruptness of the onset of symptoms, as TIAs generally occur suddenly and without prodrome. Stuttering symptoms, over hours to days, are of particular concern and warn of a highly unstable plaque.

Though the component of time has been removed from the definition of TIA, the duration of symptoms remains an important aspect of the diagnosis. The majority of TIAs are brief, with a classic study by Levy showing that 60% last < 1 hour. Once

a neurologic deficit is present for > 1 hour, there is < 15% chance that it will spontaneously resolve.⁵² Others have shown that the duration of symptoms correlates with the likelihood of experiencing a disabling stroke in the short term, and they have incorporated the element of time into risk stratification schemes.^{53,54} Other than the onset, character, and duration of symptoms, the history should investigate comorbid risk factors that have proven associations with stroke after TIA, such as advanced age, diabetes, hypertension, carotid stenosis, and prior TIA or stroke. The predictive ability of these clinical comorbidities will be discussed in the “Risk Stratification” section on page 7.

The physical examination must be thorough, as the primary objective is to determine whether baseline neurologic function has been restored. One recent study showed that, among patients referred to a same-day TIA clinic with reportedly resolved symptoms, 26% had evidence of persisting neurologic deficit on the neurologist’s assessment.⁵⁵ Every TIA patient should have a complete neurologic examination, including testing of cranial nerves, visual fields, strength, sensation, language fluency, and coordination. The National Institutes of Health Stroke Scale (NIHSS) is a standardized tool that can be applied to these patients. Certification is available using a free online resource (at <http://nihss-english.trainingcampus.net/uas/modules/trees/windex.aspx>). It should be noted, however, that a score of zero on the NIHSS does not rule out the presence of neurologic deficit or stroke. Clinical deficits correlating with posterior circulation ischemia are poorly represented on the NIHSS and can be missed if not tested independently.⁵⁶ Truncal ataxia, decreased visual acuity, Horner syndrome, and memory impairment are just a few focal neurologic deficits that would be missed by the NIHSS. Injury to the sympathetic nerves from carotid artery dissection can result in an incomplete Horner syndrome (ptosis and miosis without anhidrosis). Truncal ataxia is seen in midline lesions in the cerebellum. Amaurosis fugax, or transient monocular blindness, is caused by ischemia in the territory of the ophthalmic branch of the internal carotid artery and manifests as a “curtain” being drawn over the affected eye. This should be differentiated from hemianopia through careful visual field testing. Fundoscopy to assess for retinal plaques and pigmentation is reasonable to perform in all patients with TIA, but it is particularly important in patients with visual symptoms. Auscultate the carotids for bruits, as symptomatic carotid stenosis is an indication for intervention and can significantly reduce stroke risk, if detected. Carefully listen for valvular and structural heart lesions, since cardioembolic causes are numerous.

Even after obtaining a detailed history and performing a complete neurologic examination, atypical

Table 4. Stroke Chameleons

Symptom / Syndrome	Description / Location
Delirium, delusions, dementia	Mild behavioral symptoms can be indicative of lenticulostriate artery occlusion within the caudate. Mania or psychosis can be seen in orbitofrontal cortex, thalamus, and temporoparietal infarction.
Depression	Abulia (loss of motivation to undertake a task), aprosodia (inability to interpret or express emotional information in conversation), and akinetic mutism (decreased voluntary movement and mutism) can all be seen in frontoparietal strokes.
Coma	Coma can be due to medial thalamic and rostral midbrain perforator occlusion, as well as distal basilar artery occlusion, causing top-of-the-basilar syndrome.
Visual perception deficit	Cortical blindness with denial of being blind and confabulation can occur in Anton syndrome from bilateral occipital infarcts. Balint syndrome is caused by bilateral occipitoparietal infarcts and is characterized by an inability to recognize more than 1 object at a time.
Abnormal movements	Tremor, dystonia, clonic or jerky movements, chorea, and posturing-like movements can be seen in basal ganglia strokes. Alien hand syndrome can be mistaken for a psychogenic cause but suggests corpus callosum infarct.
Limb shaking	Transient unilateral limb shaking is more common in the upper extremities and can point to hypoperfusion of the contralateral frontosubcortical motor tracts, often from tight carotid stenosis.
Seizure	Though Todd paralysis following seizure does not suggest cerebral ischemia, seizure can occur at stroke onset. Seizure is more common in younger patients and suggests cortical stroke or cerebral venous sinus thrombosis.
Dizziness	In the minority of cases, particularly in the elderly, dizziness can be due to posterior circulation ischemia, and it can be difficult to differentiate from acute vestibular syndrome.
Isolated paresthesias or sensory loss	Although rare, this can be indicative of ischemia along the sensory axis (cortex, internal capsule, thalamus, brainstem).
Isolated dysarthria	Speech deficits most often occur with other negative neurologic symptoms; however, it may be the only reported or residual deficit if others were minor or unnoticed. Isolated dysarthria-facial paresis syndrome presents subtly and is indicative of small infarction to the internal capsule, corona radiata, or pons.

Adapted from *The Lancet Neurology*, Vol. 10, Jonathan Edlow and Magdy Selim. Atypical presentations of acute cerebrovascular syndromes, Pages 550-560, Copyright © 2011, with permission from Elsevier.

stroke syndromes and unusual presentations can be missed when they take on the appearance of another clinical syndrome. Knowledge of these stroke “chameleons” can help identify the wolf in sheep’s clothing.^{57,58} (See Table 4.)

Risk Stratification

Predicting stroke risk in patients with TIA has long been a topic of great interest to emergency medicine and neurology clinicians, and it has been the focus of several research studies in recent years. Early clinical prediction tools in TIA included the Stroke Prognosis Instruments,^{59,60} the California score¹, and the ABCD score,⁵³ published in 1991, 2000, and 2005, respectively. The authors of the latter 2 scores combined efforts to create the refined, and now well-known, ABCD2 score, designed specifically to guide nonneurologists in the prehospital setting in predicting risk among undifferentiated patients with transient stroke-like symptoms.⁵⁴ (See Table 5.) The score stratifies patients as low, moderate, or high risk for stroke at 2, 7, and 90 days following TIA, in an effort to guide appropriate triage and disposition of these patients. There have been numerous validation attempts of the ABCD2 score, with varying results, and a systematic review and meta-analysis published in 2010 found a pooled area under the curve (AUC) of 0.72 (95% confidence interval [CI], 0.63-0.80), indicating good overall discrimination.⁷¹ Nonetheless, the 7-day stroke risk was higher in the proportion of patients presenting to the ED compared to the entire population-based cohort, suggesting that extrapolation on the risk estimates of the ABCD2 score should be done with caution in the ED setting. Moreover, a recent prospective validation attempt of the ABCD2 score

exclusively in ED patients found it to be poorly sensitive (AUC 0.56, 95% CI, 0.47-0.65) and, perhaps more concerning, miscalculated in a third of patients in the ED.⁶² This was most often due to ED providers failing to give points to patients who reported a history of unilateral weakness when none was found on physical examination.

Thus, there exists little consensus as to the proper implementation of the score into clinical practice. Some have argued that the ABCD2 score helps to differentiate true TIAs from mimics,⁶³ whereas others have found that a high ABCD2 score does not predict subsequent stroke, but rather the patients in whom a stroke is likely to be significantly disabling.⁶⁴ Regardless, the ABCD2 score should be considered no more than a tool to provide a general gauge of short-term stroke risk, and it should not supersede physician judgment. Keep in mind that the ABCD2 score is mechanism blind and provides no insight as to TIA etiology, which is critically important for secondary prevention and ongoing stroke risk.

Several recent studies have combined radiographic data with the clinical ABCD2 score to create prediction models with improved discriminative ability. The clinical and imaging-based predictive (CIP) model,⁶⁵ ABCD2-MRI,⁶⁶ ABCD2-I,⁶⁷ ABCD3-I,⁶⁸ ABCDE+,⁶⁹ and recurrence risk estimator (RRE)⁷⁰ scores all incorporate magnetic resonance imaging (MRI) findings into stroke risk calculation. (See Tables 6 and 7, pages 8 and 9.) Only 1 of the aforementioned prediction tools (ABCD2-I) utilized computed tomography (CT) data, and, interestingly, CT was found to be equivalent to MRI in predicting stroke when added to the ABCD2 score.⁶⁷ Two studies showed that absence of an area of restricted diffusion on MRI and an ABCD2 score < 4 achieved 100% sensitivity in excluding stroke at 7 days.^{69,71} In contrast, classically defined TIA patients with neuroimaging evidence of infarction confer a 20-fold increased risk of stroke at 7 days than those with normal imaging.⁷² In a recent pooled cohort analysis, the overall risk of stroke at 7 days in patients with normal DWI on MRI is 0.4%, compared to 3% with normal unenhanced CT scan.⁷³ The addition of CT angiography (from the aortic arch to the vertex) to unenhanced CT increases the negative predictive value of the imaging modality in predicting stroke at 7 days to near equal that of MRI.⁷⁴ Perfusion CT is also predictive of clinical deterioration following TIA.⁷⁵

