Definition, etiology, and clinical manifestations of transient ischemic attack

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INTRODUCTION

Stroke and transient ischemic attack (TIA) are caused by one of several pathophysiologic processes involving the blood flow of the brain:

- The process may be intrinsic to the vessel, as in atherosclerosis, lipohyalinosis, inflammation, amyloid deposition, arterial dissection, developmental malformation, aneurysmal dilation, or venous thrombosis.
- The process may originate remotely, as occurs when an embolus from the heart or extracranial circulation lodges in an intracranial vessel.
- The process may result from inadequate cerebral blood flow due to decreased perfusion pressure or increased blood viscosity.
- The process may result from rupture of a vessel in the subarachnoid space or intracerebral tissue.

The first three processes can lead to transient cerebral ischemia (transient cerebral ischemic attack or TIA) or permanent cerebral infarction (ischemic stroke), while the fourth results in either subarachnoid hemorrhage or an intracerebral hemorrhage (primary hemorrhagic stroke).

This topic will discuss the definition, etiology, and clinical manifestations of TIA. The clinical diagnosis, evaluation, and treatment of TIA are discussed separately. (See "Initial evaluation and management of transient ischemic attack and minor ischemic stroke" and "Differential diagnosis of transient ischemic attack and acute stroke" and "Secondary prevention for specific causes of ischemic stroke and transient ischemic attack".)

DEFINITION OF TIA

Traditional time-based definition of TIA — TIA was originally defined as a sudden onset of a **focal** neurologic symptom and/or sign lasting less than 24 hours, brought on by a transient decrease in blood flow, which renders the brain ischemic in the area producing the symptom. The time limit was intended to separate ischemia without infarction from infarction. However, this classic, time-based definition of TIA is inadequate for several reasons. Most notably, there is risk of permanent tissue injury (ie, infarction) even when focal transient neurologic symptoms last less than one hour.

Tissue-based definition of TIA — In the tissue-based definition, TIA is a transient episode of neurologic dysfunction caused by focal brain, spinal cord, or retinal ischemia, **without** acute infarction [1]. In keeping with this definition of TIA, ischemic stroke is defined as an infarction of central nervous system tissue (brain, spinal cord, or retinal cells) attributable to ischemia, based on neuropathologic, neuroimaging, and/or clinical evidence (ie, persistence of symptoms or findings) of permanent tissue injury [2].

Thus, the benign connotation of "TIA" has been replaced by an understanding that even relatively brief ischemia can cause permanent neurologic or retinal injury. (See 'Symptom duration and infarction' below.)

The advantages of tissue-based definitions of TIA and stroke include the following [1,3]:

- The end point is biologic (tissue injury, as confirmed or excluded by neuroimaging) rather than arbitrary (24 hours)
- The definition encourages use of neurodiagnostic tests to identify brain injury and its cause, which furthers earlier therapeutic interventions
- The presence or absence of ischemic brain is more accurately reflected

The shortcomings of tissue-based definitions of TIA/stroke include the following:

- Dependency on the sensitivity and availability of neuroimaging – Infarctions associated with classically-defined TIA are often very small; most are less than 1 mL in volume [4]. Imaging methods that have low sensitivity for small infarcts, such as computed tomography (CT) or conventional magnetic resonance imaging (MRI), would result in some transient events being inappropriately classified as TIA without acute infarction. Conversely, imaging with diffusion-weighted MRI (DWI), with its higher sensitivity for acute infarction, would increase the proportion of transient events classified as ischemic stroke [5]. High variance in practice for imaging in patients with suspected TIA would reduce the ability to compare studies from different institutions as well as from different time periods.

- Dependency on population and case-mix – The diagnosis of TIA without acute infarction depends not only on the sensitivity of imaging but also on clinical judgment as to whether the signs and symptoms are consistent with an ischemic syndrome and therefore warrant an imaging study. Hence, the prevalence of TIA without acute infarction depends on the population characteristics and the case mix, particularly the mixture of typical and atypical transient spells (see 'Typical TIA' below and 'Atypical TIA' below). There is a high variance in the prevalence of brain infarcts for TIA defined by time (ie, transient symptoms lasting <24 hours), with infarct rates ranging from 4 to 34 percent by CT and 21 to 67 percent by diffusion-weighted MRI [6].

Symptom duration and infarction — The duration of ischemic symptoms does not reliably distinguish whether a symptomatic ischemic event will result in ischemic infarction [1]. A classically defined TIA with symptoms lasting for as little as a few minutes can be associated with infarction on DWI, whereas a spell lasting for many hours may show no signs of infarction on DWI. In patients with prolonged symptoms without development of infarction, concern for a nonischemic etiology of the spell should be raised [7].

Some reports suggest that increased duration of classically defined TIA (<24 hours in duration) is associated with a higher probability of infarction on DWI, but the association is not absolute [4,8-11]. A systematic analysis of patients with classically defined TIA found that symptom duration was not a reliable predictor for the presence of infarction (figure 1), even though the mean duration tended to be significantly longer in patients with infarction than in those without infarction [4].

One potential caveat is that abnormalities on initial imaging, such as DWI obtained during or soon after symptoms, may actually be reversible injuries. However, most patients with TIA seek medical attention after their symptoms fully resolve; a low proportion (≤7 percent) of patients with classically defined TIA are admitted and scanned at the height of their symptoms [8-10,12]. Therefore, infarcts

observed in patients with classically defined TIA most likely represent permanent brain injury, as the probability of DWI reversibility decreases as the time from symptom onset to imaging increases.

EPIDEMIOLOGY

TIA is a common neurologic problem [13]. In a population-based cohort study from 1948 to 2017 of over 14,000 predominantly White participants from the Framingham Heart Study, the estimated overall incidence of TIA was 1.19 per 1000 person-years [14]. The incidence increased with age; for the age group 45 to 54 years, the incidence was 0.22 per 1000 person-years, while for the age group 85 to 94 years, the incidence was 4.88 per 1000 person-years.

In a community-based registry study from Italy, the annual incidence of TIA from 2007 to 2009 was 0.52 per 1000 population [15]. In the Cincinnati and Northern Kentucky region of the United States, where the ethnic and socioeconomic demographics are similar to that of the United States as a whole, another population-based study found that the adjusted annual incidence rate for TIA from 1993 to 1994 was 0.83 per 1000 population, and that Black individuals and men had significantly higher rates of TIA than White individuals and women [16]. From these data, it was estimated that 240,000 TIAs occurred in the United States in 2002.

The estimated overall prevalence of TIA among adults in the United States is approximately 2 percent [17]. This number is felt to under-represent the true prevalence of TIA. Poor awareness by lay-persons of the signs and symptoms of cerebral or ocular ischemia and the risk of subsequent stroke, combined with a high rate of failure to seek medical attention after a TIA, may account for this finding [18].

Use of the tissue-based definition of TIA in epidemiologic studies is likely to modestly alter the incidence and prevalence rates of TIA and stroke, but these changes are encouraged because they should reflect more accurate diagnosis [1]. Data from several reports suggest that defining TIA by the absence of infarction on imaging will decrease the annual rate of TIA by approximately 30 percent and increase the annual incidence of stroke by 7 percent [19-21].

MECHANISMS AND CLINICAL MANIFESTATIONS

A TIA should be considered a syndrome. The symptoms of a TIA depend in part upon the pathophysiologic subtype, which are divided into three main mechanisms:

- Embolic TIA, which may be artery-to-artery, or due to a cardioaortic or unknown source
- Lacunar or small penetrating vessel TIA
- Large artery, low-flow TIA

Embolic TIA — Embolic TIAs are characterized by discrete, usually single (and not stereotyped if multiple), more prolonged episodes of focal neurologic symptoms. The embolus may arise from a pathologic process in an artery, usually extracranial, or from the heart (eg, atrial fibrillation or left ventricular thrombus) or aorta. A diligent search for a potential embolic source is necessary in all cases of TIA. (See "Secondary prevention for specific causes of ischemic stroke and transient ischemic attack".)

Embolic TIAs may last hours rather than minutes as in low-flow TIAs. As an example, in one study that divided patients with TIAs into those with symptoms of short duration (less than 60 minutes) or long duration (60 minutes or greater), the latter group was more likely to have an embolic source (86 versus 46 percent) [22]. Embolic TIAs also may less likely be repetitive compared with low-flow TIAs since they are the result of emboli from a specific source (eg, a one-, two-, or three-time phenomenon). When the source of the embolus is in a proximal vessel, recurrent emboli can lodge in different branches of the parent vessel giving different symptoms.

Emboli are subject to natural thrombolysis and migration since they typically break off of fresh thrombus. They may produce transient ischemia on many occasions, but an element of silent infarction remains.

Embolic TIAs are best divided into those in the anterior cerebral circulation (carotid, anterior cerebral artery, middle cerebral artery territory) and those in the posterior cerebral circulation (vertebrobasilar, posterior cerebral artery territory). Symptoms in both circulations depend upon the size of the embolic fragment in relation to the size of the artery occluded.

- **Anterior circulation embolic TIAs** – Embolic TIAs in the anterior circulation may be large enough to occlude the middle cerebral artery stem, producing a contralateral hemiplegia secondary to ischemia in the deep white matter and basal ganglion/internal capsule lenticulostriate territory (figure 2). In addition, they may produce cortical surface symptoms. These include aphasic and dysexecutive syndromes in the dominant hemisphere and anosognosia or neglect in the nondominant hemisphere.

Smaller emboli that occlude branches of the middle cerebral artery stem result in more focal symptoms, including hand alone or arm and hand numbness, weakness, and/or heaviness induced by ischemia to the frontal area of the contralateral frontal lobe motor system (figure 3). Rarely, the symptoms also may be as specific as thumb or hand numbness or a swollen feeling, suggesting focal ischemia in the hand area of the sensory strip or parietal association cortex. Isolated upper limb weakness may implicate cervical carotid atherosclerosis as the cause of cerebral ischemic symptoms [23].

Transient monocular visual loss often signifies atherothrombotic disease in the internal carotid artery proximal to the ophthalmic artery origin (see "Amaurosis fugax (transient monocular or binocular visual loss)"). Atherothrombotic disease is most often responsible for these syndromes, although carotid dissection and embolism from the aorta, heart, or an unknown source also should be considered. In a report of 129 patients with monocular visual loss of presumed ischemic origin, diffusion-weighted MRI of the brain revealed concurrent acute brain infarcts in 24 percent [24]. These infarcts were typically small, often multiple, frequently ipsilateral to the involved eye, and usually asymptomatic. The finding of concurrent acute brain infarction in a patient with transient monocular visual loss suggests a proximal source of embolic particles that travel to both the retinal and hemispheric circulations.

- **Posterior circulation embolic TIAs** – Posterior circulation territory embolic TIAs are generally produced by emboli arising from atherothrombotic disease at the origin or distal segment of one of the vertebral arteries or of the proximal basilar artery. Emboli arising from the aortic arch, the heart, an unknown source, or from a dissecting lesion in the vertebral artery should also be considered.

  Symptoms vary according to the vertebral or basilar artery branch in which the embolus lodges (figure 4). Emboli can produce transient ataxia, dizziness, diplopia, dysarthria, quadrantanopsia, hemianopsia, numbness, crossed face and body numbness, and unilateral hearing loss. When the top of the basilar artery is embolized, sudden, overwhelming stupor or coma may ensue due to bilateral medial thalamic, subthalamus, and medial rostral midbrain reticular activating system ischemia. Emboli in the more distal branches of the posterior cerebral artery may result in a homonymous field defect or in memory loss (inferior medial temporal lobe ischemia).

