



Staying on the Attack

Getting to Transient Ischemic Attacks Early

The risk of stroke is very high following a transient ischemic attack. Early diagnosis and treatment is key in reducing this risk.

In this article:

- 1. What is the link between transient ischemic attack (TIA) and stroke?**
- 2. How is TIA diagnosed?**
- 3. How is TIA treated?**

By Vanessa Palumbo, MD;
Alastair M. Buchan, MB, FRCPC;
and Michael D. Hill, MD, FRCPC

The classic definition of transient ischemic attack (TIA) is a sudden, neurologic deficit lasting less than 24 hours and caused by focal cerebral or retinal ischemia. The symptoms of TIA (Table 1) occur in varying clinical patterns, depending on the site of artery occlusion.

The establishment of a 24-hour limit for the duration of symptoms was designed to exclude patients with brain infarction and has led to the assumption that TIA is a benign clinical entity.

Subsequent clinical, experimental, and imaging data have shown that the 24-hour limit is arbitrary and often does not exclude infarction. In several studies, brain infarction is present in a substantial proportion of patients with clinical TIA. When using a computed tomography (CT) scan, infarction was found in 12% to 28% of TIA patients; when using conventional magnetic resonance imaging (MRI), it was found in 31%

to 77%.¹⁻³ However, these imaging techniques are unable to differentiate acute from chronic lesions, so it can be difficult to actually establish a causal relationship between TIA and the lesion seen on imaging. The introduction of new MRI techniques, particularly diffusion-weighted imaging (DWI), which is highly sensitive and

Mike's case

Mike, a 65-year-old man with a history of smoking and diabetes mellitus (Type 2), has a sudden, transient episode of speaking difficulty and mild right weakness of his face and arm. The episode lasts 45 minutes.

How should he be managed?

For more on Mike, see page 47.

Table 1

Typical symptoms of TIA

hemiparesis
hemiparesthesia
dysarthria/dysphasia
diplopia
imbalance
monocular blindness

TIA: Transient ischemic attack

specific in the early diagnosis of acute cerebral ischemic damage, may improve the identification of acute infarctions. In several series of patients with TIA who underwent DWI MRI, 35% to 48% showed an acute brain injury.^{4,6}

The presence of acute infarction, seen on DWI MRI, is related to symptom duration—about 70% of patients with TIA lasting > 12 hours have positive DWI findings.^{4,6}

The 24-hour limit for the clinical definition of TIA is also confusing because the majority of TIAs are resolved within 30 minutes of their onset and the likelihood of a complete recovery within 24 hours is low if symptoms last more than one hour.

What is the link between TIA and stroke?

The risk of subsequent stroke after TIA is 10.5% within 90 days. Half of this risk accrues in the first two days after TIA presentation. Five independent risk factors have been associated with an increased risk of stroke within 90 days. These risk factors are advanced age (> 60 years), Type 2 diabetes, an episode longer than 10 minutes, and weakness and speech impairment during the episode. The short-term risk of stroke increases to 34% among patients with all five risk factors.⁷

The risk of stroke after TIA is 11% in patients

with atrial fibrillation (AF) and 25% in patients with 70% to 99% internal carotid stenosis and hemispheric symptoms.⁸ Patients with pure sensory syndromes or pure dizziness are at low risk of stroke. Given these considerations, it appears that the proposed new definition of TIA, which includes symptoms lasting less than one hour, is justified, and that a different approach to evaluation and treatment is required.⁹

How is TIA diagnosed?

TIA is generally always a historical diagnosis because patients are recovered by the time they are evaluated. Any treatment should be tailored to the underlying mechanism of the attack. Because of the high short-term risk of stroke after TIA, it is important to perform a rapid evaluation and treatment of the patient, preferably within hours of the attack. The initial evaluation of a patient with symptoms suggesting a TIA should include the tests listed in Table 2. The key is to determine and then use the mechanism of the attack to guide its management.

How is TIA treated?

The treatment of TIA patients should begin as soon as possible after diagnosis. Specific man-

About the authors ...

Dr. Palumbo is a stroke fellow, department of clinical neurosciences, University of Calgary, Calgary, Alberta.

Dr. Buchan is a professor of stroke research, department of clinical neurosciences, University of Calgary, Calgary, Alberta.

Dr. Hill is the director of the stroke unit, department of clinical neurosciences, University of Calgary, Calgary, Alberta.

Transient Ischemic Attack

Table 2

Tests needed for TIA diagnosis and what they are used for

Laboratory tests

To rule out metabolic and hematologic causes of neurologic symptoms, such as hypoglycemia, hyponatremia, and thrombocytosis

Electrocardiography

To look for evidence of atrial fibrillation

Doppler ultrasonography

To determine the presence of internal carotid critical stenosis

Neuroimaging (MRI and CT scan)

To reveal the presence of a brain tumour or subdural hematoma (which can both mimic a TIA)

TIA: Transient ischemic attack
MRI: Magnetic resonance imaging
CT: Computed tomography

Table 3

Summary of antiplatelets which can be used for TIA treatment

ASA—reduces long-term risk of stroke after a TIA.