Although imaging-enhanced clinical tools improve stroke risk prediction after TIA, their performance is not perfect—or even at a level of sufficient risk tolerance for most emergency clinicians. The best way to prognosticate future events following TIA is by gaining insight into the underlying vascular mechanism responsible for the event.⁷⁶ This is the primary objective of neurologists when

Table 5. The ABCD2 Score

Predictor	Points
Age > 60 y	1
Blood pressure > 140/90 mm Hg	1
Clinical features (maximum 2) Unilateral weakness (2) Speech difficulty without weakness (1)	2
Duration (maximum 2) > 60 min (2) 10-59 min (1) < 10 min (0)	2
Diabetes	1
Maximum total score	7

Adapted from *The Lancet*, Vol. 369, S. Claiborne Johnston, Peter M. Rothwell, Mai N. Nguyen-Huynh, Matthew F. Giles, Jacob S. Elkins, Allan L. Bernstein, and Stephen Sidney. Validation and refinement of scores to predict very early stroke risk after transient ischaemic attack, Pages 283-292, Copyright © 2007, with permission from Elsevier.

caring for TIA patients, regardless of whether they are admitted to the hospital or seen in follow-up. Unfortunately, full etiologic evaluation requires time and resources not commonly available in the ED, but this is not an excuse from doing what is within the capacity in one's local ED practice environment. Etiologic algorithms such as the TOAST criteria and the automated Causative Classification System (CCS) have been developed to assist in determining stroke or TIA etiology using available data.^{77,78}

Diagnostic Studies

Laboratory Testing

There are few laboratory tests that aid in the diagnosis of TIA, except for a fingerstick glucose to exclude

hypoglycemia, which is a common stroke mimic. A complete blood count is reasonable to obtain and may uncover unusual prothrombotic conditions such as thrombocytosis or polycythemia vera.² Serum electrolytes are generally considered routine, as many forms of metabolic disarray such as hypokalemic periodic paralysis and hyponatremic encephalopathy can also mimic cerebral ischemia. Coagulation studies are typically of low yield, but they are recommended by the AHA/ASA as part of the routine acute evaluation of TIA patients (Class IIa, Level B).² Obtaining specialized coagulation studies for hereditary thrombophilias and hypercoagulable states is a reasonable consideration for young TIA patients without apparent vascular etiology, but these studies are best left to the discretion of specialists who will be continuing care beyond the ED.

Table 6. Imaging-Enhanced Risk Prediction Tools

	ABCD2-MRI	CIP	ABCD2-I	ABCD3-I	ABCDE+	RRE
Publication	<i>Int J Stroke</i>	<i>Stroke</i>	<i>Stroke</i>	<i>Lancet Neurol</i>	<i>Eur J Neurol</i>	<i>Neurology</i>
Year of publication	2008 ⁶⁶	2009 ⁶⁵	2010 ⁶⁷	2010 ⁶⁸	2011 ⁶⁹	2010 ⁷⁰
Follow-up (days)	90	2, 7	7, 90	2, 7, 28, 90	90	7, 14, 90
Imaging modality	DWI	DWI	DWI/CT	DWI/carotids	DWI	DWI
ABCD2 Score	Age > 60 y	1	1	1	1	-
	Blood pressure > 140/90 mm Hg	1	1	1	1	-
	No weakness	0	0	0	0	-
	Speech difficulty without weakness	1	1	1	1	-
	Unilateral weakness	2	2	2	2	-
	Duration: < 10 min	0	0	0	0	-
	10-59 min	1	1	1	1	-
	> 60 min	2	2	2	2	-
Diabetes	1	1	1	1	1	-
Dual / recent event	-	-	-	2	-	1
DWI lesion:						
Any DWI lesion	1	1	3	2	3	1
> 1 acute lesion	-	-	-	-	-	1
Varying ages	-	-	-	-	-	1
Different territories	-	-	-	-	-	1
Isolated cortical	-	-	-	-	-	1
Intracranial vessel occlusion	1	-	-	-	-	-
Carotid stenosis	-	-	-	2	-	-
Etiology:						
Large-artery atherosclerosis	-	-	-	-	3	-
Cardioembolic	-	-	-	-	1	-
Undetermined	-	-	-	-	1	-
Score range	0-9	7 + 1*	0-10	0-13	0-13	0-6
Predictive power (AUC)	0.88	0.81	0.80	0.79	0.67	0.85

*The CIP model is not a stepwise scale but, rather, a dichotomized ABCD2 score at ≤ 4 plus an additional point for DWI abnormalities.

Abbreviations: AUC, area under the curve; CIP, clinical and imaging-based predictive model; CT, computed tomography; DWI, diffusion-weighted imaging; ABCD2, age, blood pressure, clinical features, duration, diabetes; MRI, magnetic resonance imaging; RRE, recurrence risk estimator.

Blood biomarkers with sufficient sensitivity and accuracy for routine clinical use have, so far, remained elusive, but several have been studied and may find a place in the ED evaluation of TIA in the near future. C-reactive protein (CRP) is an acute-phase protein and marker of systemic inflammation that is predictive of recurrent events following TIA.⁷⁹ It was recently shown to modestly improve the discriminative ability of the ABCD2 score.⁸⁰ Lipoprotein-associated phospholipase A2 is thought to be a marker of atherosclerotic plaque instability and was found to be predictive of vascular events in TIA patients, whereas CRP was not.⁸¹ The D-dimer test is a nonspecific marker of coagulation that has been studied extensively in stroke and found to be very sensitive and to be a strong prognostic indicator of worsening or recurrence within the acute period.⁸²⁻⁸⁵ Additionally, D-dimer and brain natriuretic peptide have been linked to cardioembolic causes of TIA.⁸⁶ Although nonspecific by itself, incorporation of D-dimer into multimarker panels improves collective specificity in differentiating acute ischemic stroke from mimicking conditions, and it may serve as an ideal beneficial point-of-care test in rural or prehospital settings.⁸⁷

For a summary of laboratory studies in TIA, see **Table 8**.

Cardiac Evaluation

Since cardioembolism is among the most common causes of stroke and TIA, evaluation of the heart is part of the routine investigation in these patients. A 12-lead electrocardiogram (ECG) is recommended in all TIA patients to assess for dysrhythmia, left ventricular hypertrophy, and active or recent ischemia (Class I, Level B).² New-onset atrial fibrillation will be diagnosed in approximately 2% of patients.⁸⁸ Prolonged outpatient telemetry should be prescribed for TIA patients with unclear etiology, as it detects par-

Table 7. Summary Of Types Of Imaging Used In Stroke Risk Prediction Tools

Imaging Modality	Model / Score
MRI with DWI	<ul style="list-style-type: none"> • CIP • RRE • ABCD2-MRI • ABCD2-I • ABCD3-I • ABCDE+
CT	<ul style="list-style-type: none"> • ABCD2-I
Carotid duplex, CTA, MRA	<ul style="list-style-type: none"> • ABCD3-I

Abbreviations: ABCD, age, blood pressure, clinical features, duration, diabetes; CIP, clinical and imaging-based predictive model; CT, computed tomography; CTA, computed tomographic angiography; DWI, diffusion-weighted imaging; MRA, magnetic resonance angiography; MRI, magnetic resonance imaging; RRE, recurrence risk estimator.

oxysmal atrial fibrillation in 14% of patients when performed for 4 days following 24 hours of uneventful monitoring⁸⁹ and detects 23% at 21 days.⁹⁰

