

TIAs and stroke prevention

Rapid assessment, urgent treatment

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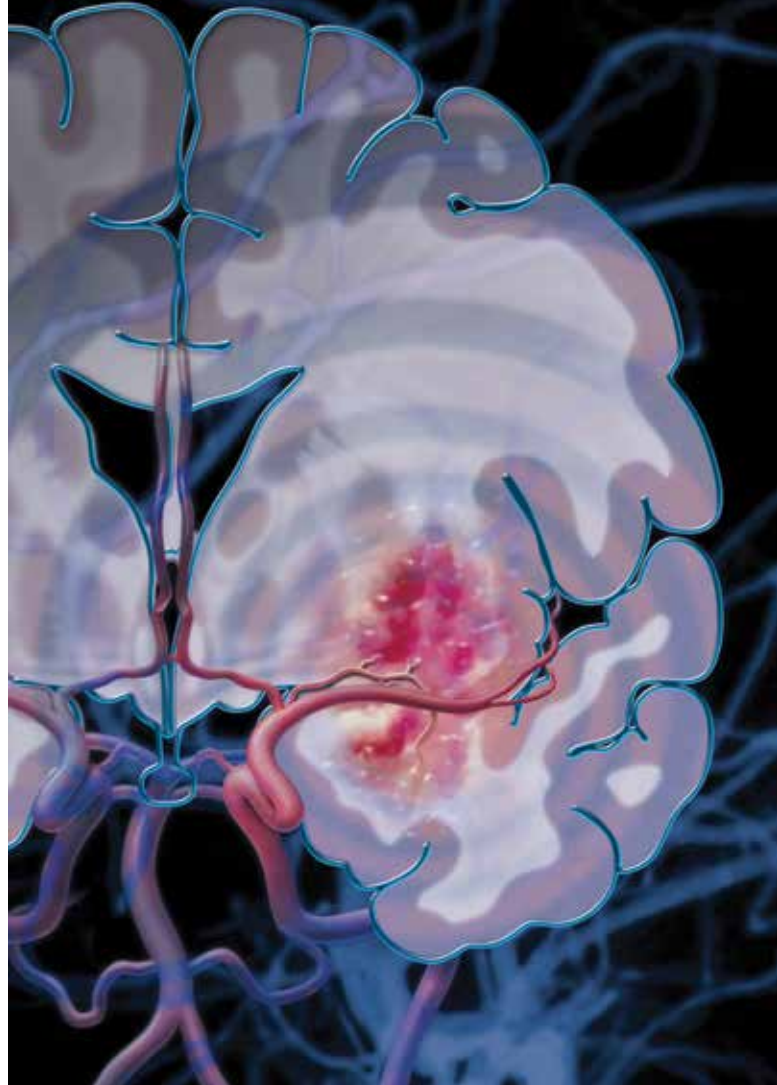
Common issues arising in the management of patients with TIA and stroke and the application of best evidence practice in managing and preventing these conditions are highlighted in this case-based article.

Key points

- A transient ischaemic attack (TIA) is a transient neurovascular event that resolves within 24 hours without acute infarction on MRI.
- Rapid assessment and treatment of TIAs can prevent disabling strokes in up to 80% of cases.
- Urgent investigations for TIA or stroke should include: imaging of the brain; imaging of the carotid and vertebral arteries; 12-channel ECG and Holter monitoring; transthoracic echocardiography; and blood pressure, fasting lipids and glucose measurements.
- The American Heart Association (AHA)/American Stroke Association (ASA) have recently updated their guidelines on primary and secondary stroke prevention, focusing on lifestyle modification and management of hypertension, hyperlipidaemia and diabetes.
- The targets for primary prevention are less strict than for secondary prevention, but the same principles for treatment and lifestyle changes apply.

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Transient ischaemic attacks (TIAs) are medical emergencies. Rapid assessment and treatment of TIAs can prevent disabling strokes in up to 80% of cases.¹ Early management of vascular risk factors together with lifestyle modification has been highly effective in lowering age-adjusted stroke incidence rates in the Western world. Primary and secondary stroke prevention is important since stroke is still the second most common cause of death and the most common cause of acquired disability in Australia.²

The introduction of a nationwide rapid access TIA outpatient service could be an important tool in improving the outcomes of patients after a stroke and overall population health, while reducing the strain on hospital inpatient resources and general healthcare costs. In most regions of Australia, however, GPs provide the full care for patients with TIAs, including initial assessment, organisation and evaluation of diagnostic investigations and preparation of a treatment plan. Patient education about the management of risk factors for primary and secondary prevention (Table)^{3,4} and proper action in the case of sudden onset of neurological symptoms (phoning 000) usually rests with the GP, the first point of contact regarding most health issues.