Dipyridamole—when used with ASA, reduces recurrence of non-fatal stroke after a TIA or stroke.

Clopidogrel—more effective than ASA in secondary prevention of vascular events in patients with previous myocardial infarction, stroke, and peripheral heart disease.

Ticlopidine—should not be used because of side effects, such as neutropenia, rash, diarrhea, and fatal thrombotic thrombocytopenic purpura.

TIA: Transient ischemic attack
ASA: Acetylsalicylic acid

agement is clear for patients with chronic or paroxysmal AF or atrial flutter. Oral anticoagulation therapy is the treatment of choice in such patients, reducing the risk of recurrent stroke by about 65%.¹⁰ Anticoagulation can be started immediately using a combination of low-molecular-weight heparin and warfarin. Heparin can be discontinued when the international normalised ratio reaches 2.5. Patients with prosthetic heart valves also require anticoagulation.

Similarly, carotid endarterectomy is beneficial in patients with symptomatic internal carotid stenosis of 70% to 99%, with an absolute risk reduction of ipsilateral stroke or death of 17% over two years.¹¹ Among patients with moderate internal carotid stenosis, the benefit of carotid endarterectomy is less, with an absolute risk

reduction of only 6.5% over five years.¹¹ Subgroups of patients who particularly benefit from carotid endarterectomy include: patients with greater stenosis, those who are over 75, those of male gender, those with a history of stroke (rather than TIA) as a qualifying event, and those with hemispheric TIA rather than transient monocular blindness.

Some radiographic factors, such as the presence of intracranial stenosis, the absence of

microvascular ischemia, and the presence of collateral vessels, predict more favourable outcomes after carotid endarterectomy. Patients with asymptomatic stenosis of any degree rarely

benefit from surgery and if they do, it is only under exceptional circumstances.

Patients with low-grade stenosis, small vessel disease, and other mechanisms of stroke are treated with antiplatelet therapy (Table 3). The use of acetylsalicylic acid (ASA), 75 mg to 150 mg daily, reduces the long-term risk of stroke. A

♥ Practical Point

Patients with TIA need rapid investigation; among high-risk patients, the risk of stroke is largely compressed into the first 48 hours, therefore, investigations must be completed quickly.

Followup on Mike

The patient has been hospitalised to undergo a rapid diagnostic workup. The following exams were done:

- *Electrocardiogram*—identified the presence of atrial fibrillation.
- *Computed tomography scan*—negative for early ischemic changes and non-vascular causes of neurologic symptoms.
- *Carotid ultrasound*—did not show the presence of concomitant carotid disease.

Anticoagulation therapy was promptly started with warfarin and low-molecular-weight heparin (until warfarin reached effective anticoagulation).

loading dose of at least 150 mg should be used in the acute phase, to obtain a rapid and complete inhibition of thromboxane-mediated platelet aggregation.

Dipyridamole, another antiplatelet drug, has not been shown to be effective in secondary stroke prevention; however, one trial showed a reduction in the recurrence of non-fatal stroke after a TIA or stroke if dipyridamole is used in addition to ASA.^{12,13}

Clopidogrel is a slightly more effective antiplatelet drug than ASA in secondary prevention of vascular events among patients with previous myocardial infarction, stroke, and peripheral heart disease.

Ticlopidine should not be used, as it is associated with a higher frequency of side effects, such as neutropenia, rash, diarrhea, and fatal thrombotic thrombocytopenic purpura.

Antiplatelet treatment with ASA is the first choice, while clopidogrel or combined ASA and dipyridamole are indicated in case of ASA intolerance or occurrence of TIA while already taking ASA. Among the aforementioned drugs,

ASA is the only antiplatelet agent to have been studied within 48 hours after a cerebrovascular event and to have shown a highly significant, but clinically modest, reduction in recurrent ischemic stroke.¹⁴

In the longer term, risk factor management and lifestyle changes are recommended to prevent recurrence of stroke after TIA. Blood pressure lowering in primary and secondary prevention can reduce the relative risk of stroke to 28% to 32%, even in normotensive patients.¹⁵

The Antihypertensive and Lipid Lowering treatment to prevent Heart Attack Trial (ALLHAT) showed that thiazide-type diuretics were better than amlodipine and lisinopril at preventing combined cardiovascular events (such as coronary heart disease, stroke, and peripheral vascular disease). This trial

suggests that chlorthalidone should be considered as the first choice drug in the treatment of hypertension.¹⁶

Statins also play a role in the secondary prevention of cerebrovascular disease, with evidence of an absolute risk reduction of 1.3% for




**For a good move
see page 8**

Transient Ischemic Attack

non-fatal stroke.¹⁵ The use of statins is indicated even when dyslipidemia is absent.