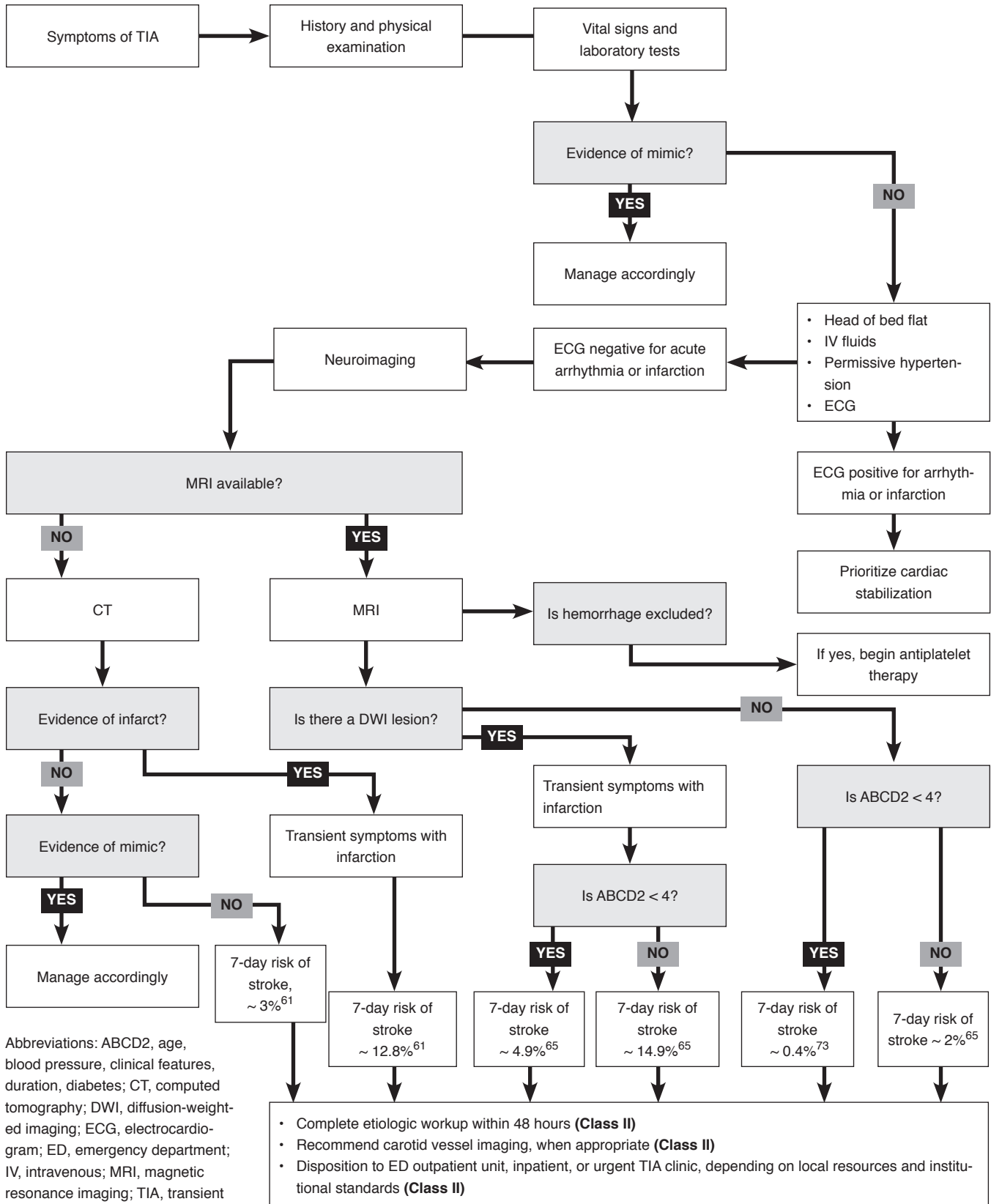
Echocardiography is a reasonable consideration in patients with a history or evidence of cardiac disease and in patients in whom other causes have been ruled out. Transesophageal echocardiography is more sensitive than transthoracic echocardiography in detecting cardiac sources of embolism, but it is semi-invasive and should be reserved for cases where detection will alter management. Transthoracic echocardiography is a good starting point in most patients, as it was shown in 1 retrospective study of 186 individuals with stroke or TIA to have detected a source of embolism in 19% of patients.⁹¹ Transthoracic echocardiography will diagnose left ventricular hypertrophy in a large proportion of acute ischemic stroke and TIA patients, many who are without a known history of hypertension.⁹² Left ventricular hypertrophy is an early finding of end-organ damage from poorly controlled hypertension and has been linked to an increased stroke risk that can be

Table 8. Laboratory Studies In Transient Ischemic Attack

Routine laboratory tests recommended by AHA/ASA ²
<ul style="list-style-type: none"> • Blood glucose • Complete blood count • Serum electrolytes • Coagulation studies (PT/INR, PTT)
Specialty laboratory tests useful in certain circumstances ⁸⁴
<ul style="list-style-type: none"> • Protein C, Protein S, antithrombin III, factor V Leiden • Fibrinogen • Lupus anticoagulant • Anticardiolipin antibody level • Prothrombin gene G20210A mutation • Factor VIII • Von Willebrand factor • Plasminogen activator inhibitor-1 • Endogenous tissue plasminogen activator activity • Homocysteine
Promising serum biomarkers of cerebral ischemia ⁸⁴
<ul style="list-style-type: none"> • High-sensitivity C-reactive protein (hsCRP) • D-dimer • Brain natriuretic peptide (BNP) • Lipoprotein-associated phospholipase A2 (PL A2) • S100B • Copeptin • Matrix metalloproteinases (MMPs) 2, 9, 13 • Glial fibrillary-associated protein (GFAP) • Brain-type fatty acid binding proteins (B-FABP) • NMDA autoantibodies • Ischemia-modified albumin (IMA)

Abbreviations: AHA/ASA, American Heart Association/American Stroke Association; INR, international normalized ratio; NMDA, N-methyl-D-aspartate; PT, prothrombin time; PTT, partial thromboplastin time.

Clinical Pathway For Transient Ischemic Attack (continued on page 11)

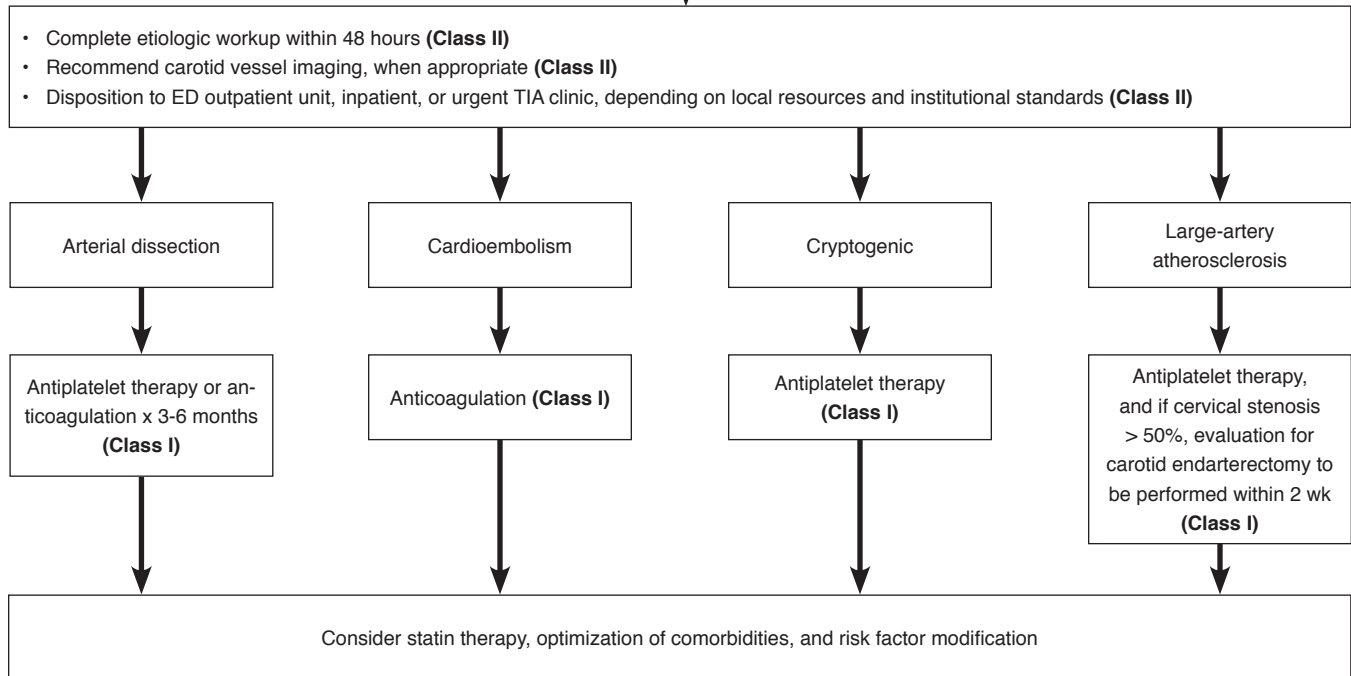


Abbreviations: ABCD2, age, blood pressure, clinical features, duration, diabetes; CT, computed tomography; DWI, diffusion-weighted imaging; ECG, electrocardiogram; ED, emergency department; IV, intravenous; MRI, magnetic resonance imaging; TIA, transient ischemic attack.

Continued on next page.

Clinical Pathway For Transient Ischemic Attack (continued from page 10)

Continued from previous page.



See Table 1 on page 3 for class of evidence definitions.

reduced with aggressive antihypertensive therapy. For this reason, some have argued that transthoracic echocardiography be considered routine,⁹² and it is currently a Class IIa, Level B recommendation of the AHA/ASA.²

See **Table 9** for a summary of cardioembolism sources.