The case reports described below from our TIA clinic at a Sydney teaching hospital illustrate common issues arising in the management of patients with TIA and stroke and highlight the application of best evidence practice in the management and prevention of these conditions.

Case 1

A 65-year-old man presented to the emergency department (ED) with a transient (5 minutes) right facial droop and arm weakness. He was a smoker, suffered from

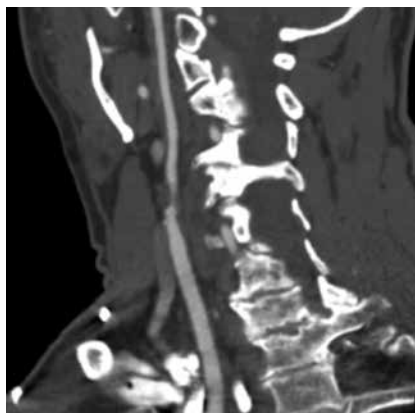


Figure 1. Case 1: high-grade stenosis (90%) of the left internal carotid artery in a 65-year-old man (CT angiogram).

hypertension, which was being treated with perindopril 5 mg daily, and had known but untreated hyperlipidaemia.

On admission to the ED, his blood pressure was 170/90 mmHg. He underwent a CT scan of his brain, which did not show ischaemia. Before discharge from the ED he was commenced on aspirin 100 mg daily and his antihypertensive medication was changed to perindopril 5 mg plus amlodipine 10 mg.

Two days later he attended our TIA clinic for a duplex scan of the carotid arteries. This indicated a high-grade stenosis of the left internal carotid artery (ICA). A CT angiogram confirmed a high-grade stenosis (90%) of the left ICA (Figure 1). Because this patient had symptomatic high-grade ICA stenosis, he was referred to a vascular surgeon, and subsequently underwent a carotid endarterectomy (CEA) within a week of its onset.

Secondary stroke prevention for this

patient followed the recently updated (2014) guidelines by the American Heart Association (AHA)/American Stroke Association (ASA).³ The medication plan for him after surgery included:

- antiplatelet therapy with aspirin 100 mg daily
- perindopril 5 mg plus amlodipine 10 mg daily, with a blood pressure target of less than 140/90 mmHg
- atorvastatin 40 mg, with targets for total cholesterol of less than 4.0 mmol/L and LDL less than 1.8 mmol/L (his fasting blood tests had revealed a total cholesterol level of 6.5 mmol/L and LDL of 4.2 mmol/L).

The patient's fasting glucose level of 5.9 mmol/L led to the suspicion that he had prediabetes (fasting glucose levels between 6.1 and 6.9 mmol/L)⁵ He was referred for an oral glucose tolerance test and follow

Table. Primary and secondary stroke prevention: important modifiable vascular risk factors and targets*^{3,4}

Risk factor	Primary prevention recommendation	Secondary prevention recommendation
Physical inactivity	Moderate-to-vigorous-intensity activity for 40 minutes per day, three to four days per week	Moderate-to-vigorous-intensity activity for at least 150 minutes per week
Diet	Mediterranean diet supplemented with nuts and reduced sodium intake	Mediterranean diet supplemented with nuts and reduced sodium intake
Hypertension	Regular blood pressure screening; treat to target <140/90 mmHg	Regular blood pressure screening; treat to target <140/90 mmHg
Dyslipidaemia	Statin therapy if high (>10%) 10-year cardiovascular risk, lifestyle changes	LDL target <1.8 mmol/L, total cholesterol level <4.0 mmol/L
Diabetes	Glycaemic control; statin therapy; strict blood pressure target <140/90 mmHg; aspirin if high 10-year cardiovascular risk	HbA _{1c} target <6.5%; statin therapy; strict blood pressure target <130/85 mmHg
Smoking	Cessation, using counselling plus drug therapy	Cessation, using counselling plus drug therapy
Alcohol intake	No more than two drinks per day for men or one drink per day for women	No more than two drinks per day for men or one drink per day for women
Obesity	Aim for a BMI target 25 kg/m ² or below	Aim for a BMI target 25 kg/m ² or below
Ischaemic vascular event (e.g. stroke, MI)	–	Antiplatelet therapy with aspirin 50–325 mg or clopidogrel 75 mg daily or sustained-release dipyridamole 200 mg combined with aspirin 25 mg twice daily unless atrial fibrillation is present (see below)
Atrial fibrillation	Screening in patients over 65 years of age once a year with 12-channel ECG, commence oral anticoagulation depending on risk stratification using CHA2DS2-VASc score	Screening in patients over 65 years of age once a year with 12-channel ECG, commence oral anticoagulation immediately if atrial fibrillation is found

* For more detailed information refer to references 3 and 4.

up was arranged with his GP.