Lacunar or small vessel TIA — Lacunar or penetrating or small vessel TIAs are due to transient cerebral ischemia induced by stenosis of one of the intracerebral penetrating vessels arising from the middle cerebral artery stem, the basilar artery, the vertebral artery

(figure 5), or the circle of Willis (figure 6 and figure 7). Occasionally, recurrent stereotyped TIAs occur; in this setting, the term lacunar or small vessel TIAs seems appropriate.

Most often, lacunar or small vessel TIAs are thought to be caused either by atherothrombotic obstructive lesions at the origin of the penetrating vessel or by lipohyalinosis distally within the penetrating vessel. Less commonly, embolism may cause lacunar or small vessel TIAs. (See "Lacunar infarcts", section on 'Etiology'.)

These small vessel TIAs cause symptoms similar to the lacunar strokes that are likely to follow. Thus, face, arm, and leg weakness or numbness due to ischemia in the internal capsule, pons, or thalamus may occur, similar to the symptoms due to ischemia from embolism or large vessel atherothrombotic disease or dissection. As a result, serious disease in the parent vessel must be excluded before the diagnosis of lacunar or small vessel TIA can be established with confidence.

Lacunar infarcts may be preceded by lacunar TIAs consisting of brief repetitive stereotyped clinical symptoms and signs, and lacunar stroke onset may be stepwise and progressive rather than abrupt [25-27]. Such a pattern of TIAs, or non-sudden onset in association with a lacunar syndrome, is highly suggestive of small vessel lipohyalinotic etiology [28]. (See "Lacunar infarcts".)

Low-flow TIA — Large artery low-flow TIAs are often associated with a tightly stenotic atherosclerotic lesion at the internal carotid artery origin or in the intracranial portion of the internal carotid artery (siphon) when collateral flow from the circle of Willis to the ipsilateral middle or anterior cerebral artery is impaired (figure 6 and figure 7). Other important causes include atherosclerotic stenotic lesions in the middle cerebral artery stem (figure 3) or at the junction of the vertebral and basilar artery. Any obstructive vascular process in the extracranial or intracranial arteries can cause a low-flow TIA syndrome if collateral flow to the potentially ischemic brain also is diminished.

Low-flow TIAs usually are brief (minutes) and often recurrent. They may occur as little as several times per year but typically occur more often (once per week or up to several times per day).

- **Anterior circulation low-flow TIAs** – Low-flow TIAs are generally stereotyped, especially when they are due to hemodynamically significant stenotic lesions at the origin of the internal carotid artery, at the siphon portion of the internal carotid artery where collateral flow to the circle of Willis is inadequate, or in the middle cerebral artery stem. Symptoms due to ischemia from these

lesions often include weakness or numbness of the hand, arm, leg, face, tongue, and/or cheek. Recurrent aphasic syndromes appear when there is focal ischemia in the dominant hemisphere, and recurrent neglect occurs in the presence of focal ischemia in the nondominant hemisphere ischemia. Limb-shaking TIAs are a rare, but classic, hypoperfusion syndrome of repetitive jerking movements of the arm or leg due to a severe stenosis or occlusion of the contralateral internal carotid or middle cerebral artery [29-31].

- **Posterior circulation low-flow TIAs** – In contrast, recurrent symptoms are often **not** stereotyped when the stenotic lesion that obstructs flow involves the vertebrobasilar junction or the basilar artery. The many closely packed neuronal structures in the brainstem preclude consistent manifestations of recurrent focal ischemia in this area.

  Nevertheless, certain generalizations about recurrent low-flow TIA symptoms in the posterior circulation can be made.

  - Obstructive lesions in the distal vertebral artery or at the vertebrobasilar junction usually cause dizziness that may or may not include spinning or vertigo. The patient may complain that the room is tilting or that the floor is coming up at them, rather than spinning dizziness. Patients may use the word dizziness to describe a myriad of symptoms, not necessarily spinning. Other symptoms can include numbness of one side of the body or face, dysarthria, or diplopia.

  - Ischemia in the pons from stenotic lesions in the proximal to mid-basilar artery can cause bilateral leg and arm weakness or numbness and a feeling of heaviness in addition to dizziness.

  - Ischemia in the territory of the top of the basilar artery or proximal posterior cerebral artery may present with all of the above recurrent symptoms as well as overwhelming drowsiness, vertical diplopia, eyelid drooping, and an inability to look up. Transient ischemia at the top of the basilar artery is usually due to embolism rather than low-flow TIA.

URGENCY OF EVALUATION

TIA is a neurologic emergency (table 1). Patients with TIA and minor, nondisabling stroke have a high early risk of recurrent stroke (see 'Risk of recurrent stroke' below). Recognition of TIAs can identify patients who may benefit from preventive therapy. Therefore, the initial management of suspected TIA and minor ischemic stroke includes immediate antiplatelet treatment and urgent evaluation

(algorithm 1). This is reviewed in detail separately. (See "Initial evaluation and management of transient ischemic attack and minor ischemic stroke".)

DIAGNOSIS

The diagnosis of TIA is based upon the clinical features of the transient attack and the neuroimaging findings [6]. Since few patients with suspected TIA present when fully symptomatic [32], determining the likelihood of ischemia as the cause of the event often depends upon the history as reported by the patient and witnesses.

Typical TIA — Typical TIAs are characterized by transient, focal neurologic symptoms, generally with sudden onset, that can be localized to a single vascular territory within the brain, including one or more of the following:

- Transient monocular blindness (amaurosis fugax)
- Aphasia or dysarthria
- Hemianopia
- Hemiparesis and/or hemisensory loss

In such cases, the likelihood of ischemia is relatively high. However, events consistent with typical TIA may sometimes occur due to nonischemic mechanisms such as seizure, migraine, intracerebral hemorrhage, and others. (See "Differential diagnosis of transient ischemic attack and acute stroke".)

A key problem with the diagnosis of TIA is how to determine if symptoms are caused by ischemia when brain imaging is normal. Although clinical features are not definitive for etiology, an ischemic insult is the most likely cause when the attack is consistent with a typical TIA (ie, one with transient, focal neurologic symptoms localizing to a single vascular territory).

Atypical TIA — The clinical characteristics of transient symptoms considered to be atypical of an ischemic attack include the following [33-35]:

- Gradual build-up of symptoms (more than five minutes)

- March of symptoms from one body part to another (without passing the midline)
- Progression of symptoms from one type to another
- Isolated disturbance of vision in both eyes characterized by the occurrence of positive phenomena (eg, flashing lights)
- Isolated sensory symptoms with remarkably focal distribution, such as in a finger, chin, or tongue
- Very brief spells (less than 30 seconds)
- Identical spells occurring over a period of more than one year
- Isolated brainstem symptoms, such as dysarthria, diplopia, or hearing loss
- Amnesia, confusion
- Incoordination of limbs

With atypical attacks as defined above, the likelihood of an ischemic cause may be relatively low. In several reports, the proportion of patients with atypical attacks who had acute brain infarction on diffusion weighted magnetic resonance imaging (MRI) was approximately 10 percent, suggesting that a minority of atypical spells have an ischemic cause and are therefore TIAs [6,36,37]. Alternatively, it may be the case that the sensitivity of MRI is not sufficient to reveal the ischemic lesions associated with atypical spells. One report that evaluated 275 patients with definite vertebrobasilar territory infarction found that preceding transient isolated brainstem symptoms occurred in 16 percent, suggesting that isolated brainstem symptoms can sometimes signify an ischemic attack [38].

However, there is evidence that patients with atypical TIAs characterized by negative focal symptoms (where "negative" indicates a loss of some neurologic function) have similar short- and long-term risks of subsequent ischemic stroke as do patients with typical TIAs and should therefore be investigated and treated as true TIAs. A population-based longitudinal cohort study from the United Kingdom prospectively evaluated patients with minor ischemic stroke (n = 1287), classic TIA (n = 1021), or nonconsensus TIA (n = 570), the latter defined by isolated vertigo, isolated ataxia, isolated diplopia, isolated speech disturbance (slurred speech) without aphasia, isolated bilateral decreased vision, or isolated unilateral sensory loss involving only one body part (face, arm, hand, or leg) [37]. All patients were treated according to secondary prevention guidelines; the median follow-up was 5.2 years. At baseline, the prevalence of stroke risk factors including atrial fibrillation, arterial stenoses, and patent foramen ovale was similar for nonconsensus and classic TIA. Furthermore, the 90-day stroke risk after the index event was similar for nonconsensus TIA (10.6 percent [95% CI 7.8-12.9]) and classic TIA (11.6 percent [95% CI 9.6-13.6]), as was the 10-year risk of major vascular events (27.1 versus 30.9 percent).

Differential diagnosis — The differential diagnosis of TIA (table 1) is discussed in detail separately. (See "Differential diagnosis of transient ischemic attack and acute stroke".)

RISK OF RECURRENT STROKE

TIA is a neurologic emergency because patients with time-based TIA and minor, nondisabling stroke are at increased risk of recurrent stroke, especially in the days following the event.

Factors that affect stroke risk — The risk of stroke after TIA appears to vary according to several factors, including time after the index event, presence of vascular pathologies, and the presence of acute infarction on MRI scan.

- **The first days after the event** – The risk of stroke is highest in the first days after a TIA, ranging from 1.5 to 3.5 percent in the first 48 hours after TIA, making up approximately 40 percent of the 90-day stroke risk [39-42]. The urgency associated with TIA derives also from the observation that TIAs are most likely to occur in the hours and days immediately preceding ischemic stroke. As an example, a study that analyzed four cohorts of patients who had recent ischemic stroke found that TIAs occurred most often in the 48 hours prior to the stroke [43]. Another study found that the risk of ischemic stroke occurring within 24 hours of a probable or definite TIA was approximately 5 percent [42]. Of all ischemic strokes during the 30 days after a first TIA, 42 percent occurred within the first 24 hours. This may be an overestimate related to the difficulty distinguishing a single ischemic event (stroke) with fluctuating symptoms from separate events (TIA followed by stroke) within a short period of time. Nevertheless, these observations underscore the high early risk of developing a permanent deficit after transient ischemic symptoms and the importance of urgent assessment, risk stratification, and treatment.

  Given this short time window and high risk of stroke (1.5 to 3.5 percent in the first 48 hours after TIA [39,40]) neurologic evaluation of and intervention for TIA should occur urgently. Recognition and urgent evaluation of TIAs can identify patients who may benefit from preventive therapy or from revascularization of large vessels such as the carotid artery. Premonitory carotid territory TIAs occur in approximately 50 to 75 percent of patients with ischemic stroke from extracranial carotid disease [44-46], and vertebrobasilar TIAs are associated with a risk of subsequent stroke or death that is similar to or possibly higher than that seen with carotid TIAs [47].

- **Higher risk with vascular pathologies** – TIA caused by vascular pathologies (ie, large artery atherosclerosis and small vessel disease) appears to confer a higher risk of subsequent stroke than cardiac and other nonvascular subtypes of TIA. A study from the prospective TIAregistry.org project, with over 4700 patients, found that large artery atherosclerosis was an independent risk factor for recurrent stroke [39].