Brain Imaging

Acquisition of neuroimaging excluding acute infarction is inherent in the new, tissue-based definition of TIA, regardless of resolution of symptoms. This was born out of a wealth of data demonstrating that clinically transient symptoms are often not transient at the tissue level. As such, the AHA/ASA currently recommends that all patients with suspected TIA undergo neuroimaging within 24 hours of symptom onset (Class I, Level B), with DWI MRI being the preferred modality.² CT, however, is the most common imaging modality performed in the acute evaluation of TIA in the ED, with studies reporting its use in 56% to 92% of cases.^{13,93,94} A nonvascular pathology is identified in 1% to 5% of patients,^{95,96} whereas evidence of infarction is present in 4% to 34% of patients.^{94,97} DWI shows areas of restricted diffusion consistent with cytotoxic edema formation in the early phase of infarction as hyperintense, making this modality far more sensitive than CT or traditional MRI. Approximately one-third of patients with normal CT or standard MRI will have small, acute lesions detectable on DWI.⁹⁸ Despite its improved sensitivity, MRI is chosen as the first-line imaging modality in only 5% to 15% of TIA patients.^{13,99} Around-the-clock accessibility of MRI is limited to < 40% of United States hospitals, with only 13% reporting an inhouse MRI technologist 24

Table 9. Sources Of Cardioembolism

- Atrial fibrillation
- Atrial flutter
- Sick sinus syndrome
- Left atrial thrombus
- Left atrial myxoma
- Patent foramen ovale
- Atrial septal aneurysm
- Mitral stenosis
- Mitral annular calcification
- Mitral valve prolapse
- Calcified aortic valve
- Infective and noninfective endocarditis
- Left ventricular thrombus
- Left ventricular myxoma
- Ventricular wall hypokineses
- Dilated or hypertrophic cardiomyopathy

Adapted from *The Lancet Neurology*, Vol. 2, Jose M. Ferro. Cardioembolic stroke: an update, Pages 177-188, Copyright © 2003, with permission from Elsevier.

hours a day, 7 days a week.⁹⁹ Additionally, MRI is contraindicated in approximately 10% of patients, due to indwelling hardware or shrapnel.¹⁰⁰ Further limitations include body habitus, claustrophobia, inability to remain still or supine for several minutes, prolonged scan times, and increased cost.

MRI with gradient-echo imaging detects acute intracerebral hemorrhage with equal sensitivity to CT.^{101,102} Therefore, given the low yield of noncontrast CT, multimodal MRI is a reasonable consideration as the lone neuroimaging technique utilized in undifferentiated TIA patients if it is available and is not contraindicated. However, MRI with DWI is not perfect, and the overall sensitivity is between 83% and 97% when compared to final clinical diagnosis.^{101,103,104} Reasons for false-negative DWI include very early ischemia and small infarcts, particularly in the internal capsule and brainstem. DWI can also be falsely positive following seizure.⁵⁸ Obtaining thin slices with coronal and axial reconstructions in regions of interest, based on clinical suspicion, can help improve sensitivity.

See **Figures 1-3** for brain imaging examples.

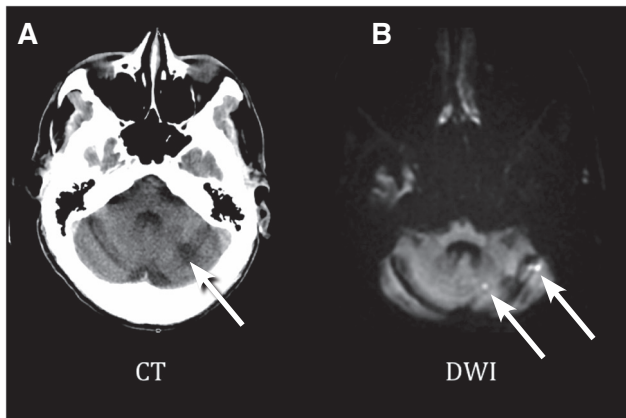
Vascular Imaging

All patients should undergo some form of intracranial and extracranial vascular imaging study as part of the routine evaluation of suspected TIA, though not necessarily in the ED. This is reflected in a Class I, Level A recommendation by the AHA/ASA² and is based, in part, on the finding that between 8% and 31% of patients with TIA and minor stroke have treatable carotid atherosclerosis.^{105,106} Additionally, approximately half of TIA patients with DWI lesions have significant stenosis or occlusion of a large cervicocephalic vessel.¹⁰⁷ Carotid ultrasound and transcranial Doppler, CT angiography, and magnetic resonance (MR) angiography are all reasonable, noninvasive modalities that have largely supplanted the traditional gold standard catheter-based digital subtraction angiography.¹⁰⁸ (See **Table 10, page 14.**)

Carotid ultrasound detects significant (> 50%) stenosis of the extracranial internal carotid artery with a sensitivity and specificity of 88% and 76%, respectively,¹⁰⁹ compared to 86% and 89% for high-grade (> 70%) stenosis.¹¹⁰ It measures intraluminal diameter and peak systolic velocity and can provide a good overall assessment of flow through the extracranial portion of the internal carotid artery. It is generally thought that when the luminal diameter is reduced to ≤ 1.5 mm (normal = 5-7 mm), hemodynamic changes increase the risk of occlusion.¹¹¹ Doppler ultrasonography is insensitive in detecting carotid artery dissection, cannot assess the intracranial portion of the internal carotid artery, and is operator-dependent. The addition of transcranial Doppler and transcranial color Doppler ultrasonography can reliably exclude intracranial stenosis in the

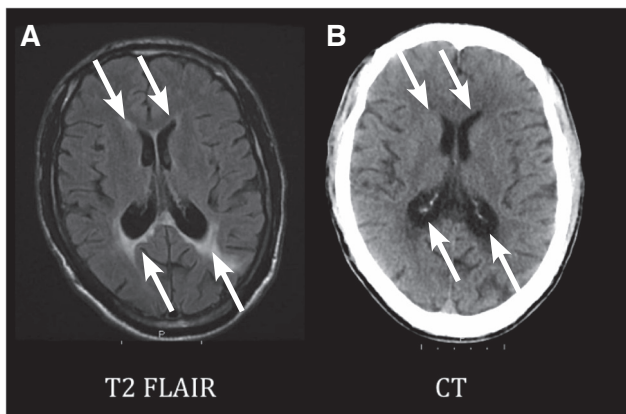
anterior and posterior circulations, and it has been shown to have a negative predictive value of 86%.¹¹² Transcranial Doppler can be performed in real time during ED assessment and is being explored in other applications to assess the response to thrombolysis or to augment thrombolysis in acute ischemic stroke.

Figure 1. Prior And New Cerebellar Infarct On Computed Tomography And Magnetic Resonance Imaging



CT (image A) and MRI (image B) images obtained from a man with a history of prior cerebellar stroke who presented with acute dizziness. NIHSS was 0, and CT (image A) showed prior left cerebellar infarct (arrow). Subsequent corresponding DWI image (image B) shows a punctate area of new infarct (arrows).
Images courtesy of Matthew S. Siket, MD.

Figure 2. Leukoaraiosis On Magnetic Resonance Imaging And Computed Tomography



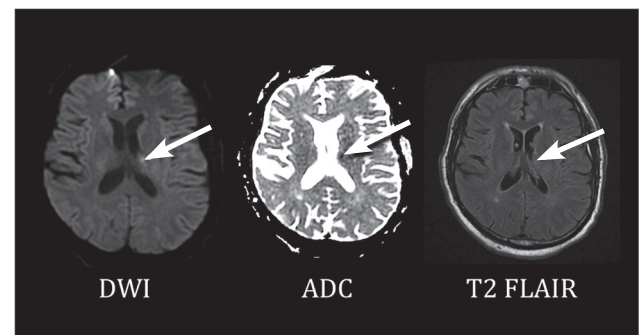
MRI (image A) and CT (image B) images from the same patient showing extensive periventricular, subcortical white matter disease (leukoaraiosis), which is thought to be indicative of underlying cerebrovascular disease. Leukoaraiosis appears hyperintense on T2 FLAIR and hypointense on CT, (arrows) but it is easily appreciated with both modalities.
Images courtesy of Matthew S. Siket, MD.

It has also been shown to be independently predictive of recurrent vascular events in a retrospective analysis of a high-volume TIA clinic database.¹¹³ Doppler ultrasonography is relatively low cost and does not require the use of potentially nephrotoxic intravenous contrast as in the other modalities, but it is operator-dependent and requires availability of skilled ultrasound technicians. The performance of bedside carotid ultrasound and transcranial Doppler by emergency clinicians has not been assessed.

MR angiography with gadolinium enhancement has been shown to have superior discriminatory power compared to Doppler ultrasonography in detecting high-grade carotid stenosis,¹¹⁰ but it is less cost-effective. It is also a reasonable consideration in patients who will be obtaining a MRI of the brain. Additionally, in patients unable to receive gadolinium due to allergy or renal failure, unenhanced MR angiography using time-of-flight sequences is a reasonably sensitive alternative.

CT angiography is a fast and highly accurate vascular imaging modality, and it is widely available in most EDs. It can visualize the entire cervicocephalic vascular network with 1 fixed dose of contrast, and delayed images can also be obtained to add to overall sensitivity. CT angiography with newer 64-slice CT scanners has a negative predictive value of 97% of excluding significant internal carotid artery stenosis, which is a diagnostic accuracy rivaling digital subtraction angiography, without the associated complications.^{114,115} Nonetheless, this information is obtained at the expense of additional radiation exposure, which has been shown to be 2 to 3 times

Figure 3. Transient Ischemic Attack On Magnetic Resonance Images



MRI from a man who presented with right-sided weakness and speech difficulty (NIHSS of 6) that rapidly improved in the ED. CT scan was unremarkable. The left image shows a small hyperdensity in the left thalamus and putamen (arrow) on DWI. The middle image is the corresponding apparent diffusion coefficient, which is dark (arrow), suggesting the lesion is acute. The right image shows slight hyperintensity on the T2 FLAIR sequence (arrow), suggesting the lesion is early subacute (> 3 h old).
Images courtesy of Matthew S. Siket, MD.

the dose of a standard brain CT.¹¹⁶ Collectively, CT/CT angiography has been shown to be equal to MRI in predicting 90-day recurrent events following TIA and minor stroke, and it is a reasonable modality to provide diagnostic, prognostic, and etiologic data in suspected TIA patients, particularly when MRI is not readily available.⁷⁴ (See Figures 4 and 5.)