Antihypertensive and lipid-lowering agents have not been studied specifically in patients with TIA, but are likely to be effective in preventing recurrent cerebrovascular events. Moreover, several studies have tested the efficacy of different treatments in acute coronary syndromes, but no trial, to date, has evaluated the efficacy of an early intervention after TIA.

TIA is an unstable state, especially in high-risk patients. Early diagnosis and treatment is required in these cases, in order to prevent stroke in the 90 days following the attack. An ongoing trial, the Fast Assessment of Stroke and Transient ischemic attack to prevent Early Recurrence (FASTER), is currently testing the efficacy and safety of early use of clopidogrel and ASA after TIA or minor stroke to prevent early recurrence. 

References

1. Dennis M, Bamford J, Sandercock P, et al: Computed tomography in patients with transient ischemic attacks: When is a transient ischemic attack not a transient ischemic attack but a stroke? *J Neurol* 1990; 237(4):257-61.
2. Koudstaal PJ, vanGijn J, Frenken CW, et al: TIA, RIND, minor stroke: A continuum, or different subgroup. Dutch TIA Study Group. *J Neurol Neurosurg Psychiatry* 1992; 55(2):95-7.
3. Evans GW, Howard G, Murros KE, et al: Cerebral infarction verified by cranial computed tomography and prognosis for survival following transient ischemic attack. *Stroke* 1991; 22(4):431-6.
4. Kidwell SC, Alger JR, DiSalle F, et al: Diffusion MRI in patients with transient ischemic attacks. *Stroke* 1999; 30(6):1174-80.
5. Ay H, Oliveira-Filho J, Buonanno FS, et al: "Footprints" of transient ischemic attacks: A diffusion-weighted MRI study. *Cerebrovasc Dis* 2002; 14(3-4):177-86.
6. Engeleter ST, et al: Diffusion MRI imaging and transient ischemic attacks (letter). *Stroke* 1999; 30:2762-3
7. Clairborne SJ, Sidney S, Bernstein AL, et al: A comparison of risk factors for recurrent TIA and stroke in patients diagnosed with TIA. *Neurology* 2003; 60(2):280-5.
8. Streifler JY, Eliasziw M, Benavente OR, et al: The risk of stroke in patients with first ever retinal vs. hemispheric transient ischemic attacks and high-grade carotid stenosis: North American Symptomatic Carotid Endarterectomy Trial. *Arch Neurol* 1995; 52(3):246-9.
9. Albers GW, Caplan LR, Easton JD, et al: Transient ischemic attack—Proposal for a new definition. *New Engl J Med* 2002; 347(21):1713-6.

10. Ezekowitz MD, Levine JA: Preventing stroke in patients with atrial fibrillation. *JAMA* 1999; 281(19):1830-5.
11. North American Symptomatic Carotid Endarterectomy Trial Collaborators: Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *New Engl J Med* 1991; 325(7):445-53.
12. Antithrombotic Trialists' Collaboration Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction and stroke in high-risk patients. *BMJ* 2002; 324(7329):71-86.
13. Diener HC, Cunha L, Forbes C, et al: European Stroke Prevention Study-2. Dipyridamole and acetylsalicylic acid in the secondary prevention of stroke. *J Neurol Sci* 1996; 143:1-13.
14. International Stroke Trialists Collaborative Group: The International Stroke Trial (IST): A randomised trial of aspirin, subcutaneous heparin, both, or neither among 19,435 patients. *Lancet* 1997; 349(9065):1569-81.
15. Heart Protection Study Collaborative Group: MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002; 360(9326):7-22.
16. PROGRESS Collaborative Group: Randomised trial of a perindopril-based blood-pressure lowering regime among 6105 individuals with previous stroke or TIA. *Lancet* 2001; 358(9287):1033-41.

Practical Point

For more information on TIA, visit:

- ♥ **The National Institute of Neurological Disorders and Stroke, at**
www.ninds.nih.gov
- ♥ **The National Institute of Health, at:**
www.nih.gov

Take-home message

- The typical symptoms of TIA are hemiparesis, hemiparesis, dysarthria/dysphasia, diplopia, imbalance, and monocular blindness.
- Important diagnostic tests include laboratory tests, electrocardiography, Doppler ultrasonography, MRI, and CT scan.
- Treatment of TIA should be started as soon as possible after diagnosis, with antiplatelet therapy being the treatment of choice.

For some frequently asked questions on TIA, please go to page 22.