  Another prospective population-based study of 1000 patients from the United Kingdom reported that TIA due to small vessel vasculopathy was associated with a higher risk of early stroke than TIA due to other causes [48]. The stroke risk was particularly elevated after multiple stereotyped small vessel TIAs occurring in a brief period of time and characterized by motor symptoms but no cortical signs, the so-called "capsular warning syndrome" [27] or "stuttering lacunar syndrome." Although data are limited, the risk of early (within seven days) stroke after such events may be as high as 40 percent or more [27,48].

- **Higher risk with infarction** – There is accumulating evidence suggesting that the findings of acute infarction on diffusion-weighted MRI (DWI) [32,49-52] or acute or chronic ischemic lesions on computed tomography (CT) [53] after a transient ischemic event are important predictors of stroke. As an example, in a pooled analysis of 3206 patients with TIA who were evaluated with DWI, the risk of stroke at seven days was much lower in patients with no infarction compared with those with infarction (0.4 versus 7.1 percent) [20]. In patients with an imaging-positive transient event, the 90-day risk of stroke appears to be as high as 14 percent [32,49,50,54]. In contrast, after an imaging-negative transient event, the corresponding risk is <1 percent.

- **Is the stroke risk after TIA declining over time?** – In a 2016 report from the TIAregistry.org project, a prospective multinational registry of over 4700 patients with TIA or minor stroke (defined by a modified Rankin scale score of 0 or 1 when first evaluated), the estimated risks of stroke at 2, 30, 90, and 365 days after the index event were 1.5, 2.8, 3.7, and 5.1 percent, respectively [39]. In a 2018 follow-up study, the estimated cumulative risk of stroke at five years after the index event was 9.5 percent [55]. These rates are lower than those previously reported [40,56,57], possibly due to the more rapid implementation of newer and more effective strategies for the secondary prevention of ischemic stroke; the registry included only sites with dedicated systems for the urgent evaluation of TIA, and most patients were seen by a stroke specialist within 24 hours of symptom onset. Independent risk factors for recurrent stroke were multiple infarctions on brain imaging, large artery atherosclerosis, and an $ABCD^2$ score of 6 or 7. (See 'Stroke risk stratification' below.)

A systematic review and meta-analysis of 68 studies published from 1971 to March 2019 that included over 200,000 patients found that the risk of stroke after TIA was 2.4 percent within two days, 3.8 percent within seven days, 4.1 percent within 30 days, and 4.7 percent within 90 days [41]. The incidence of stroke was lower among study populations enrolled after 1999. Similarly, in a longitudinal population-based cohort study from the Framingham Heart Study that included over 14,000 participants from 1948 to 2017 with no history of TIA or stroke at baseline, the risk of stroke after TIA was lower in the epoch of 2000 to 2017 compared with 1948 to 1985 [14].

High-risk lesions — There are four pathologic processes that give rise to embolic TIAs or low-flow TIAs and that can produce sudden devastating stroke if not recognized and treated.

- **Internal carotid artery atherosclerosis** – An atherothrombotic stenotic lesion at the origin of the internal carotid artery that is narrowed to more than 70 percent of its normal lumen diameter poses a threat of embolic or low-flow TIA or stroke [58-61]. Even a 50 percent stenosis may be important when considering carotid endarterectomy for prevention of a secondary stroke or of a primary stroke when a TIA has occurred. In this setting, embolism is more common than low flow as a cause of TIA or stroke. (See "Management of symptomatic carotid atherosclerotic disease".)

  Prospective natural history studies of asymptomatic atherothrombotic disease at the origin of the internal carotid artery (mostly asymptomatic carotid artery bruits) suggest that the rate of ipsilateral stroke increases dramatically when the residual lumen diameter narrows to greater than 70 percent stenosis (figure 8 and figure 9) [62-64]. In one series of 500 patients with asymptomatic cervical bruits, the incidence of stroke was 1.7 percent per year overall but 5.5 percent per year in those with more than a 75 percent carotid artery stenosis [63].

  This degree of stenosis corresponds to a residual lumen diameter of 1.5 mm, the precise point at which pressure drops across the stenotic lesion [65,66]. When the pressure drops, flow to the ipsilateral middle cerebral artery stem is in part supplied by collateral circulation from the circle of Willis and from the external carotid to ophthalmic to distal internal carotid artery system (figure 6 and figure 7). Less flow is provided by the internal carotid artery as the lesion further narrows. We believe that this provides a milieu for thrombus formation at the site of the stenosis and subsequent embolism. When the circle of Willis is compromised, low-flow TIA ensues.

- **Intracranial atherothrombotic disease** — Intracranial atherothrombotic disease that produces low-flow or embolic TIA most commonly occurs at the distal vertebral artery/vertebrobasilar junction/proximal basilar artery site. The potential of this lesion to precipitate a disastrous stroke by thrombosis, thrombus propagation, and embolism is extremely important. The other two most important, but less common, sites include the siphon portion of the internal carotid artery and the middle cerebral artery stem. The common carotid artery origin and the vertebral artery origin are much less problematic since they only rarely give rise to artery-to-artery emboli.

  The ability to noninvasively diagnose and follow these intracranial arterial lesions with precision through MRI angiography, CT angiography, duplex Doppler, and transcranial Doppler flow assessment allows for important preventive therapeutic considerations. (See "Intracranial large artery atherosclerosis: Treatment and prognosis" and "Secondary prevention for specific causes of ischemic stroke and transient ischemic attack".)

- **Arterial, aortic, or cardiac sources of emboli** — Emboli at the top of the basilar artery or the middle cerebral artery stem that come from a source below — arterial, aortic, or cardiac — are extremely important to recognize since they may produce fluctuating symptoms or TIAs prior to a devastating stroke. Transient focal symptoms due to an embolus at these sites occur because blood flow reestablishes itself around the embolus.

  The symptoms may return in abundance and produce a stroke when the embolus itself causes a thrombus that further occludes the artery. This can occur hours or even days after the embolus has lodged at the site because it did not migrate or lyse.

- **Dissection lesions** — Dissection lesions at the origin of the petrous portion of the internal carotid artery or at the C1-2 level of the vertebral artery as it enters the foramen transversarium cause symptoms of cerebral ischemia due to low flow or embolism, which occur within minutes, hours, or even days prior to a devastating stroke. Modern neurovascular imaging technology can establish the diagnosis noninvasively. (See "Cerebral and cervical artery dissection: Clinical features and diagnosis" and "Cerebral and cervical artery dissection: Treatment and prognosis".)

Stroke risk stratification — Methods that can reliably assess the risk of stroke after TIA in individual patients would be useful for triaging patients. The discussion that follows applies to the traditional time-based definition of TIA, which is characterized clinically by the temporary nature (<24 hours) of the associated neurologic symptoms.

ABCD2 score — A simple but suboptimal assessment called the ABCD^2 score (ie, ABCD squared, for Age, Blood pressure, Clinical features, Duration of symptoms, and Diabetes) was designed to identify patients at high risk of ischemic stroke in the first seven days after TIA (table 2) [67]. Despite the score's simplicity, it is often miscalculated [68]. The ABCD^2 score is tallied as follows (calculator 1):

- Age (≥60 years = 1 point)
- Blood pressure elevation when first assessed after TIA (systolic ≥140 mmHg or diastolic ≥90 mmHg = 1 point)
- Clinical features (unilateral weakness = 2 points; isolated speech disturbance = 1 point; other = 0 points)
- Duration of TIA symptoms (≥60 minutes = 2 points; 10 to 59 minutes = 1 point; <10 minutes = 0 points)
- Diabetes (present = 1 point)

Estimated two-day stroke risks determined by the ABCD^2 score in the combined derivation and validation cohorts were as follows [67]:

- Score 6 to 7: High two-day stroke risk (8 percent)
- Score 4 to 5: Moderate two-day stroke risk (4 percent)
- Score 0 to 3: Low two-day stroke risk (1 percent)

The ABCD^2 score was designed to be used in primary care settings to stratify patients according to stroke risk and thus identify those who required emergency assessment by specialists. However, its predictive performance is not satisfactory. A systematic review and meta-analysis of 29 studies that included over 13,700 patients with TIA found that the ABCD^2 score did not reliably distinguish those with a low and high risk of recurrent stroke, or those with TIAs and TIA mimics [69].

An earlier meta-analysis found that the score performance was poor in settings of low baseline risk and in TIA diagnosed by nonspecialists [70].

The predictive power of the ABCD^2 score is generally lower in hospital settings compared with population-based settings, thus limiting its utility for high-risk populations [67,71,72].

Other risk models — Risk models that combine information from acute DWI, noninvasive angiography, and presumed TIA etiology improve the accuracy of stroke risk prediction after TIA [20,32,49,73-77]. There are a number of examples:

- Several scores are based upon the conventional $ABCD^2$ score:
  - The Clinical- and Imaging-based Prediction (CIP) model incorporates diffusion-weighted MRI findings with a dichotomized $ABCD^2$ score [32].
  - The $ABCD^2$-I score adds information about brain infarction on diffusion-weighted MRI or CT [20].
  - The $ABCD^3$-I score assigns points for an earlier TIA within seven days of the index event and further incorporates data from initial diagnostic brain and carotid imaging [73].
- The Canadian TIA Score (table 3) estimates the probability of stroke within seven days of a TIA and is based upon nine items from the history and examination and four items from investigations that were correlated with having an impending stroke [78]. The total score ranges from -3 to 23. In the derivation study, scores ≤5 were associated with a low risk (≤0.5 percent) of subsequent stroke, while scores from 6 to 9 were associated with an intermediate risk (approximately 1 to 3 percent), and scores ≥10 were associated with a high risk (≥5 percent). In a prospective cohort study of over 7000 patients with TIA, the Canadian TIA Score was more accurate compared with the $ABCD^2$ or the $ABCD^2$-I for predicting subsequent stroke or carotid artery revascularization [79].
- The Recurrence Risk Estimator (RRE) score combines clinical (recent history of stroke or TIA plus admission stroke subtype) and imaging information (location, multiplicity, distribution, and age of brain infarcts) [74] for predicting recurrent stroke following TIA with infarction [80,81]. As mentioned above, time-based TIA associated with acute brain infarction is a high-risk condition, and the RRE is the only predictive score that can be used to further stratify the risk in this particular population. The score identifies subsets of patients with a seven-day stroke risk that is as low as 1 percent and as high as 40 percent. The RRE score was externally validated in a multicenter cohort of over 1400 patients with acute ischemic stroke [82].

Additional research and validation of these models is needed to determine whether these stroke risk stratification models have any utility for clinical practice. The requirement for MRI limits the widespread applicability of advanced risk prediction models.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Stroke in adults".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Transient ischemic attack (The Basics)")
- Beyond the Basics topic (see "Patient education: Transient ischemic attack (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Time-based definition** – The classic, time-based definition of transient ischemic attack (TIA) is a sudden onset of a focal neurologic symptom and/or sign lasting less than 24 hours, caused by a transient decrease in blood supply to the brain, spinal cord, or retina. Although still widely used, this classic definition is inadequate because even relatively brief ischemia can cause permanent neurologic or retinal injury. A substantial proportion of patients with a classically defined TIA (<24 hours in duration) have corresponding ischemic lesions on diffusion-weighted or perfusion-weighted magnetic resonance imaging (MRI) that could explain the transient clinical manifestations. The associated infarctions are often very small. (See 'Traditional time-based definition of TIA' above.)