Perfusion Imaging

Although not considered part of routine evaluation in TIA patients, CT and MR perfusion imaging have been shown to provide additional diagnostic and prognostic information. MR perfusion abnormalities are present in 30% to 40% of TIA patients, and they are the only abnormalities in otherwise-normal MRI scans in 14% to 16% of patients.¹¹⁷⁻¹²⁰ Combined diffusion and perfusion MRI reveals an acute ischemic lesion in roughly 60% of TIA patients¹²¹ and has recently been shown to have a role in predicting recurrent events within 1 week.¹²² CT perfusion detects abnormalities in one-third of TIA patients, which was predictive of short-term morbidity and was independent of DWI lesions or clinical prediction tools in one study. It appears that perfusion imaging has a complimentary role, and, in keeping with the revised definition of TIA, it may currently be the best tissue-based imaging modality to detect ischemia without infarction. However, this comes at added cost and, in the case of CT, further radiation exposure. The United States Food and Drug Administration issued a warning about excess radiation during CT brain perfusion scans on November 9, 2010, so the clinical application of perfusion imaging remains unresolved. (<http://www.fda.gov/medicaldevices/safety/alertsandnotices/ucm185898.htm>)

Treatment

Once the diagnosis of TIA is suspected, the immediate treatment objectives are to optimize cerebral perfusion and prevent stroke. (See Table 11.) Consider the following treatment strategies: (1) Keep the head of the bed flat. This has been shown to increase cerebral perfusion by 20%, compared to a 30° incline.¹²³ Patients may find this uncomfortable or intolerable, but it is a reasonable consideration during the first 24 hours if cerebral perfusion is thought to be at risk. (2) Maintain euvolemia and proper electrolyte balance. (3) Optimize tissue oxygenation by preventing hypoxia. Routine supplementary oxygen was found to be associated with a transient improvement in neurologic impairments in 2 small pilot studies of acute ischemic stroke,^{124,125} and it has been suggested as a strategy for neuroprotection¹²⁶; however, as yet, no randomized trial has shown clear benefit, so its routine administration is not recommended.

Antihypertensive Treatment

Although blood pressure is the most important modifiable risk factor in primary and secondary prevention of stroke, caution is advised in the ED setting.^{3,127,128} In fact, permissive hypertension up to a blood pressure of 220/120 mm Hg is currently favored by the AHA/ASA in the acute setting of cerebral ischemia.¹²⁹ The rationale is that the ischemic brain may lose the ability for autoregulation and a higher mean arterial pressure may be required to maximize perfusion to ischemic tissue via collateral vessels. Nonetheless, this is more likely to be true in disabling acute ischemic stroke than in TIA, and, unlike in stroke, no acutely initi-

Table 10. Summary Of Carotid Imaging Modalities

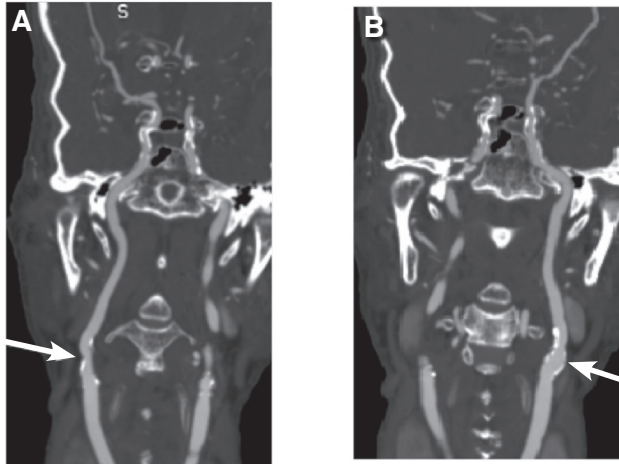
Test	Negative Predictive Value, ≥ 50% Stenosis	Advantages	Disadvantages
Duplex ultrasound	0.91	<ul style="list-style-type: none"> • Less expensive • Does not require contrast or radiation 	<ul style="list-style-type: none"> • Operator-dependent • Does not visualize intracranial carotid (unless combined with transcranial Doppler) • Less sensitive for ulcerated plaque • May not be available 24/7
Computed tomographic angiography	0.97	<ul style="list-style-type: none"> • Sensitive for dissection • Fast and widely available • Can visualize entire cervicocephalic vascular tree with 1 dose of contrast • Can obtain delayed images 	<ul style="list-style-type: none"> • Additional radiation • Requires potentially nephrotoxic contrast • Bone averaging at skull base
Magnetic resonance angiography	0.99	<ul style="list-style-type: none"> • Can visualize entire cervicocephalic vascular tree • Time-of-flight sequence alternative in those not able to receive gadolinium 	<ul style="list-style-type: none"> • Limited availability • Most expensive and time-consuming option • Contraindicated in patients with some forms of indwelling hardware/shrapnel

Adapted from *Emergency Medicine Clinics of North America*, Matthew S. Siket, Jonathan A. Edlow. Transient ischemic attack: reviewing the evolution of the definition, diagnosis, risk stratification, and management for the emergency physician, Pages 745-770, Copyright © 2012, with permission from Elsevier.

ated antihypertensive trial has been associated with worsened outcomes.^{23,24,130}

For patients who remain stable beyond the first 24 hours following a TIA or stroke, the initiation of antihypertensives is indicated. Treatment goals

Figure 4. Coronal Computed Tomographic Angiography Showing Carotid Stenosis



In image A, arrow points to moderate proximal stenosis. In image B, arrow points to mild stenosis.

Images courtesy of Matthew S. Siket, MD.

Figure 5. Coronal Computed Tomographic Angiography Showing Severe Stenosis Of The Basilar Artery



Arrow points to severe stenosis of the basilar artery.

Image courtesy of Matthew S. Siket, MD.

should be individualized, but, in general, benefits have been linked to an absolute reduction of approximately 10/5 mm Hg or to a normalization of < 120/80 mm Hg with a diuretic or angiotensin-converting enzyme inhibitor.² Angiotensin-receptor blocker agents have shown mixed results in randomized controlled trials, and a clear role has yet to be confirmed.^{127,131}

Antiplatelet Therapy

Antiplatelet therapy is generally considered appropriate in patients with cerebrovascular disease, and it is indicated in most etiologic subtypes of TIA and acute ischemic stroke unless full anticoagulation or thrombolysis is warranted. Aspirin, clopidogrel (Plavix[®]), combination aspirin plus dipyridamole (Aggrenox[®]), and ticlopidine (Ticlid[®]) are currently the 4 FDA-approved antiplatelet therapies for secondary prevention in acute ischemic stroke and TIA. A meta-analysis encompassing over 200,000 patients showed that the average reduction of the relative risk of serious vascular events was 22% in patients on antiplatelet therapy.¹³²

Aspirin

Aspirin is the most well studied and widely prescribed of the approved antiplatelet medications, and it is a reasonable consideration for initial therapy. Overall, it confers a risk reduction of roughly 15% for stroke recurrence, compared to placebo, at a variety of doses ranging from 50 mg to 1500 mg, over a follow-up period of at least 2 years.¹³³ Lower doses (61 mg to 325 mg per day) appear to be as effective, with a lower incidence of gastrointestinal bleeding. Low-dose (≤ 325 mg/day) aspirin users are 2.5 times more likely to have a serious gastrointestinal hemorrhage than nonusers (annual risk 0.4%) and have a small absolute increase in the risk of hemorrhagic stroke (12 events per 10,000 persons).^{134,135}

Other Antiplatelet Agents And Combinations

Ticlopidine is a platelet adenosine diphosphate receptor antagonist that has shown mixed results in comparison to aspirin in preventing vascular events after stroke¹³⁶⁻¹³⁸; however, it was associated with a

Table 11. General Management Considerations For Suspected Transient Ischemic Attack

1. Optimize cerebral perfusion: keep the head of the bed flat unless otherwise contraindicated.
2. Maintain euolemia and proper electrolyte balance: administer intravenous fluids if clinically dehydrated.
3. Ensure adequate tissue oxygenation: provide supplemental oxygen if hypoxic.
4. Allow cerebral autoregulation: maintain permissive hypertension to blood pressure up to 220/120 mm Hg.

small but significant risk for hematologic dyscrasias, so it is rarely used.¹³⁹

Clopidogrel and aspirin/dipyridamole combination therapy has also been studied. In a head-to-head trial of over 20,000 patients who were followed an average of 2.5 years, the patients on clopidogrel therapy versus aspirin/dipyridamole combination therapy showed similar recurrent stroke and hemorrhagic complication rates.¹⁴⁰ The combined use of aspirin and clopidogrel does not confer an added benefit and has been associated with increased hemorrhagic risk compared to either agent alone.^{141,142} Additionally, the Secondary Prevention of Small Subcortical Strokes (SPS3) Trial, which randomized patients to either aspirin plus clopidogrel or aspirin alone, was recently terminated prematurely because of increased risk of hemorrhage and death in the combined treatment group.¹²⁸ Short-term and early combination therapy with aspirin and clopidogrel may be of benefit. A pilot study showed a 90-day stroke recurrence risk of 7.1% with combination therapy compared to 10.1% in those treated with aspirin alone.¹⁴³ This is the focus of the Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke (POINT) Trial, which is currently underway.¹²⁸

A summary of secondary strategies that are controversial and/or currently under investigation is included in **Table 12**.