The patient's necessary lifestyle modifications included, most importantly, smoking cessation and a Mediterranean-type diet, emphasising vegetables, fruits, whole grains, low-fat dairy products, poultry, fish, legumes, olive oil and nuts.

At his three-month follow up, the patient's target levels had been achieved; he had also stopped smoking, maintained a significantly healthier diet and started cycling for 30 to 45 minutes three times a week.

Case 2

A 59-year-old salesman presented to the ED with two transient episodes (5 and 20 minutes) of right arm weakness and word-finding difficulties. His medical history was significant for type 2 diabetes and untreated hypertension. He was overweight, with a BMI of 31 kg/m², and the only regular medication he took regularly was metformin 500 mg once daily.

The patient's blood pressure in the ED was 155/90 mmHg and his LDL-cholesterol was found to be elevated at 3.0 mmol/L. His random blood glucose level was 9.5 mmol/L and his HbA_{1c} 8.0%. A CT scan did not show any abnormality, but MRI showed a small stroke in the left middle cerebral artery (MCA) territory and magnetic resonance angiography (MRA) showed severe stenosis of the left middle cerebral artery (MCA; M1 segment; Figure 2), which is a high-risk condition.

The Stenting versus Aggressive Medical Therapy for Intracranial Arterial Stenosis (SAMMPRIS) trial showed that stenting is inferior to medical treatment in the treatment of intracranial stenosis.⁶ According to the protocol used in this trial, our patient was commenced on dual antiplatelet medication with aspirin 100 mg and clopidogrel 75 mg for three months, followed by permanent single antiplatelet therapy with aspirin 100 mg. The beneficial effect of dual antiplatelet therapy has not been shown to outweigh increased bleeding risk beyond a three-month period after a neurovascular event.⁷

The patient was also started on amlodipine 10 mg and perindopril 5 mg daily, aiming

to reach a blood pressure target of less than 130/85 mmHg (this blood pressure recommendation takes into account the patient's type 2 diabetes), and atorvastatin 40 mg, with an LDL target of less than 1.8 mmol/L.

The patient was referred to a diabetes clinic, where his medications were adjusted with the aim of reaching the target HbA_{1c} of less than 6.5%. He was provided with information on an appropriate diet for patients with diabetes (BMI target 25 kg/m² or below) and advised to perform at least 20 minutes of daily exercise.

Although the patient usually drove to work, he was unable to do so as driver licensing authorities prohibit driving after stroke for at least four weeks and require a medical clearance assessment before driving is resumed. After a TIA, licensing authorities recommend patients do not drive for at least two weeks.⁸

The discharge letter from the TIA clinic to the patient's GP outlined targets for his vascular risk factors. Long-term management of hypertension, hyperlipidaemia and diabetes in this patient is crucial and he requires continuous care by his GP.

Case 3

An 81-year-old woman presented to the emergency department with a transient episode (10 minutes) of vertigo. The neurological examination revealed no deficit indicating a stroke in the cerebellum or brainstem-like dysarthria, ataxia, fine-motor skill impairment or double vision. The Dix-Hallpike test (positioning manoeuvre to identify benign paroxysmal positional vertigo [BPPV]) and head-impulse test (used to assess the function of the vestibular organ) were both normal.

The woman appeared to be very fit. Her past medical history included hypertension, treated with telmisartan 40 mg daily, and palpitations. In the ED, her blood pressure was 130/80 mmHg, blood tests (including kidney function levels) were normal and an ECG showed sinus rhythm. She was discharged home with advice to return to the ED in the case of a recurrent event.

Three days later at the TIA clinic, the patient's MRI showed no ischaemia.

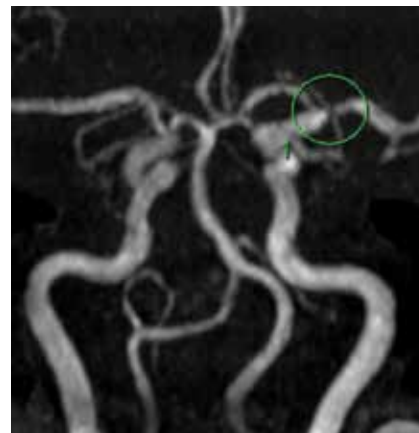


Figure 2. Case 2: severe stenosis of the proximal left middle cerebral artery in a 59-year-old man (magnetic resonance angiogram).