- **Tissue-based definition** – The tissue-based definition of TIA is defined as a transient episode of neurologic dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction. Defining TIA by the absence of infarction means that the end point is biological (tissue injury) rather than arbitrary (24 hours). In addition, this tissue-based definition encourages the use of neurodiagnostic tests to identify brain injury and its cause. (See 'Tissue-based definition of TIA' above.)

- **Mechanisms** – The symptoms of a TIA depend in part upon the pathophysiologic subtype, which are divided into three main mechanisms (see 'Mechanisms and clinical manifestations' above):

  - Embolic TIA, which may be artery-to-artery, or due to a cardioaortic or unknown source. (See 'Embolic TIA' above.)
  - Lacunar or small penetrating vessel TIA. (See 'Lacunar or small vessel TIA' above.)
  - Large artery, low-flow TIA. (See 'Low-flow TIA' above.)

- **Neurologic emergency** – TIA is a neurologic emergency. Therefore, the initial evaluation of suspected TIA and minor ischemic stroke requires urgent evaluation (algorithm 1). (See 'Urgency of evaluation' above and "Initial evaluation and management of transient ischemic attack and minor ischemic stroke", section on 'Urgent investigations'.)

- **Clinical features and diagnosis** – The diagnosis of TIA is based upon the clinical features of the transient attack and the neuroimaging findings. (See 'Diagnosis' above.)

  - **Typical TIAs** – Typical TIAs are characterized by transient, focal neurologic symptoms that can be localized to a single vascular territory within the brain, including one or more of the following (see 'Typical TIA' above):

    - Transient monocular blindness (amaurosis fugax)
    - Aphasia or dysarthria
    - Hemianopia
    - Hemiparesis and/or hemisensory loss

  - **Atypical TIAs** – Atypical spells suggestive of TIA (table 1) may be less likely to have an ischemic cause, but atypical TIAs characterized by negative focal symptoms (where "negative" indicates a loss of some neurologic function) have similar short-

and long-term risks of subsequent ischemic stroke, as do patients with typical TIAs, and should therefore be investigated and treated as true TIAs. (See 'Atypical TIA' above.)

- **Differential diagnosis** – The differential diagnosis of TIA is summarized in the table (table 1) and discussed in detail separately. (See "Differential diagnosis of transient ischemic attack and acute stroke".)

- **Risk of stroke** – Both traditionally defined TIA (ie, time-based, lasting <24 hours) and minor ischemic stroke are associated with a high early risk of recurrent stroke. The stroke risk in the first two days after TIA is approximately 1.5 to 3.5 percent. The $ABCD^2$ score (table 2) was designed to identify patients at high risk of ischemic stroke in this time period, but its predictive performance is not optimal. Risk stratification models that combine information from brain imaging, vascular imaging, and presumed TIA etiology in addition to the clinical $ABCD^2$ score may improve the accuracy of stroke risk prediction after TIA. (See 'Risk of recurrent stroke' above.)

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REFERENCES

1. Easton JD, Saver JL, Albers GW, et al. Definition and evaluation of transient ischemic attack: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association Stroke Council; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; and the Interdisciplinary Council on Peripheral Vascular Disease. The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists. Stroke 2009; 40:2276.

2. Sacco RL, Kasner SE, Broderick JP, et al. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2013; 44:2064.
3. Albers GW, Caplan LR, Easton JD, et al. Transient ischemic attack--proposal for a new definition. N Engl J Med 2002; 347:1713.
4. Ay H, Koroshetz WJ, Benner T, et al. Transient ischemic attack with infarction: a unique syndrome? Ann Neurol 2005; 57:679.
5. Förster A, Gass A, Kern R, et al. Brain imaging in patients with transient ischemic attack: a comparison of computed tomography and magnetic resonance imaging. Eur Neurol 2012; 67:136.
6. Sorensen AG, Ay H. Transient ischemic attack: definition, diagnosis, and risk stratification. Neuroimaging Clin N Am 2011; 21:303.
7. Toole JF. The Willis lecture: transient ischemic attacks, scientific method, and new realities. Stroke 1991; 22:99.
8. Kidwell CS, Alger JR, Di Salle F, et al. Diffusion MRI in patients with transient ischemic attacks. Stroke 1999; 30:1174.
9. Engelter ST, Provenzale JM, Petrella JR, Alberts MJ. Diffusion MR imaging and transient ischemic attacks. Stroke 1999; 30:2762.
10. Crisostomo RA, Garcia MM, Tong DC. Detection of diffusion-weighted MRI abnormalities in patients with transient ischemic attack: correlation with clinical characteristics. Stroke 2003; 34:932.
11. Rovira A, Rovira-Gols A, Pedraza S, et al. Diffusion-weighted MR imaging in the acute phase of transient ischemic attacks. AJNR Am J Neuroradiol 2002; 23:77.
12. Ay H, Oliveira-Filho J, Buonanno FS, et al. 'Footprints' of transient ischemic attacks: a diffusion-weighted MRI study. Cerebrovasc Dis 2002; 14:177.
13. Virani SS, Alonso A, Aparicio HJ, et al. Heart Disease and Stroke Statistics-2021 Update: A Report From the American Heart Association. Circulation 2021; 143:e254.
14. Lioutas VA, Ivan CS, Himali JJ, et al. Incidence of Transient Ischemic Attack and Association With Long-term Risk of Stroke. JAMA 2021; 325:373.
15. Cancelli I, Janes F, Gigli GL, et al. Incidence of transient ischemic attack and early stroke risk: validation of the ABCD2 score in an Italian population-based study. Stroke 2011; 42:2751.
16. Kleindorfer D, Panagos P, Pancioli A, et al. Incidence and short-term prognosis of transient ischemic attack in a population-based study. Stroke 2005; 36:720.

17. Johnston SC, Fayad PB, Gorelick PB, et al. Prevalence and knowledge of transient ischemic attack among US adults. Neurology 2003; 60:1429.
18. Wang Y, Zhao X, Jiang Y, et al. Prevalence, knowledge, and treatment of transient ischemic attacks in China. Neurology 2015; 84:2354.
19. Ovbiagele B, Kidwell CS, Saver JL. Epidemiological impact in the United States of a tissue-based definition of transient ischemic attack. Stroke 2003; 34:919.
20. Giles MF, Albers GW, Amarenco P, et al. Addition of brain infarction to the ABCD2 Score (ABCD2I): a collaborative analysis of unpublished data on 4574 patients. Stroke 2010; 41:1907.
21. Mullen MT, Cucchiara BL. Redefinition of transient ischemic attack improves prognosis of transient ischemic attack and ischemic stroke: an example of the will rogers phenomenon. Stroke 2011; 42:3612.
22. Kimura K, Minematsu K, Yasaka M, et al. The duration of symptoms in transient ischemic attack. Neurology 1999; 52:976.
23. Topcuoglu MA, Rocha EA, Siddiqui AK, et al. Isolated Upper Limb Weakness From Ischemic Stroke: Mechanisms and Outcome. J Stroke Cerebrovasc Dis 2018; 27:2712.
24. Helenius J, Arsava EM, Goldstein JN, et al. Concurrent acute brain infarcts in patients with monocular visual loss. Ann Neurol 2012; 72:286.
25. Fisher CM. Lacunar strokes and infarcts: a review. Neurology 1982; 32:871.
26. Kappelle LJ, van Latum JC, Koudstaal PJ, van Gijn J. Transient ischaemic attacks and small-vessel disease. Dutch TIA Study Group. Lancet 1991; 337:339.
27. Donnan GA, O'Malley HM, Quang L, et al. The capsular warning syndrome: pathogenesis and clinical features. Neurology 1993; 43:957.
28. Hervé D, Gautier-Bertrand M, Labreuche J, et al. Predictive values of lacunar transient ischemic attacks. Stroke 2004; 35:1430.
29. Persoon S, Kappelle LJ, Klijn CJ. Limb-shaking transient ischaemic attacks in patients with internal carotid artery occlusion: a case-control study. Brain 2010; 133:915.
30. Ali S, Khan MA, Khealani B. Limb-shaking Transient Ischemic Attacks: case report and review of literature. BMC Neurol 2006; 6:5.

31. Richardson TE, Beech P, Cloud GC. Limb-shaking TIA: a case of cerebral hypoperfusion in severe cerebrovascular disease in a young adult. BMC Neurol 2021; 21:260.
32. Ay H, Arsava EM, Johnston SC, et al. Clinical- and imaging-based prediction of stroke risk after transient ischemic attack: the CIP model. Stroke 2009; 40:181.
33. Fisher CM. Late-life migraine accompaniments--further experience. Stroke 1986; 17:1033.
34. Special report from the National Institute of Neurological Disorders and Stroke. Classification of cerebrovascular diseases III. Stroke 1990; 21:637.
35. Amarenco P. Transient Ischemic Attack. N Engl J Med 2020; 382:1933.
36. Lavallée PC, Sissani L, Labreuche J, et al. Clinical Significance of Isolated Atypical Transient Symptoms in a Cohort With Transient Ischemic Attack. Stroke 2017; 48:1495.
37. Tuna MA, Rothwell PM, Oxford Vascular Study. Diagnosis of non-consensus transient ischaemic attacks with focal, negative, and non-progressive symptoms: population-based validation by investigation and prognosis. Lancet 2021; 397:902.
38. Paul NL, Simoni M, Rothwell PM, Oxford Vascular Study. Transient isolated brainstem symptoms preceding posterior circulation stroke: a population-based study. Lancet Neurol 2013; 12:65.
39. Amarenco P, Lavallée PC, Labreuche J, et al. One-Year Risk of Stroke after Transient Ischemic Attack or Minor Stroke. N Engl J Med 2016; 374:1533.
40. Wu CM, McLaughlin K, Lorenzetti DL, et al. Early risk of stroke after transient ischemic attack: a systematic review and meta-analysis. Arch Intern Med 2007; 167:2417.
41. Shahjouei S, Sadighi A, Chaudhary D, et al. A 5-Decade Analysis of Incidence Trends of Ischemic Stroke After Transient Ischemic Attack: A Systematic Review and Meta-analysis. JAMA Neurol 2021; 78:77.
42. Chandratheva A, Mehta Z, Geraghty OC, et al. Population-based study of risk and predictors of stroke in the first few hours after a TIA. Neurology 2009; 72:1941.
43. Rothwell PM, Warlow CP. Timing of TIAs preceding stroke: time window for prevention is very short. Neurology 2005; 64:817.
44. Mohr JP, Caplan LR, Melski JW, et al. The Harvard Cooperative Stroke Registry: a prospective registry. Neurology 1978; 28:754.

