Elaine S Leung
M Anne Hamilton-Bruce
Simon A Koblar

Transient ischaemic attacks

Assessment and management

Background
Transient ischaemic attacks (TIAs) can be challenging to diagnose, but early assessment and effective management can reduce the subsequent risk of stroke.

Objective
This article reviews the assessment and management of TIAs for general practitioners.

Discussion
Transient ischaemic attacks can be a trap for the unwary, with difficulty in making a diagnosis and varied assessment and management pathways. There is a significant risk of subsequent stroke. Early assessment and initiation of treatment, which can take place in the general practice setting, could lower the risk of stroke. Liaising with regional stroke care centres is required to establish an optimal pathway of care.

Keywords: ischaemic attack, transient; stroke; secondary prevention

CPD

Transient ischaemic attacks (TIAs) are a warning sign of stroke, with 20% of patients having a subsequent stroke within 90 days.[1] Stroke is a leading cause of disease in Australia, with approximately 50 000 strokes occurring per year.[2] The subsequent consequences can be devastating, with 20% of patients dying within 1 month of their first stroke[3] and of survivors, one-third remaining disabled.[4]

The assessment and management of TIAs can be difficult, particularly as symptoms resolve quickly and patients may be unaware of their importance and the urgency of early medical attention.[5] With difficulty in ascertaining cases, and cases undiagnosed in the community, there is limited data on the incidence of TIAs both within Australia and internationally. Studies overseas have estimated the incidence of TIA to be 68–83 per 100 000 population, with the majority of cases occurring in the 75–84 years age group.[6] This provides an opportunity for stroke prevention, with evidence suggesting that early assessment and management of TIAs reduce the risk of stroke by up to 80%.[7]

Definition of TIA

In 1978, the World Health Organization defined TIA as an 'episode of sudden focal neurological deficit lasting less than 24 hours and of vascular origin'.[8] A stroke in contrast, is defined as 'rapidly developing symptoms and/or signs of focal (or global) loss of brain function lasting longer than 24 hours or leading to death with no apparent cause other than of vascular origin'.[9] With advances in imaging, in particular magnetic resonance imaging (MRI), up to 48% of patients with a diagnosis of TIA have evidence of infarction on diffusion weighted imaging and so have actually had an ischaemic stroke.[10] Furthermore, the use of intravenous thrombolysis in acute ischaemic stroke has been shown to be effective up to 4.5 hours from the onset of symptoms.[11] Thus, the American Stroke Association has recently adopted a new definition for TIA, being a 'transient episode of neurological dysfunction caused by focal brain, spinal cord or retinal ischaemia, without acute infarction' and they recommend that all TIA patients undergo neuro-imaging, preferably MRI scanning.[12] This new definition has not yet been adopted fully but it is clear the

previous definition was hampered by an arbitrary time restraint which is now less meaningful.

Diagnosis

The diagnosis of TIA remains a clinical one, and even for neurologists can be a challenge, with many other medical conditions posing as mimics.[13] One study reviewed 100 patients with transient neurological symptoms presenting at a hospital emergency department and found only 40 were confirmed cases of TIA (*Table 1*).[14]

Symptoms more suggestive of a TIA include:

- sudden onset
- focal symptoms (eg. unilateral weakness, speech disturbance).

Many transient episodes that present in general practice have mixed symptoms and posterior circulation symptoms, which can be difficult to interpret. Taking a detailed history from both the patient and, if possible, any witnesses, is very important in diagnosing any transient neurological episode.

In educating patients about the symptoms of stroke and TIA, the mnemonic FAST (Face, Arm, Speech, Time to act) should be discussed, having been shown to identify 88.9% of TIAs in one study.[15]

While the use of imaging, particularly MRI scans, has been advocated with the new proposed definition, in Australia there is no Medicare rebate available for general practitioners ordering this investigation and there are major issues surrounding access and costing, which make its routine use unrealistic currently. The presence of protein biomarkers in blood, similar to troponin in ischaemic heart disease, would be useful in assisting in diagnosing or stratifying TIAs, but as yet none have been found particularly useful.[16] Studies have also demonstrated that a genetic risk for stroke and genetic biomarkers may contribute to stratifying risk and preventing stroke.[17,18]

Assessment

In general practice the diagnosis can be a challenge, especially given that a TIA is a medical emergency with the risk of stroke varying between 10–20% in the following 90 days.[1] Half of such patients will have a stroke within 48 hours of the TIA.[19]

Risk stratification can assist GPs in assessing this early risk of stroke. Johnston et al devised the 'Age, Blood pressure, Clinical features, Duration, Diabetes' tool ($ABCD^2$ score) (*Table 2*) to assist with predicting the risk of stroke in TIAs at 48 hours.[20] This easy assessment provides clinicians with a tool to determine how urgently and where the TIA patient might be best managed. There is limited research on where best to manage TIA patients and, in particular, the usefulness of acute stroke units for patients with TIAs. Opinions on the most appropriate setting differ within the neurology community and as a result there are variable models of care both nationally and internationally.[21]

A recent survey of Australian hospitals co-ordinated by the National Stroke Foundation confirmed the variable services for TIA assessment and management. These ranged from admitting all patients (15%) to specialist follow up (35%) in neurology outpatient clinics, specialist rooms or a TIA clinic. With delays in both assessment and treatment, the study suggested there is a significant gap between the evidence and current practice, concluding that determining the best model of care requires urgent investigation.[22]