Although a TIA as a cause for her vertigo cannot be completely excluded, a peripheral cause is more likely. Vertigo is extremely rare as an isolated stroke symptom and is far more often caused by BPPV.⁹ Holter monitoring demonstrated episodes of intermittent atrial fibrillation. Her echocardiogram was normal, showing an ejection fraction of 60% and no evident thrombus.

Although this woman had had recurrent falls (five in the previous year), her risk for a cardioembolic stroke far exceeded her risk from major bleeding and falls.¹⁰ Therefore, after thorough patient education, she was started on oral anticoagulation. The new oral anticoagulation agents dabigatran, rivaroxaban and apixaban have been shown to be at least as effective as warfarin in preventing ischaemic events and are associated with fewer intracerebral bleeding complications.¹¹ In cases of significantly impaired renal function, however, warfarin with an INR target between 2.0 and 3.0 would be preferred.

In the discharge letter from the TIA clinic to her GP, blood monitoring and further investigation to address her falls risk were recommended.

Case 4

A 40-year-old teacher presented with headache and visual disturbance that seemed to be similar to her migraine with aura but had persisted for more than three days. Apart from frequent migraine attacks with visual

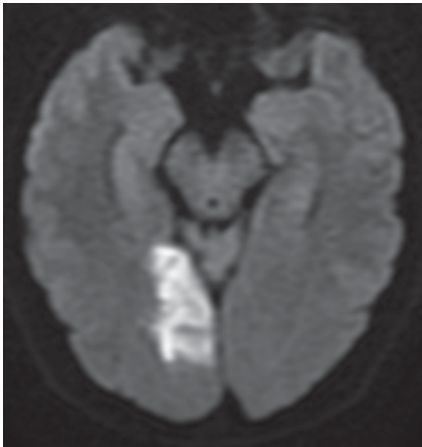


Figure 3. Case 4: an acute ischaemia in the right posterior cerebral artery territory in a 40-year-old woman (magnetic resonance image).

field deficits she had no relevant past medical history. She was a smoker and her only regular medication was oral contraception. Her family history was unremarkable.

Examination revealed a clear right-sided hemianopia but no other focal neurological deficits. An MRI showed an acute ischaemia (stroke) in the right posterior cerebral artery (PCA) territory (Figure 3). Her blood pressure and cholesterol levels were within the normal ranges. The duplex ultrasound, echocardiogram and Holter monitoring did not indicate a cause for her stroke.

A thrombophilia screen revealed positive Lupus anticoagulant antibodies and after confirmation of this finding, the patient was started on oral anticoagulation with warfarin, with an INR target of between 2.0 and 3.0.¹² Since there are no randomised trial data on the treatment of young patients who have had a stroke and who test positive for thrombophilia, an evidence-based recommendation cannot be made. Nevertheless, this patient fulfils the clinical criteria for antiphospholipid syndrome and can therefore be treated with oral anticoagulation. She was strongly

advised to stop smoking and cease hormonal contraception. She was told that in case of a planned pregnancy she would need to take low-molecular weight heparin instead of warfarin.

At follow-up presentations one, two and three years later the patient remained free of new symptoms. Unfortunately, a residual left lower field deficit prevented her from resuming driving.

Discussion

In 2009 the AHA/ASA endorsed a change in the definition of TIAs from a purely clinical and time-based definition to one including tissue-based information. Currently, TIAs are defined as transient episodes of neurological dysfunction caused by presumed focal brain, spinal cord or retinal ischaemia without infarction on MRI and resolving within 24 hours.¹³ If MRI shows evidence of infarction but the symptoms last for less than

24 hours the diagnosis is a minor stroke.

Typical symptoms of TIAs and stroke usually occur with sudden onset and include one-sided weakness or numbness, impairment of speech or language, visual disturbance (e.g. visual field deficit, double vision or loss of vision in one eye), incoordination and imbalance (Box 1). Some of the deficits – for example, visual field deficits – may become evident only when a thorough neurological examination is conducted. Patients with aphasia as their presenting symptom are often misdiagnosed as being disoriented or confused. Acute onset of vertigo can also indicate a neurovascular event, although it is mostly caused by vestibular dysfunction such as BPPV. Patients with any of these symptoms should be considered as

having had a possible TIA or stroke and should be investigated thoroughly. Most TIA symptoms last for several minutes to up to one hour, but sometimes they can last up to 24 hours. If symptoms persist beyond this time the patient must be referred immediately to the ED.