45. Pessin MS, Hinton RC, Davis KR, et al. Mechanisms of acute carotid stroke. Ann Neurol 1979; 6:245.
46. Russo LS Jr. Carotid system transient ischemic attacks: clinical, racial, and angiographic correlations. Stroke 1981; 12:470.
47. Flossmann E, Rothwell PM. Prognosis of vertebrobasilar transient ischaemic attack and minor stroke. Brain 2003; 126:1940.
48. Paul NL, Simoni M, Chandratheva A, Rothwell PM. Population-based study of capsular warning syndrome and prognosis after early recurrent TIA. Neurology 2012; 79:1356.
49. Calvet D, Touzé E, Oppenheim C, et al. DWI lesions and TIA etiology improve the prediction of stroke after TIA. Stroke 2009; 40:187.
50. Asimos AW, Rosamond WD, Johnson AM, et al. Early diffusion weighted MRI as a negative predictor for disabling stroke after ABCD2 score risk categorization in transient ischemic attack patients. Stroke 2009; 40:3252.
51. Purroy F, Montaner J, Rovira A, et al. Higher risk of further vascular events among transient ischemic attack patients with diffusion-weighted imaging acute ischemic lesions. Stroke 2004; 35:2313.
52. Al-Khaled M, Eggers J. MRI findings and stroke risk in TIA patients with different symptom durations. Neurology 2013; 80:1920.
53. Sciolla R, Melis F, SINPAC Group. Rapid identification of high-risk transient ischemic attacks: prospective validation of the ABCD score. Stroke 2008; 39:297.
54. Giles MF, Albers GW, Amarenco P, et al. Early stroke risk and ABCD2 score performance in tissue- vs time-defined TIA: a multicenter study. Neurology 2011; 77:1222.
55. Amarenco P, Lavallée PC, Monteiro Tavares L, et al. Five-Year Risk of Stroke after TIA or Minor Ischemic Stroke. N Engl J Med 2018; 378:2182.
56. Giles MF, Rothwell PM. Risk of stroke early after transient ischaemic attack: a systematic review and meta-analysis. Lancet Neurol 2007; 6:1063.
57. van Wijk I, Kappelle LJ, van Gijn J, et al. Long-term survival and vascular event risk after transient ischaemic attack or minor ischaemic stroke: a cohort study. Lancet 2005; 365:2098.
58. North American Symptomatic Carotid Endarterectomy Trial Collaborators, Barnett HJM, Taylor DW, et al. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. N Engl J Med 1991; 325:445.
59. Kistler JP, Buonanno FS, Gress DR. Carotid endarterectomy--specific therapy based on pathophysiology. N Engl J Med 1991; 325:505.

60. MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70-99%) or with mild (0-29%) carotid stenosis. European Carotid Surgery Trialists' Collaborative Group. Lancet 1991; 337:1235.
61. Mayberg MR, Wilson SE, Yatsu F, et al. Carotid endarterectomy and prevention of cerebral ischemia in symptomatic carotid stenosis. Veterans Affairs Cooperative Studies Program 309 Trialist Group. JAMA 1991; 266:3289.
62. Roederer GO, Langlois YE, Jager KA, et al. The natural history of carotid arterial disease in asymptomatic patients with cervical bruits. Stroke 1984; 15:605.
63. Chambers BR, Norris JW. Outcome in patients with asymptomatic neck bruits. N Engl J Med 1986; 315:860.
64. Meissner I, Wiebers DO, Whisnant JP, O'Fallon WM. The natural history of asymptomatic carotid artery occlusive lesions. JAMA 1987; 258:2704.
65. Suwanwela N, Can U, Furie KL, et al. Carotid Doppler ultrasound criteria for internal carotid artery stenosis based on residual lumen diameter calculated from en bloc carotid endarterectomy specimens. Stroke 1996; 27:1965.
66. Can U, Furie KL, Suwanwela N, et al. Transcranial Doppler ultrasound criteria for hemodynamically significant internal carotid artery stenosis based on residual lumen diameter calculated from en bloc endarterectomy specimens. Stroke 1997; 28:1966.
67. 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.
68. Perry JJ, Sharma M, Sivilotti ML, et al. Prospective validation of the ABCD2 score for patients in the emergency department with transient ischemic attack. CMAJ 2011; 183:1137.
69. Wardlaw JM, Brazzelli M, Chappell FM, et al. ABCD2 score and secondary stroke prevention: meta-analysis and effect per 1,000 patients triaged. Neurology 2015; 85:373.
70. Sanders LM, Srikanth VK, Blacker DJ, et al. Performance of the ABCD2 score for stroke risk post TIA: meta-analysis and probability modeling. Neurology 2012; 79:971.
71. Stead LG, Suravaram S, Bellolio MF, et al. An assessment of the incremental value of the ABCD2 score in the emergency department evaluation of transient ischemic attack. Ann Emerg Med 2011; 57:46.

72. Amarenco P, Labreuche J, Lavallée PC. Patients with transient ischemic attack with ABCD2 <4 can have similar 90-day stroke risk as patients with transient ischemic attack with ABCD2 ≥4. Stroke 2012; 43:863.

73. Merwick A, Albers GW, Amarenco P, et al. Addition of brain and carotid imaging to the ABCD^2 score to identify patients at early risk of stroke after transient ischaemic attack: a multicentre observational study. Lancet Neurol 2010; 9:1060.

74. Ay H, Gungor L, Arsava EM, et al. A score to predict early risk of recurrence after ischemic stroke. Neurology 2010; 74:128.

75. Yaghi S, Rostanski SK, Boehme AK, et al. Imaging Parameters and Recurrent Cerebrovascular Events in Patients With Minor Stroke or Transient Ischemic Attack. JAMA Neurol 2016; 73:572.

76. Kelly PJ, Albers GW, Chatzikonstantinou A, et al. Validation and comparison of imaging-based scores for prediction of early stroke risk after transient ischaemic attack: a pooled analysis of individual-patient data from cohort studies. Lancet Neurol 2016; 15:1238.

77. Lemmens R, Smet S, Thijs VN. Clinical scores for predicting recurrence after transient ischemic attack or stroke: how good are they? Stroke 2013; 44:1198.

78. Perry JJ, Sharma M, Sivilotti ML, et al. A prospective cohort study of patients with transient ischemic attack to identify high-risk clinical characteristics. Stroke 2014; 45:92.

79. Perry JJ, Sivilotti MLA, Émond M, et al. Prospective validation of Canadian TIA Score and comparison with ABCD2 and ABCD2i for subsequent stroke risk after transient ischaemic attack: multicentre prospective cohort study. BMJ 2021; 372:n49.

80. Arsava EM, Furie KL, Schwamm LH, et al. Prediction of early stroke risk in transient symptoms with infarction: relevance to the new tissue-based definition. Stroke 2011; 42:2186.

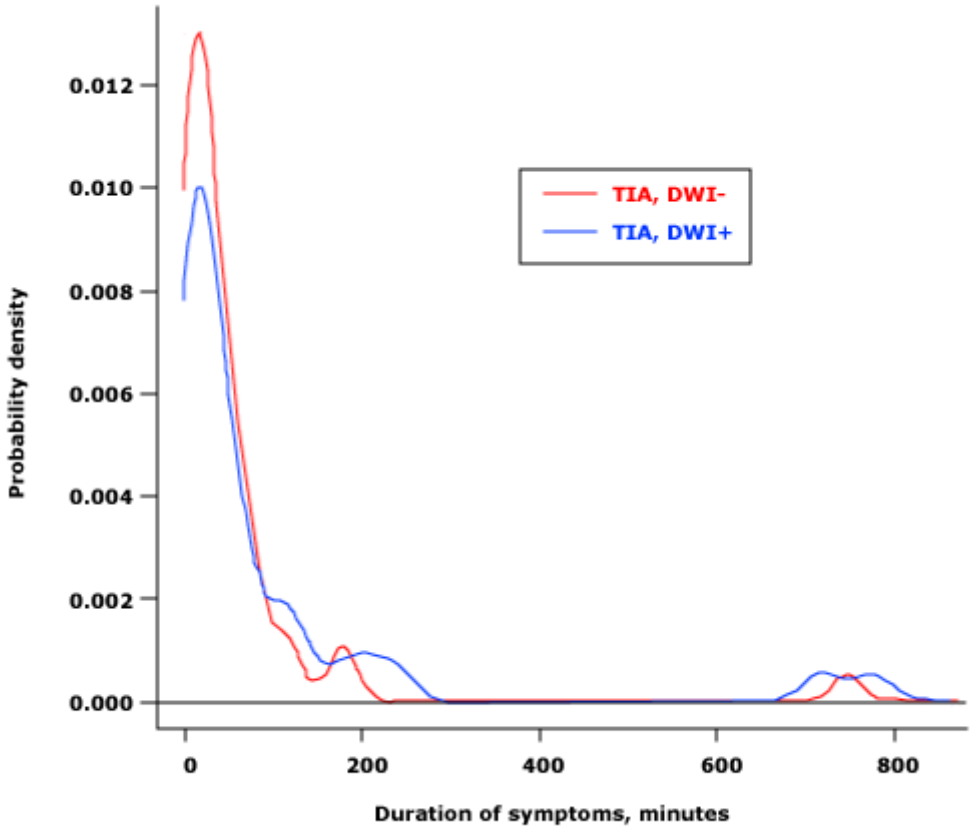
81. Maier IL, Bauerle M, Kermer P, et al. Risk prediction of very early recurrence, death and progression after acute ischaemic stroke. Eur J Neurol 2013; 20:599.

82. Arsava EM, Kim GM, Oliveira-Filho J, et al. Prediction of Early Recurrence After Acute Ischemic Stroke. JAMA Neurol 2016; 73:396.

Topic 1088 Version 24.0

GRAPHICS

Temporal behavior of symptoms in patients with transient ischemic attack (TIA)



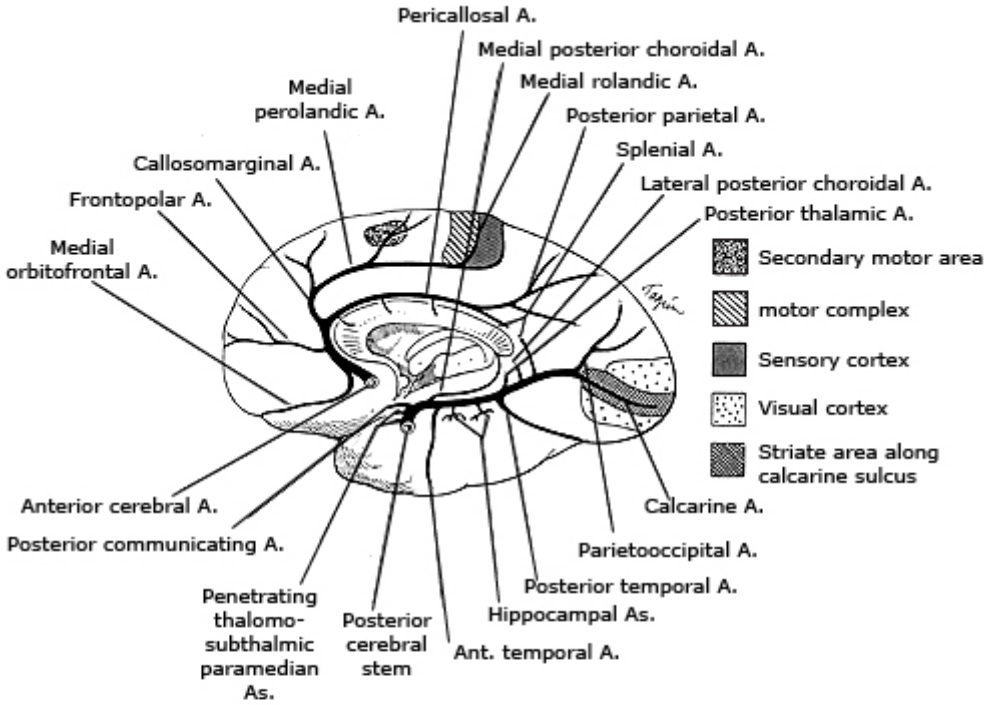
The probability density function curve of symptom duration for transient symptoms associated with infarction (TSI) indicates the absence of continuity within the first 24 hours. The probability density function is the probability that the variable takes a value in a given interval and is equal to 1 over its entire range of values. The area under curve is almost equal to 1 at around 200 minutes. Also note that the curves for TIA with or without infarction overlap (p

= 0.82). The distribution of duration of symptoms as seen here suggests that symptom duration is not a reliable feature to be used for predicting whether a transient neurological spell is associated with infarction.