Anticoagulation

In patients with atrial fibrillation or another cardioembolic source of TIA (other than infective endocarditis) or acute ischemic stroke, anticoagulation with a vitamin K antagonist is currently recommended (Class I, Level A).³ A meta-analysis of trials comparing warfarin to placebo or aspirin found that the risk of stroke was reduced by 60% and 40%, respectively,

over a follow-up period of at least 3 months.¹⁴⁶ In patients with atrial fibrillation, warfarin has shown superior efficacy to aspirin or aspirin plus clopidogrel in the secondary prevention of stroke.^{147,148} Conversely, in patients with noncardioembolic etiologies, oral anticoagulation with warfarin has shown no benefit and, in most cases, a significantly higher risk of hemorrhage.¹⁴⁹⁻¹⁵² Acute heparinization following TIAs or minor strokes, as practiced in the past, is to be avoided. The target international normalized ratio (INR) for patients with atrial fibrillation on warfarin is 2.5 (range, 2.0-3.0).

A new generation of oral anticoagulants that do not require monitoring are FDA approved and are increasingly replacing warfarin in these patients. Dabigatran (Pradaxa[®]), a direct thrombin inhibitor, was found to be superior to warfarin in preventing stroke, and had a similar rate of bleeding complications, but a lower incidence of intracranial hemorrhage, at a dose of 150 mg twice per day.¹⁵³ A lower dose of 110 mg twice per day was found noninferior to warfarin and had an overall lower risk of bleeding complications. Factor Xa inhibitors, including rivaroxaban (Xarelto[®]) and apixaban (Eliquis[®]) have also shown efficacy in randomized clinical trials in reducing stroke risk in patients with atrial fibrillation. Rivaroxaban has been shown to be noninferior to warfarin with a lower risk of bleeding,¹⁵⁴ whereas apixaban has shown superiority, with a lower risk of bleeding and reduced mortality.¹⁵⁵ Apixaban is also superior to aspirin in patients deemed unsuitable for vitamin K antagonist.¹⁵⁶

See **Table 13** for more information about novel anticoagulants and stroke risk compared to warfarin.

Note: The optimal timing of initiation of anticoagulant therapy is unknown. Intravenous thrombolysis is contraindicated in patients on oral

Table 12. Current, Controversial, And Investigational Strategies In Transient Ischemic Attack^{128,144,145}

Diagnosis	Current Strategy	Controversy / Investigation Status
Antiplatelet therapy	<ul style="list-style-type: none"> Aspirin 81-325 mg daily, or Clopidogrel 75 mg daily, or Aspirin/dipyridamole combination therapy 200 mg daily 	Combination therapy with aspirin and clopidogrel has been associated with increased bleeding risk, but it may be beneficial if initiated early after TIA and minor stroke. Under investigation.
Atrial fibrillation	<ul style="list-style-type: none"> Warfarin to INR 2.0-3.0, or Dabigatran 150 mg twice daily 	Apixaban and rivaroxaban showed similar efficacy to dabigatran when compared to warfarin in patients with atrial fibrillation. Apixaban is pending FDA approval.
Carotid stenosis	Carotid endarterectomy or stenting within 2 wk of TIA if stenosis \geq 70%	To date, literature suggests that preferred choice varies with age and short-term vs long-term risk tolerance.
Carotid dissection	Any antiplatelet regimen or anticoagulation for 6-12 mo	No clearly superior treatment, although a trial of aspirin vs warfarin is underway.
Intracranial stenosis	Antiplatelet therapy	The role of intracranial stenting is unclear. One trial (SAMMPRIS) showed no benefit ¹⁴⁴ ; others are underway.
Patent foramen ovale	Antiplatelet therapy	The utility of percutaneous closure is unclear. One trial (CLOSURE I) showed no benefit ¹⁴⁵ ; others are underway.

Abbreviations: FDA, Food and Drug Administration; INR, international normalized ratio; SAMMPRIS, Stenting and Aggressive Medical Management for Preventing Recurrent stroke in Intracranial Stenosis Trial; TIA, transient ischemic attack.

anticoagulants with an INR > 1.7, and so it would seem reasonable to withhold initiation of this therapy (at least initially) when the stroke risk is the highest.

Endovascular Treatment

Carotid endarterectomy is currently recommended for patients with nondisabling acute ischemic stroke or TIA who have high-grade ($\geq 70\%$) carotid stenosis (Class I, Level A) or in select patients who are symptomatic with moderate stenosis (50%-69%) (Class I, Level B).³ The North American Symptomatic Carotid Endarterectomy Trial (NASCET) reported an absolute risk reduction of 17% and a relative reduction of 65% in the risk of ipsilateral stroke at 18 months in patients with high-grade carotid stenosis.¹⁵⁷ The benefit was modest (6.5%) in patients with moderate stenosis.¹⁵⁸ Since the risk is highest immediately following stroke and TIA, it is understandable that the benefits of carotid endarterectomy diminish the longer it is delayed. It has been shown that the number needed to treat to prevent 1 ipsilateral stroke in patients with > 50% carotid stenosis was 5 in patients receiving carotid endarterectomy within 2 weeks, compared to 125 if carotid endarterectomy was delayed beyond 12 weeks.¹⁵⁸ As a result, it is currently recommended that it be performed within 2 weeks of the event or onset of symptoms (Class IIa, Level B).³

Carotid artery stenting is a controversial alternative to carotid endarterectomy. On the one hand, it is less invasive than carotid endarterectomy and is associated with a more-rapid recovery, with fewer surgical complications (such as cranial nerve palsies). Nonetheless, it has been associated with higher rates of periprocedural death and recurrent stroke at 30 days.¹⁵⁹⁻¹⁶² The Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) noted these risks, but it found no difference in mortality, due to fewer myocardial infarctions in the carotid artery stenting group.¹⁶² The periprocedural risk of stroke and death is equivalent between the 2 procedures in patients ≤ 70 years of age, making carotid artery stenting a reasonable alternative in younger

patients.^{159,163} At this point, carotid endarterectomy appears to be the safer choice in older patients. Ultimately, this is a highly individualized decision best made after careful consideration of the risks and benefits of both procedures, in consultation with a specialist.

Lipid Modification

Lowering cholesterol levels using statins has proven to be effective as both a primary and secondary stroke prevention strategy. The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Trial was a randomized placebo-controlled trial of atorvastatin (Lipitor[®]) (80 mg/day) in patients with elevated low-density lipoprotein (LDL) who experienced a recent TIA or acute ischemic stroke. The treatment group had an absolute risk reduction of 2.2 for stroke over 5 years.¹⁶⁴ Reduction of baseline LDL $\geq 50\%$ conferred the greatest reduction in stroke risk.¹⁶⁵ Although statins have shown an overall benefit, a post hoc analysis of the SPARCL data showed a small increase in the proportion of patients with intracerebral hemorrhage in the treatment group. Evaluation for hyperlipidemia and lipid modification should be recommended upon discharge from the ED. If a fasting lipid panel was obtained as part of an ED observation unit evaluation, then there is justification for prescription of a statin.

Risk Factor Control

Regular exercise and abstinence from smoking have been independently associated with lower all-cause mortality after stroke.¹⁶⁶ In 1 study, failure to adhere to a low-risk lifestyle, as measured by 5 parameters, including: (1) maintenance of a body mass index < 25 kg/m², (2) moderate exercise > 30 minutes daily, (3) abstinence from smoking, (4) modest alcohol intake, and (5) a healthy diet (top 40% by a diet score), was attributed to over 50% of ischemic strokes in a cohort of over 114,000 individuals.¹⁶⁷ Expressed another way, adherence to these parameters would have prevented 444 ischemic strokes in that cohort. Moderate physical activity, alone, has been shown to reduce stroke risk by 20%.¹⁶⁸

Table 13. Novel Anticoagulants And Stroke Risk, Compared To Warfarin

Medication	Dose	Hazard Ratio for Ischemic Stroke or Systemic Embolism (95% CI)	Hazard Ratio for All Major Bleeding (95% CI)	Hazard Ratio for Intracranial Hemorrhage (95% CI)
Warfarin	Target INR 2-3	NA	NA	NA
Dabigatran	110 mg twice daily	0.91 (0.74-1.11)	0.8 (0.69-0.93)	0.31 (0.2-0.47)
	150 mg twice daily	0.66 (0.53-0.82)	0.93 (0.81-1.07)	0.40 (0.27-0.6)
Apixaban	5 mg twice daily	0.79 (0.66-0.95)	0.69 (0.6-0.8)	0.42 (0.3-0.58)
Rivaroxaban	20 mg once daily	0.79 (0.66-0.96)	1.04 (0.9-1.2)	0.67 (0.47-0.93)

Abbreviations: CI, confidence interval; INR, international normalized ratio; NA, not applicable.