Urgent investigations should be performed within a few days and include:

- imaging of the brain (by CT and/or MRI, which has significantly higher sensitivity, especially in cases of minor strokes)
- imaging of the carotid and vertebral arteries (CT angiography or duplex ultrasonography of the cervical arteries)
- 12-channel ECG

1. Typical TIA/stroke symptoms

- Visual disturbance (visual field deficit, double vision or loss of vision in one eye)
- Facial droop
- Unilateral paresis (weakness)
- Unilateral sensory deficit
- Speech difficulties (slurred speech)
- Language difficulties (difficulties understanding or expressing)
- Impaired fine motor skills
- Incoordination

- transthoracic echocardiography
- blood pressure measurement
- full blood cell count
- fasting lipids and glucose measurements.

2. Vascular risk factors and lifestyle questionnaire*

To be completed by the patient

Are you a **smoker**? Yes No Are you an ex-smoker? Yes No How many years ago did you stop? ____ If you smoke/smoked, how many cigarettes per day ____ and for how many years ____ ?

Physical exercise (i.e. jogging, swimming, gym, brisk walking): How many times a week do you exercise? ____ In total how many hours a week do you exercise? ____

Diet: How many times a week do you eat: Eggs ____ Meat ____ Fish ____ Full fat dairy ____ Cheese ____ Sweets ____ Vegetables ____ Fruits ____

Alcohol: How many standard drinks do you have per week (1 standard drink equals 1 stubby or small glass of wine) ____

Known risk factors: High blood pressure High cholesterol Diabetes Previous stroke/TIA Atrial fibrillation Palpitations Ischaemic heart disease (angina pectoris, heart attack, cardiac stent)

For women: Are you on any kind of **hormonal therapy** (i.e. oral contraceptive, HRT)? Yes No

Family history: Did a family member have a stroke/heart attack at the age of 60 years or younger? Yes No

Do you have concerns about your **mood**? Yes No If yes, please describe _____

To be completed by the physician

Blood pressure: ____ / ____ mmHg **Heart rate:** ____ bpm regular irregular **Weight:** ____ kg **Height:** ____ cm

LDL: ____ mmol/L **Total cholesterol:** ____ mmol/L **Glucose:** ____ mmol/L Not done

Stenosis in duplex? Yes No Not done If yes, grade and localisation _____

Holter monitor? Yes No

Follow up? Yes No If yes, when? ____ month

Comments _____

* Risk factor assessment tool used at the TIA/stroke clinic, Royal North Shore Hospital, Sydney, NSW.

3. Useful websites on TIAs and stroke

Tips on symptom recognition, risk factors, management of TIA or stroke and information for patients and their relatives

National Stroke Foundation: <http://strokefoundation.com.au>

Medical standards for road licensing and assessment guidelines (including stroke and epilepsy)

Austroroads: www.austroroads.com.au

Official stroke guidelines from the American Heart Association/American Stroke Association

AHA/ASA website: http://my.americanheart.org/professional/StatementsGuidelines/ByTopic/TopicsQ-Z/Stroke-Statements-Guidelines_UCM_320600_Article.jsp

Holter monitoring to exclude paroxysmal atrial fibrillation should also be performed as soon as possible. It has been shown that long-term monitoring with an insertable cardiac monitor detects a significantly higher rate of paroxysmal atrial fibrillation than standard Holter monitoring in cases of cryptogenic strokes – that is, when no cause has been found despite extensive investigation.⁴

Optional tests might be performed in selected cases and can include transthoracic echocardiography, thrombophilia screen and angiography. All these tests should be performed and assessed within a few days after a patient has had a TIA.

The risk factor assessment tool used in our TIA/stroke clinic at The Royal North Shore Hospital, a teaching hospital in Sydney, is shown in Box 2. This questionnaire provides the patient with an opportunity to review lifestyle aspects and known risk factors while they are waiting to see the neurologist. The patient and doctor can then together evaluate the list and discuss important modifications in lifestyle and medical treatment.

The targets for primary prevention are less strict compared with those for secondary prevention, but the same principles for treatment and lifestyle changes apply.⁴ The most important modifiable risk factors for primary and secondary stroke prevention are listed in the Table.^{3,4}

Useful websites on TIAs and stroke for health professionals and patients and their families are listed in Box 3.

Summary

The introduction of a nationwide rapid access TIA outpatient service could be an important tool in improving patient outcomes and overall population health, while reducing the strain on hospital inpatient resources and general healthcare costs. In most regions of Australia, however, GPs provide the care for patients with TIAs, manage vascular risk factors for primary and secondary prevention as well as educating patients on recognising signs of an acute stroke. The population needs to be informed about the importance of phoning 000 in the case of any neurological deficit of sudden onset. **CT**

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