DWI: diffusion-weighted magnetic resonance imaging.

Graphic 82729 Version 1.0

Anterior cerebral artery distribution and signs and symptoms of occlusion



Signs and symptoms of occlusion	Structures involved
Paralysis of opposite foot and leg	Motor leg area
A lesser degree of opposite arm paresis	Involvement of arm cortex or fibers descending to corona radiata
Cortical sensory loss over toes, foot, and leg	Sensory area for foot and leg
Urinary incontinence	Sensorimotor area in paracentral lobule
Contralateral grasp reflex, sucking reflex, gegenhalten (paratonic rigidity)	Medial surface of the posterior frontal lobe ?Supplemental motor area
Abulia (akinetic mutism), slowness, delay, intermittent interruption, lack of spontaneity, whispering, reflex distraction to sights and sounds	Uncertain localization - probably cingulate gyrus and medial inferior portion of frontal, parietal, and temporal lobes
Impairment of gait and stance (gait apraxia)	Frontal cortex near leg motor area
Dyspraxia of left limbs, tactile aphasia in left limbs	Corpus collusum

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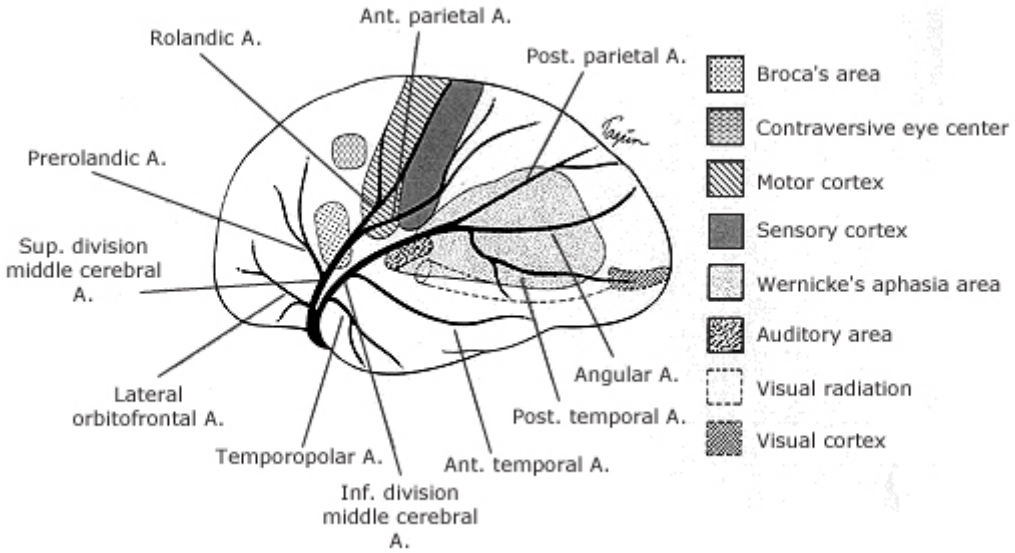
Companies, Inc.

Graphic 60945 Version 3.0

Middle cerebral artery distribution and signs and symptoms of occlusion



Signs and symptoms of occlusion	Structures involved
Paralysis of contralateral face, arm, and leg; sensory impairment over the same area (pinprick, cotton touch, vibration, position, two-point discrimination, stereognosis, tactile localization, barognosis, cutaneographia	Somatic motor area for face and arm and the fibers descending from the leg area to enter the corona radiata and corresponding somatic sensory system
Motor aphasia	Motor speech area of the dominant hemisphere
Central aphasia, word deafness, anomia, jargon speech, sensory agraphia, acalculia, alexia, finger agnosia, right-left confusion	Central, suprasylvian speech area and parieto-occipital cortex of the dominant hemisphere
Apractognosia of the minor hemisphere (amorphosynthesis), anosognosia, hemisomatognosia, unilateral neglect, agnosia for the left half of external space, dressing "apraxia," contstructional "apraxia," distortion of visual coordinates, innacurate localization in the half field, impaired ability to judge distance, upside-down reading, visual illusions	Nondominant parietal lobe (area corresponding to speech area in dominant hemisphere); loss of topographic memory is usually due to a nondominant lesion, occasionally to a dominant one
Homonymous hemianopsia (often homonymous inferior quadrantonopsia	Optic radiation deep to [redacted]

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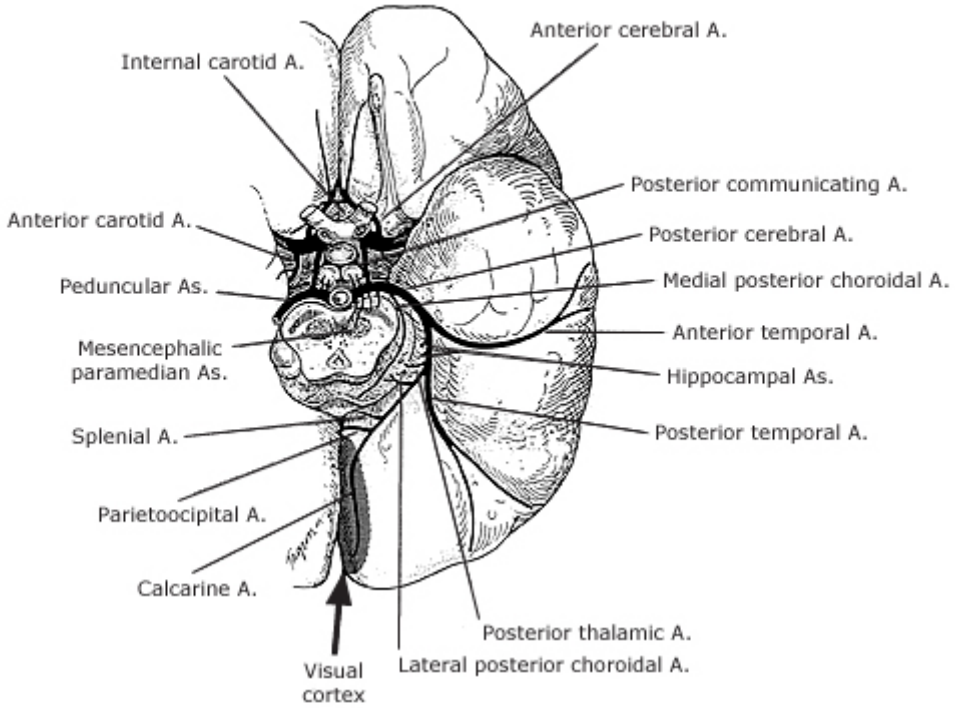
Graphic 81813 Version 2.0

Posterior cerebral artery distribution and signs and symptoms of occlusion



Signs and symptoms of occlusion	Structures involved
Peripheral territory	
Homonymous hemianopsia (often upper quadrantic)	Calcarine cortex or optic radiation nearby
Bilateral homonymous hemianopsia, cortical blindness, awareness or denial of blindness, tactile naming, achromatopsia (color blindness), failure to see to and fro movements, inability to perceive objects not centrally located, apraxia of ocular movements, inability to count or enumerate objects	Bilateral occipital lobe with possibly parietal lobe
Verbal dyslexia without agraphia, color anomia	Dominant calcarine lesion, posterior corpus callosum
Memory defect	Hippocampal lesion bilaterally or dominant side only
Topographic disorientation and prosopagnosia	Usually nondominant calcarine and lingual gyrus
Simultagnosia, hemivisual neglect	Dominant visual cortex, contralateral hemisphere
Unformed visual hallucinations, peduncular hallucinosis, metamorphopsia, teleopsia, illusory visual spread, distortion of outlines, central photophobia	Calcarine cortex
Complex hallucinations	Usually nondominant hemisphere
Central territory	
Thalamic syndrome: sensory loss (all modalities), spontaneous pain and dysesthesias, choreoathetosis, intention tremor, hand spasm, mild hemiparesis	Posteroventral nucleus of thalamus, involvement of adjacent subthalamus body or its afferent tracts
Thalamoperforate syndrome: crossed cerebellar ataxia with ipsilateral third nerve palsy	Dentatothalamic tract and issuing third nerve
Third nerve palsy and contralateral hemiplegia	Third nerve and cerebral peduncle

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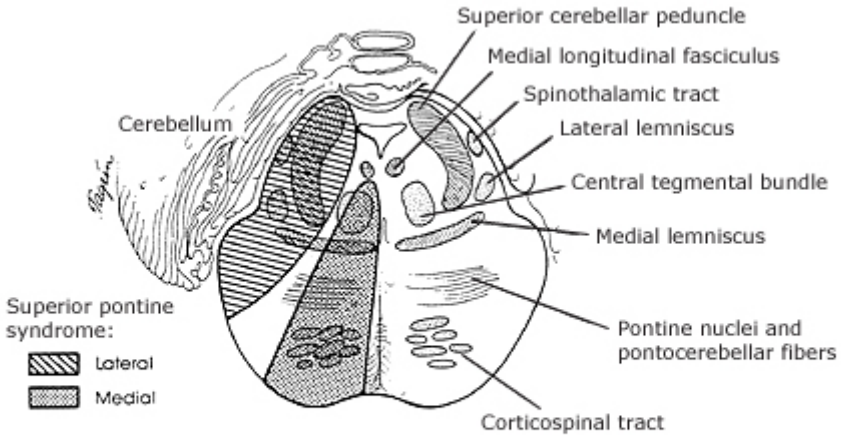
Graphic 60416 Version 2.0

Superior pontine syndrome



Signs and symptoms of occlusion	Structures involved
Medial superior pontine syndrome (paramedian branches of upper basilar artery)	
On side of lesion:	
Cerebellar ataxia (probably)	Superior and/or middle cerebellar peduncle
Internuclear ophthalmoplegia	Medial longitudinal fasciculus
Myoclonic syndrome, palate, pharynx, vocal cords, respiratory apparatus, face, occulomotor, etc..	Localization uncertain
On side opposite lesion:	
Paralysis of face, arm and leg	Corticobulbar and corticospinal tract
Rarely touch, vibration, and position affected	Medial lemniscus
Lateral superior pontine syndrome (syndrome of superior cerebellar artery)	
On side of lesion:	
Ataxia of limbs and gait, falling to side of lesion	Middle and superior cerebellar peduncles, superior surface of cerebellum, dentate nucleus
Dizziness, nausea, vomiting, horizontal nystagmus	Vestibular nucleus
Paresis of conjugate gaze (ipsilateral)	Pontine contralateral gaze
Skew deviation	Uncertain
Miosis, ptosis, decreased sweating over face	Descending sympathetic fibers
On side opposite lesion:	
Impaired pain and thermal sense on face, limbs, trunk	Spinothalamic tract
Impaired touch, vibration, and position sense, more in leg than arm (there is a tendency to incongruity of pain and touch deficits)	Medial lemniscus (lateral portion)