Thrombolysis

Though not typically relevant to TIA, TIA patients have a high risk for acute stroke, so discussing the issues of recombinant tissue-type plasminogen activator (rt-PA) is reasonable, should the situation arise when it might be indicated. Most importantly, the emergency clinician should gauge the patient's potential access to thrombolytics if discharge is planned. If access to rt-PA within the treatment window is not possible, consider empiric hospital admission for the first 24 to 48 hours while the risk of stroke is the highest. One study found that 24-hour admission of high-risk TIA patients was cost-effective on the grounds of improved access to thrombolytics alone.¹⁶⁹ Cost-effectiveness of hospital admission for access to thrombolysis does not appear to be the case when compared to a same-day TIA clinic.¹⁷⁰ Thrombolysis is not currently recommended in cases of clinical TIA with abnormal imaging (transient symptoms with infarction), and specific treatments at this time are unclear.

Disposition

The determination of the patients who require inpatient services versus those who are suitable for discharge is controversial, and significant practice variability exists. Variables such as inpatient bed availability, ED advanced imaging capabilities, access to follow-up versus inhouse neurologist consultation, medicolegal concerns, and patient expectations all likely contribute to admission thresholds. (See **Table 14.**) A retrospective analysis of 34,000 TIAs across 11 states, published in 2008, found that 53% of patients were admitted.¹⁷¹ After controlling for comorbidities, the hospital, and sociodemographic factors such as female gender, having Medicare insurance and presenting to the ED on a weekend increased the likelihood of admission. Patients already on oral anticoagulants were more likely to be discharged.

Based on the robust data emerging from stroke risk prediction tools, some have advocated for admission criteria based solely on clinical factors, such as the ABCD2 score. The National Institute for

Clinical Excellence (NICE) recommended outpatient evaluation of TIA patients with an ABCD2 score < 4 within 1 week.¹⁷² Nonetheless, these patients may have a similar 90-day risk of stroke as patients with an ABCD2 score ≥ 4 (3.9% vs 3.4%, respectively),¹⁷³ and such a strategy may not be sufficiently sensitive to use as the sole guide for stroke prediction in the ED.⁶¹ The AHA / ASA now endorses a more liberal admission policy, suggesting that hospitalization be considered for patients with an ABCD2 score > 2, evidence of focal ischemia, or for any patient in whom rapid follow-up as an outpatient cannot realistically be obtained within 2 days.² One group recently showed that in a cohort of 2056 patients with TIA, an ABCD2 score of > 2 had a sensitivity of 94.7% but a specificity of only 12.5% in predicting stroke at 7 days.⁶² The ABCD2 score has also been criticized for its weak interrater reliability and for being poorly correlative with imaging findings.¹⁷⁴ For these reasons, the authors discourage basing disposition solely on the ABCD2 or another clinical prediction score.

ED-based observation units have taken their place in emergency medicine as an efficient and cost-effective means to provide thorough, yet protocol-driven, care to patients with various conditions. In many ways, TIA is an ideal condition to pursue in an ED-based observation unit, in which an etiologic workup, which may include MRI, vascular imaging, cardiac telemetry, echocardiography, and neurology assessment, can occur. There have been multiple prospective trials of ED-based observation unit TIA care, which have proven efficacy, cost-effectiveness, and no increase in short-term morbidity.^{26,175-177} Lifestyle modification and stroke awareness education initiatives can also be deployed from the ED-based observation unit.

TIA clinics have been successfully rolled out around the world and are a means to provide rapid-access, 24/7 TIA evaluation by neurologists. The French SOS-TIA and British EXPRESS models have been shown to reduce hospital-bed days and associated healthcare costs, while being comprehensive and associated with a very low incidence of short-

Table 14. Summary Of Disposition Options

Modality	Advantages	Disadvantages
Hospital admission	Optimized access to care / thrombolysis during the time of highest stroke risk	<ul style="list-style-type: none"> • Highest cost • Risk of healthcare-associated illness/iatrogenesis • Greatest hospital resource consumption
Observation unit	Rapid, efficient, and cost-effective alternative to admission	Requires additional personnel and bed space as well as access to advanced imaging
TIA clinic referral	Rapid access to specialist-driven care	Not widely available
Discharge with urgent neurologist follow-up	Short, focused assessment in the ED, and appropriate referral for advanced diagnostic evaluation	<ul style="list-style-type: none"> • Most patients are unlikely to receive follow-up within period of highest stroke risk • Additional liability

Abbreviations: ED, emergency department; TIA, transient ischemic attack.

Risk Management Pitfalls For Transient Ischemic Attack

1. **“The patient denied symptoms of a stroke, so I did not consider TIA.”**

In TIA, history is often difficult, with vague symptoms that may not be suspected to be of ischemic etiology if they are not meticulously ascertained by an astute provider. Patients may dismiss or even fail to recognize certain symptoms.

2. **“Although the patient reported multiple, brief episodes, she felt normal in the ED, so I sent her home.”**

Stuttering symptoms are of particular concern and warrant aggressive care. Be sure to ask about multiple episodes and take them very seriously, even if the patient is normal at the time of the ED encounter.

3. **“I thought the patient’s neurologic examination was normal.”**

Subtle, persistent neurologic deficits are frequently missed in the ED—in over a quarter of TIA patients in 1 study. Performing a stepwise, thorough, and complete neurologic examination can help reduce the incidence of missed ischemic stroke.

4. **“The patient was too young to be having a TIA.”**

Though TIA and stroke are far more common in the elderly, they can occur in young adult and pediatric patients. Consider arterial dissection, structural heart defects, and hereditary or acquired thrombophilias in these patients.

5. **“The CT scan was normal, so I told him to follow up with neurology in a few weeks.”**

In patients with clinically silent infarctions, CT is falsely negative in at least one-third of cases. Patients receiving only a CT scan in the ED should be seen by a neurologist within 48 hours for additional etiologic testing and complete risk stratification.

6. **“The ECG showed a sinus rhythm, so I didn’t pursue cardioembolic causes further.”**

Paroxysmal atrial fibrillation is a common cardioembolic culprit in TIA patients without

evidence of large-vessel disease. A single 12-lead ECG is insufficient, and these patients should be considered for prolonged Holter or event monitor recording following discharge.

7. **“I discharged the patient because the neurologist said the ABCD2 score wasn’t high enough to admit.”**

The ABCD2 score is a useful research tool and may serve as an adjunct to available imaging for risk stratification, but it should not be used as a threshold by which to screen patients for hospital admission.

8. **“The symptoms lasted only 4 hours, so I knew it had to be a TIA.”**

The revised AHA/ASA-endorsed definition of TIA has moved away from a time-based definition to a tissue-based definition, wherein the arbitrary timeline of 24 hours no longer applies. In fact, the vast majority of TIAs last < 1 hour, and beyond that, infarction is much more likely.

9. **“The patient was already taking aspirin, so I didn’t think there was anything to add.”**

It is still possible to have a TIA or ischemic stroke while already on antiplatelet therapy, and these patients should be considered for alternative antiplatelet agents such as clopidogrel or aspirin/dipyridamole combination therapy. Additional secondary prevention measures include lipid modification, antihypertensive therapy, selective anticoagulation, and lifestyle modification measures.

10. **“TIA is a diagnosis to be worked up either as an inpatient or an outpatient, but not in the ED.”**

Since the risk of ischemic stroke following a TIA is highest within the first 48 hours, the emergency clinician is often the only provider to evaluate the patient in this narrow window of opportunity. Patients should receive frontloaded care and protocolized ED observation units offer a rapid, safe, and efficient means by which to conduct a complete evaluation.

term stroke.^{23,24,178} Both models reported a reduction of stroke after TIA by 80% at 90 days. An additional advantage is the ability of primary care providers to directly refer patients to the clinic the same day, thereby preserving the urgency of the evaluation without requiring the patient go to the ED. These clinics provide specialist-driven comprehensive testing and initiation of secondary prevention medications at the time of the initial visit. With the increasing regionalization of stroke care, it seems likely that rapid-access clinics such as these will become increasingly common.

Regardless of the means by which TIA patients receive their definitive etiologic evaluation, we encourage providers to ensure that all TIA patients are evaluated thoroughly as soon as possible. The stroke risk following TIA is highest immediately following the event, so it makes little sense to encourage patients to wait to follow up at a later date. Centralized and comprehensive workup, be it on the wards, in an ED-based observation unit, or a same-day TIA clinic, is the most logical solution to minimize short-term stroke risk.