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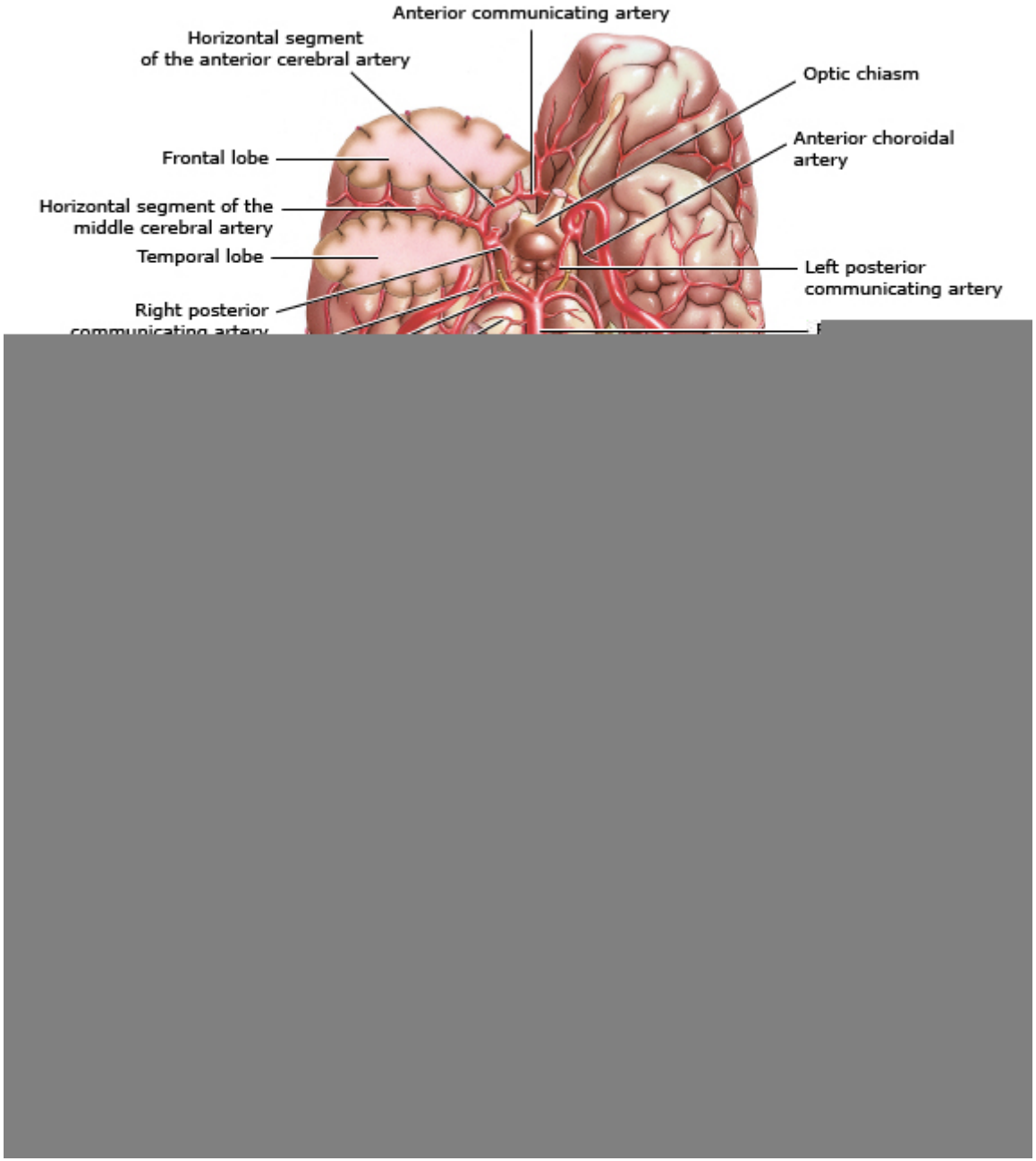
Graphic 53412 Version 1.0

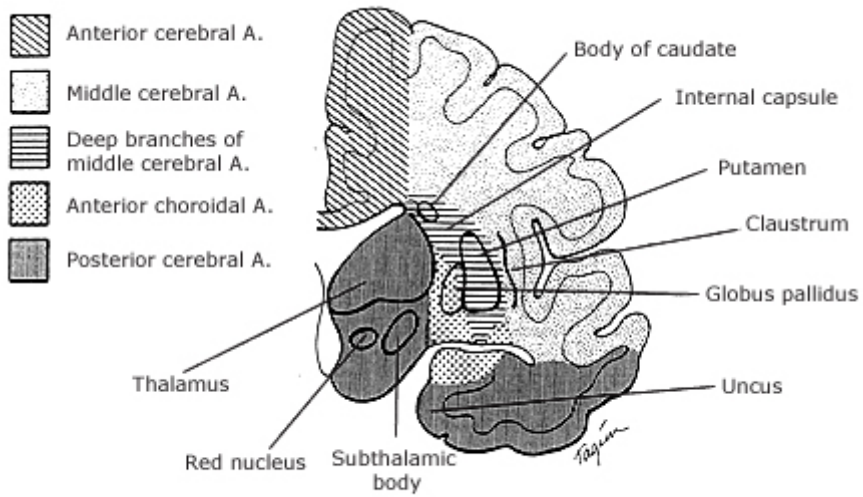
Anatomy of the cerebral arterial circulation


Anterior communicating artery
Horizontal segment of the anterior cerebral artery
Optic chiasm
Anterior choroidal artery
Frontal lobe
Horizontal segment of the middle cerebral artery
Temporal lobe
Left posterior communicating artery
Right posterior

Frontal view of the carotid arteries, vertebral arteries, and intracranial vessels and their communication with each other via the circle of Willis.

Graphic 51410 Version 6.0

Major cerebral vascular territories



Representation of the territories of the major cerebral vessels shown in a coronal section of the brain.

Graphic 65199 Version 2.0

Transient ischemic attack (TIA) and minor ischemic stroke: Rapid overview of emergency management

Clinical features

- **Typical TIAs** are characterized by transient, focal neurologic symptoms that can be localized to a single vascular territory within the brain, including one or more of the following:
  - Transient monocular blindness (amaurosis fugax)
  - Aphasia or dysarthria
  - Hemianopia
  - Hemiparesis and/or hemisensory loss (complete or partial)
- **Atypical TIAs** may present with transient isolated neurologic symptoms:
  - Isolated vertigo
  - Isolated ataxia
  - Isolated diplopia
  - Isolated speech disturbance (slurred speech) without aphasia
  - Isolated bilateral decreased vision
  - Isolated unilateral sensory loss involving only one body part

Differential diagnosis

- Seizure
- Migraine aura
- Syncope
- Transient global amnesia
- Central nervous system demyelinating disorder (eg, multiple sclerosis)
- Peripheral vestibulopathy
- Metabolic disorder (eg, hypoglycemia)
- Myasthenia gravis
- Cranial/peripheral neuropathy
- Cerebral amyloid angiopathy
- Subdural hematoma

- Subarachnoid or intracerebral hemorrhage
- Transient neurologic attack not otherwise specified

Immediate treatment while evaluating the ischemic mechanism

- For patients with TIA or minor, nondisabling acute ischemic stroke (and thus not eligible for thrombolytic therapy or mechanical thrombectomy), start antiplatelet therapy immediately while the evaluation is in progress:
  - Start DAPT (aspirin plus clopidogrel, or aspirin plus ticagrelor) for patients with one of the following:
    - High-risk TIA, defined by an $ABCD^2$ score ≥4
    - Time-based TIA with a relevant large artery stenosis or DWI lesion on MRI (if imaging available at this stage)
    - Minor, nondisabling ischemic stroke, defined by an NIHSS score ≤5
  - Start aspirin monotherapy for patients who do not meet the above criteria (ie, TIA with an $ABCD^2$ score <4 and no relevant large artery stenosis or DWI lesion on MRI [if imaging available at this stage])
- Once the ischemic mechanism is determined, antithrombotic therapy can be modified as necessary

Urgent evaluation

- Brain imaging with diffusion-weighted MRI (preferred) or CT to identify infarction and rule out nonischemic causes
- Vascular imaging of extracranial and intracranial large arteries with MRA or CTA to identify large artery cause
- Cardiac evaluation (ECG, cardiac monitoring, echocardiography) to identify atrial fibrillation or other cardioembolic source
- Laboratories: CBC, PT and PTT, serum electrolytes, creatinine, fasting blood glucose or HbA1c, lipids, and (as indicated for selected patients) ESR and CRP

Targeted treatment by mechanism for secondary prevention

- Cardiogenic embolism due to atrial fibrillation: Stop antiplatelet agents and start long-term anticoagulation
- Symptomatic internal carotid artery stenosis: Carotid revascularization with CEA or CAS and long-term antiplatelet therapy
- Intracranial large artery atherosclerosis with 70 to 99% stenosis: Continue DAPT for 21 to 90 days, then switch to long-term single-agent antiplatelet therapy
- Small vessel disease, extracranial vertebral artery stenosis, intracranial large artery atherosclerosis with 50 to 69% stenosis, or cryptogenic:
  - Continue DAPT for 21 days, then switch to long-term single-agent antiplatelet therapy for:
    - High-risk TIA ($ABCD^2$ score ≥4), or TIA with a relevant DWI lesion on MRI, or extracranial stenosis not amenable to revascularization
    - Minor ischemic stroke (NIHSS ≤5)

- Continue long-term single-agent antiplatelet therapy for low-risk TIA (ABCD^2 score <4), and TIA without a relevant large artery stenosis or DWI lesion on MRI