Case Conclusions

The 59-year-old obese patient's detailed description of abrupt, negative symptoms appropriately raised your concern for a right anterior circulation TIA. You calculated her ABCD2 score as a 2, correctly counting her reported facial droop and unilateral weakness. Knowing recent risk stratification data, you counseled her that her 7-day stroke risk was very low; however, you also remembered that the periventricular white matter hypointensities on CT may be indicative of underlying small-vessel cerebrovascular disease, and her report of multiple recent episodes raised your concern. Since your observation unit was at capacity, you insisted on hospital admission. As an inpatient, she underwent MRI/MR angiography, revealing extensive small-vessel disease and multiple lacunar infarctions of varying ages. She was seen by a neurologist, started on antiplatelet therapy, and counseled on diet and exercise

Time- and Cost-Effective Strategies

A thorough and complete evaluation of a patient with suspected TIA can seem time-consuming and resource-draining; however, frontloaded care likely reduces overall healthcare costs by minimizing the risk when the odds of stroke recurrence are highest. Careful differentiation of TIA from mimics with a thorough history and physical examination can significantly reduce unnecessary testing, radiation and contrast dye exposure, and the hospital and specialty consultation burden.

strategies. She remained stroke-free at a 3-month follow-up appointment.

Although the 80-year-old patient was status post right carotid endarterectomy, you were concerned about left-sided large vessel disease causing his stuttering symptoms. Additionally, his history of cardiomyopathy raised concern for a cardioembolic source. His pacemaker precluded MRI, but you were able to obtain a CT angiography of his cervicocephalic vessels, which revealed critical left carotid stenosis. After starting him on antiplatelet therapy, you admitted him to the hospital, where he underwent transthoracic echocardiography. No obvious intracardiac thrombus was identified, and he was maintained on a single antiplatelet agent until he could undergo left carotid surgery 4 days later. He remained symptom-free 1 year later.

You correctly identified that the 72-year-old woman was at a high short-term risk of stroke with an ABCD2 score of 6 and multiple recent episodes in different vascular territories as well as evidence of an old infarct on CT scan. At your recommendation, she agreed to admission. You arranged expedited etiologic workup, including carotid duplex and transcranial Doppler ultrasound, which was initially unrevealing. She experienced a brief episode of atrial fibrillation, which was captured on the cardiac monitor, before leaving the ED. Knowing that cardioembolic causes correlate with increased stroke severity and stroke mortality, you arranged for transthoracic echocardiography the next morning, which revealed a left atrial thrombus. She was started on anticoagulation and was recurrence-free at 3 months.

This Month In EM Practice Guidelines Update

The January 2013 issue of *EM Practice Guidelines Update* reviews the 2011 American Academy of Pediatrics (AAP) guideline entitled "The Neurodiagnostic Evaluation of a Child With a Simple Febrile Seizure." Although simple febrile seizures are typically benign events with good prognoses, when should emergency clinicians perform laboratory studies or neurodiagnostic imaging to rule out bacterial meningitis in pediatric patients? What about lumbar puncture when immunization status is unavailable or in children who are under antibiotic treatment? In this issue, Dr. Lou Spina and Dr. Trevor Pour excerpt the guideline and offer commentary on the recent changes in the AAP recommendations. Subscribers to *Emergency Medicine Practice* have free access to this online publication at www.ebmedicine.net/PedFebSeizure.

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more

weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study will be included in bold type following the reference, where available. In addition, the most informative references cited in this paper, as determined by the authors, are noted by an asterisk (*) next to the number of the reference.

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CME Questions



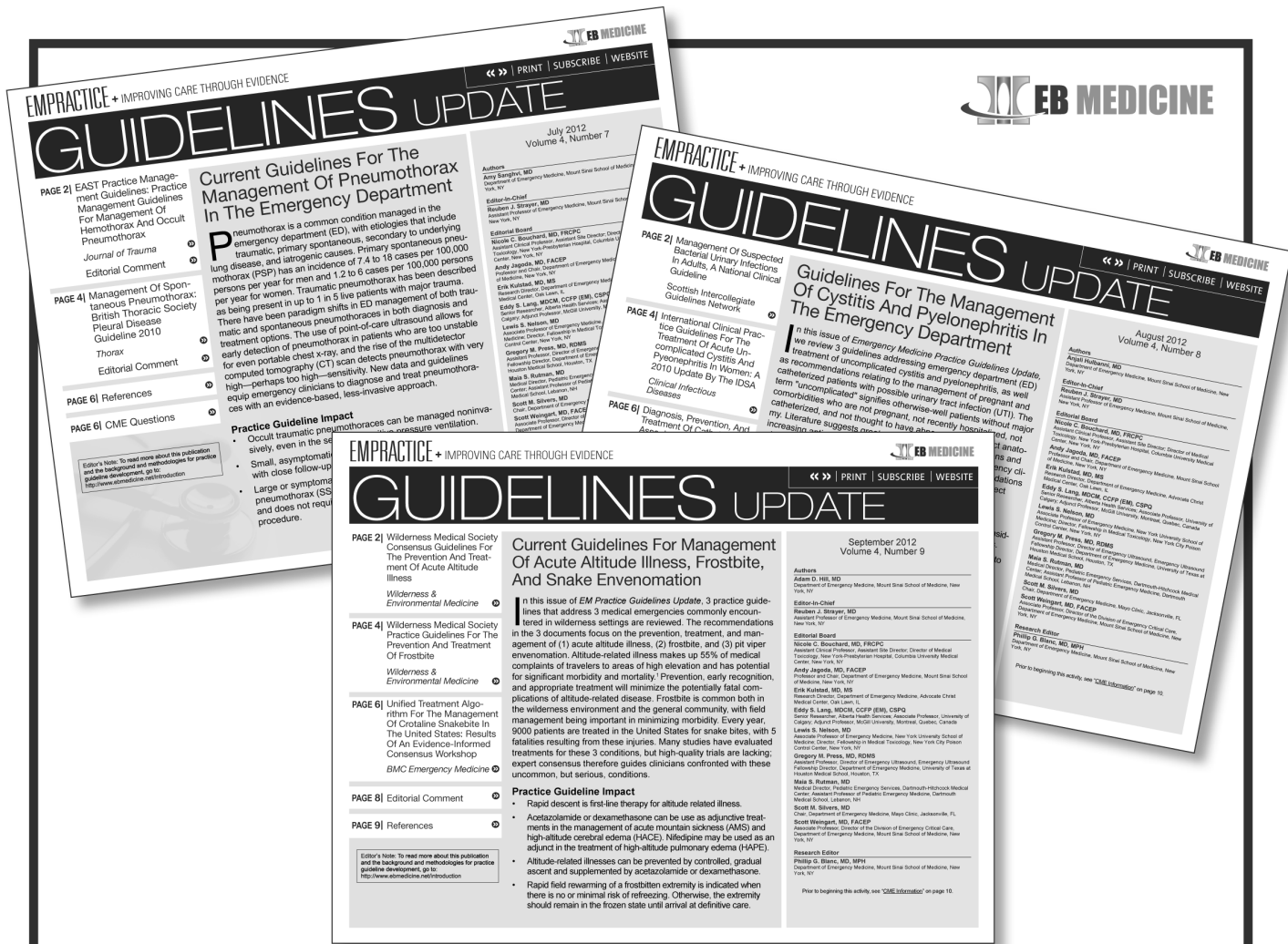
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1. The AHA/ASA now endorses a tissue-based definition of TIA described as "a transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction."
- True
 - False

2. Which of the following symptoms tends to be predictive of TIA?
- Confusion
 - Lightheadedness
 - Loss of sensation
 - Incontinence
3. Imaging-enhanced risk stratification tools include all of the following EXCEPT:
- RRE score
 - CIP model
 - ABCD2 score
 - ABCD2-I score
4. Routine serologic testing in TIA should include all of the following EXCEPT:
- Electrolytes
 - Hemoglobin and hematocrit
 - PT/INR
 - D-dimer
5. The most sensitive brain imaging sequence for detecting cytotoxic edema formation in early ischemia is:
- CT
 - Gradient echo
 - DWI
 - Fluid attenuated inversion recovery (T2-FLAIR)
6. Which vascular imaging modality is most sensitive for arterial dissection?
- CT angiography
 - MR angiography
 - Time-of-flight
 - Carotid duplex
7. Antiplatelet therapy should be given to all patients with TIA unless specifically contraindicated.
- True
 - False
8. Presently, reasonable antiplatelet regimens after TIA include all of the following EXCEPT:
- Aspirin
 - Clopidogrel
 - Aspirin/dipyridamole
 - Aspirin and clopidogrel
9. Reasonable disposition options of TIA from the ED include all of the following EXCEPT:
- Discharge with reassurance based on ABCD2 score < 4
 - Immediate TIA clinic referral
 - Observation unit admission
 - Hospital admission



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Target Audience: This enduring material is designed for emergency medicine physicians, physician assistants, nurse practitioners, and residents.

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.

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