Intensive risk factor management

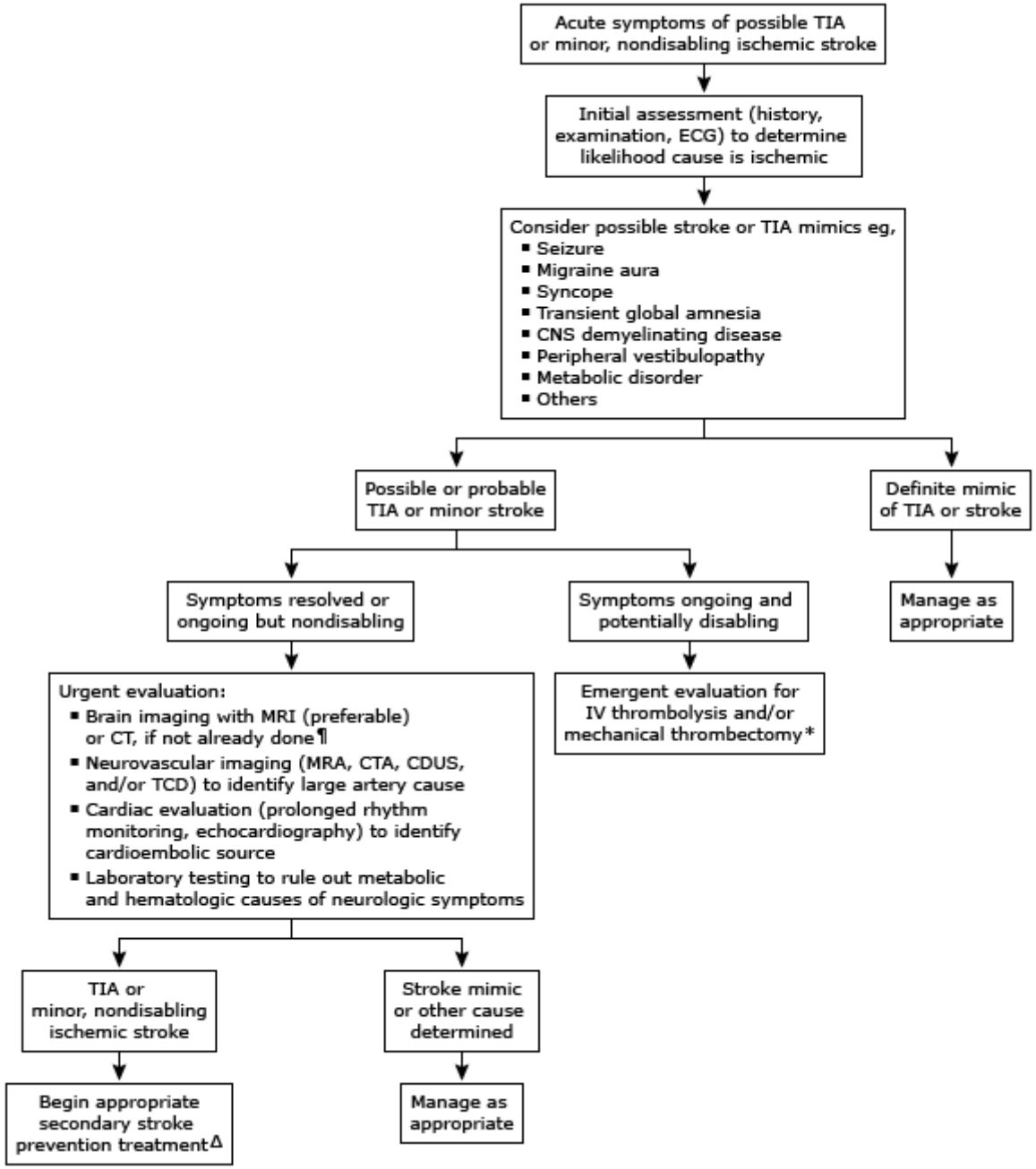
- Antihypertensive therapy for patients with known or newly established hypertension
- LDL-cholesterol lowering with high-intensity statin therapy
- Glucose control to near normoglycemic levels for patients with diabetes
- Lifestyle modification as appropriate:
  - Moderate to vigorous exercise most days of the week for those capable
  - Smoking cessation for recent or current tobacco users
  - Mediterranean diet
  - Weight reduction for patients with obesity
  - Reduced alcohol consumption for heavy drinkers

This rapid overview presents a general approach to the management of TIA and minor stroke. Please refer to UpToDate content for details, including descriptions and calculators for the NIHSS and ABCD^2 scores.

DAPT: dual antiplatelet therapy; ABCD^2: Age, Blood pressure, Clinical features, Duration of symptoms, and Diabetes; NIHSS: National Institutes of Health Stroke Scale; DWI: diffusion-weighted imaging; MRI: magnetic resonance imaging; CT: computed tomography; MRA: magnetic resonance angiography; CTA: computed tomographic angiography; ECG: electrocardiography; CBC: complete blood count; PT: prothrombin time; PTT: partial thromboplastin time; HbA1c: glycated hemoglobin; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; CEA: carotid endarterectomy; CAS: carotid artery stenting; LDL: low density lipoprotein; ICAS: intracranial larger artery atherosclerosis.

Graphic 131201 Version 4.0

Evaluation of patient presenting with acute symptoms of possible TIA or minor ischemic stroke


Acute symptoms of possible TIA or minor, nondisabling ischemic stroke
Initial assessment (history, examination, ECG) to determine likelihood cause is ischemic
Consider possible stroke or TIA mimics eg,
Seizure
Migraine aura
Syncope
Transient global amnesia
CNS demyelinating disease
Peripheral vestibulopathy
Metabolic disorder
Others
Possible or probable TIA or minor stroke
Definite mimic of TIA or stroke
Symptoms resolved or ongoing but nondisabling
Symptoms ongoing and potentially disabling
Manage as appropriate
Urgent evaluation:
Brain imaging with MRI (preferable) or CT, if not already done¶
Neurovascular imaging (MRA, CTA, CDUS, and/or TCD) to identify large artery cause
Cardiac evaluation (prolonged rhythm monitoring, echocardiography) to identify cardioembolic source
Laboratory testing to rule out metabolic and hematologic causes of neurologic symptoms
Emergent evaluation for IV thrombolysis and/or mechanical thrombectomy*
TIA or minor, nondisabling ischemic stroke
Stroke mimic or other cause determined
Begin appropriate secondary stroke prevention treatmentΔ
Manage as appropriate

This algorithm should be used in conjunction with UpToDate topics on the initial evaluation and management of TIA and ischemic stroke.

CDUS: carotid duplex ultrasonography; CNS: central nervous system; CT: computed tomography; CTA: computed tomography angiography; ECG: electrocardiography; IV: intravenous; MRA: magnetic resonance angiography; MRI: magnetic resonance imaging; TIA: transient ischemic attack; TCD: transcranial Doppler.

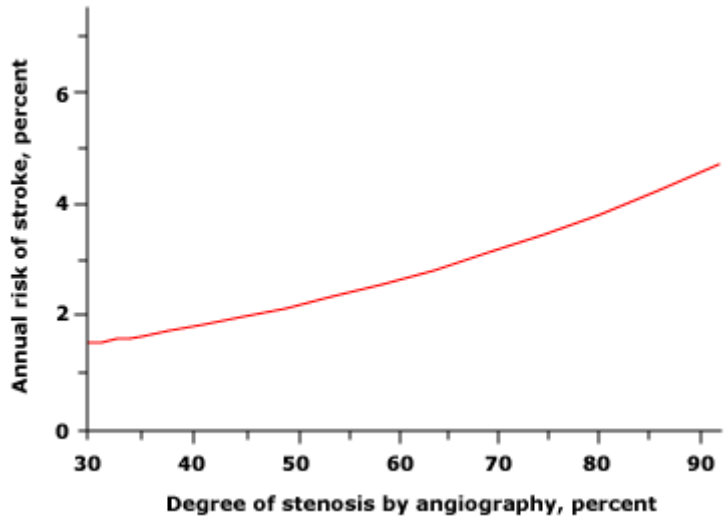
* Patients who present within the appropriate time window after ischemic symptom onset and have a persistent neurologic deficit that is potentially disabling, despite improvement of any degree, should be treated with intravenous thrombolysis and/or mechanical thrombectomy in the absence of other contraindications. Further management of these patients is similar to that of other patients with a potentially disabling stroke.

¶ Can begin aspirin and statin therapy while awaiting results of remaining diagnostic studies if imaging is negative for hemorrhage and other nonischemic cause of symptoms.

Δ Viable strategies include antihypertensive therapy, antithrombotic therapy, statin therapy, and lifestyle modification; select patients with symptomatic cervical internal carotid artery disease may benefit from carotid revascularization.

Graphic 107065 Version 1.0

Severity of carotid stenosis predicts stroke risk

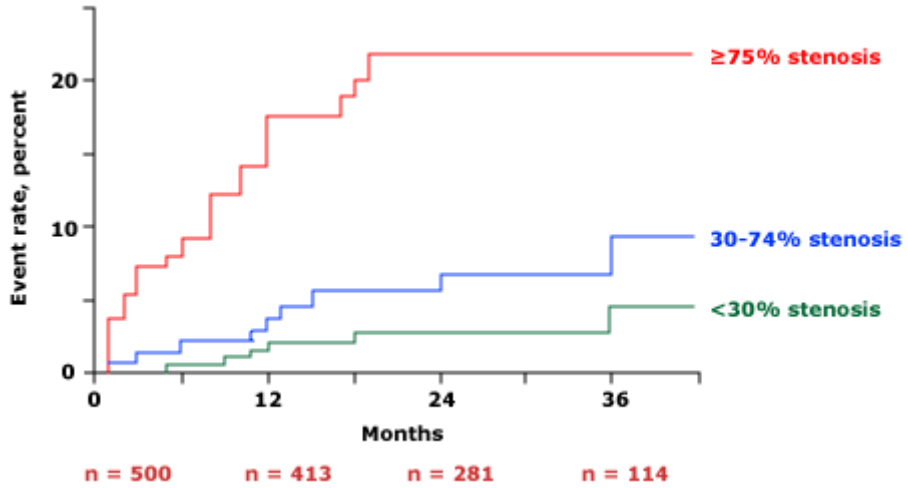


Relation between the degree of carotid artery stenosis and the annual risk of stroke.

Data from Barnett, HJ, Eliasziw, M, Meldrum, HE, Taylor, DW, Neurology 1996; 46:603.

Graphic 60048 Version 1.0

Cerebral ischemia events with asymptomatic carotid artery bruits



Incidence of ischemic events in 500 patients with asymptomatic carotid artery bruits according to the severity of carotid artery stenosis on initial Doppler ultrasonography. Patients with ≥75 percent stenosis were at significantly increased risk (P <0.0001).

Data from Chambers BR, Norris JW. Outcome in patients with asymptomatic neck bruits. N Engl J Med 1986; 315:860.

Graphic 66153 Version 3.0

ABCD^2 score

The ABCD^2 score can be used to estimate the risk of ischemic stroke in the first two days after TIA. The score is tallied as follows:	
Age:	
≥60 years	1 point
<60 years	0 points
Blood pressure elevation when first assessed after TIA:	
Systolic ≥140 mmHg **or** diastolic ≥90 mmHg	1 point
Systolic <140 mmHg **and** diastolic <90 mmHg	0 points
Clinical features:	
Unilateral weakness	2 points
Isolated speech disturbance	1 point
Other	0 points
Duration of TIA symptoms:	
≥60 minutes	2 points
10 to 59 minutes	1 point
<10 minutes	0 points
Diabetes:	
Present	1 point
Absent	0 points

Data from: 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.

Graphic 62381 Version 3.0

Canadian TIA score

Items	Points
Clinical findings	
First TIA (in lifetime)	2
Symptoms ≥10 min	2
History of carotid stenosis	2
Already on antiplatelet therapy	3
History of gait disturbance	1
History of unilateral weakness	1
History of vertigo	-3
Initial triage diastolic blood pressure ≥110 mm Hg	3
Dysarthria or aphasia (history or examination)	1
Investigations in emergency department	
Atrial fibrillation on ECG	2
Infarction (new or old) on CT	1
Platelet count ≥400×10^9/L	2
Glucose ≥15 mmol/L	3
Total score (-3 to 23)	

TIA: transient ischemic attack; ECG: electrocardiography; CT: computed tomography.

From: Perry JJ, Sharma M, Sivilotti ML, et al. A prospective cohort study of patients with transient ischemic attack to identify high-risk clinical characteristics. Stroke 2014; 45:92. DOI: 10.1161/STROKEAHA.113.003085. Copyright © American Heart Association. Reproduced with permission from Wolters Kluwer Health. Unauthorized reproduction of this material is prohibited.

Graphic 134718 Version 1.0

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