Until the evidence is clearer, the most accepted recommendation is that patients classified at higher risk ($ABCD^2$ score greater than 4) should be referred urgently for a comprehensive assessment in an acute unit, either a dedicated hospital TIA clinic or stroke unit. Patients with atrial fibrillation (AF) or crescendo TIAs should also be considered high risk. A study of a 24 hour hospital TIA clinic reported that 74%

Table 1. TIA mimics

Mimic	Timing/onset	Suggested by
Migraine	Progressive	Nausea, vomiting, aura, headache
Partial seizures	'March' of symptoms	No recall of events
Vestibular disorders	Recurrent episodes	Hearing loss, tinnitus, balance disturbance
Intracranial lesion	Gradual, fluctuating	Headache, vomiting Episodic symptoms may be from oedema, bleeding or focal seizures
Metabolic, eg. hypoglycaemia	Variable, recurrent	Co-existing morbidities and medications
Transient global amnesia	Sudden, duration hours	No recall of events, no loss of personal identity, repetitive questioning, no loss of consciousness
Syncope	Sudden	Nonfocal symptoms, loss of consciousness
Delirium, eg. sepsis	Variable, fluctuating	History of dementia, confusion rather than speech disturbance, fluctuating consciousness
Other neurological disorders, eg. multiple sclerosis, motor neuron disease, myasthenia gravis	Progressive	Recurrent episodes and deterioration
Psychogenic	Recurrent, situational	Lack of vascular risk factors, hyperventilation, nonorganic signs

Table 2. ABCD^2 tool

Age
60 years or older (1 point)
Blood pressure
Systolic ≥140 mmHg (1 point) Diastolic ≥90 mmHg (1 point)
Clinical features
Any unilateral weakness (2 points) Speech impairment without weakness (1 point)
Duration
60 minutes or more (2 points) 10–59 minutes (1 point)
Diabetes mellitus (1 point)
ABCD^2 >4 = high risk, ≤4 = low risk (maximum is 7)[23]

of patients were discharged home after prompt assessment and treatment, potentially lowering costs.[24] There is limited data on the cost effectiveness of the variable models of care.[25,26] Liaising with a regional stroke centre is required to establish a pathway of care. In metropolitan Adelaide (South Australia) for example, a model of TIA care is being investigated which uses TIA clinics in the hospital and within the community for rapid assessment and management in close association with the regional stroke unit.[27] The community TIA service utilises GPs who have been trained in stroke medicine, with a 'special interest in stroke'. Other pathways may also address delays in assessment and treatment. One group has suggested that a 24 hour, 7 day telephone hotline with access to a stroke physician is effective and feasible.[28]

Irrespective of location, patients with a lower risk (ABCD^2 score equal to or less than 4) should have a computerised topography (CT) brain scan to exclude haemorrhage and other space occupying lesions (eg. tumour), and carotid duplex ultrasound (if symptoms are within the carotid artery territory and the patient would be potentially suitable for carotid re-vascularisation) as soon as possible (within 48–72 hours).[23]

Other routine investigations should include:

- full blood count, electrolytes, renal function, lipids, blood glucose levels, and erythrocyte sedimentation rate, and
- electrocardiogram.[29]

Given the risk of subsequent stroke and its devastating consequences, if there is any doubt about the diagnosis or concerns about assessing the patient, the safest approach would be to refer the patient to an acute care hospital. The evidence surrounding the value of the ABCD^2 score remains uncertain and the American Stroke Association has a different approach. Their guidelines are more conservative and suggest that it is reasonable to hospitalise patients with TIA if they present within 72 hours of the event and any of the following criteria are present:

- ABCD^2 score of equal to or greater than 3
- ABCD^2 score of 0–2 and uncertainty that diagnostic workup can be completed within 2 days as an outpatient
- ABCD^2 score of 0–2 and other evidence that indicates the patient's event was caused by focal ischemia.[12]

Management

The treatment of a suspected TIA aims to prevent further TIAs and subsequent ischaemic stroke. This management may be best carried out by the patient's GP in the community setting following initial acute and focused management by a TIA clinic or acute stroke unit. The close communication between GP and TIA physician for optimum secondary prevention is fundamental (*Figure 1*).

Lifestyle modifications

All patients with a suspected TIA should be counselled to:

- quit smoking
- adopt a low fat, low sodium diet
- exercise regularly, and
- avoid excessive alcohol consumption.[23]

Antiplatelets

Long term antiplatelets should be commenced in all patients with TIA who are not on anticoagulant therapy. Studies have demonstrated that antiplatelet treatment significantly reduces the risk of stroke,[30] with the combination of aspirin and dipyridamole shown to be more effective than aspirin alone.[31] Low dose aspirin and modified release dipyridamole or clopidogrel alone should be commenced.[32]

Anticoagulation

After a CT has excluded haemorrhage, warfarin should be commenced in all TIA patients who have atrial fibrillation, cardio-embolic stroke from valvular heart disease, or recent myocardial infarction. A Cochrane review in 2004 concluded that anticoagulation can reduce the risk of stroke in patients with non-rheumatic atrial fibrillation.[33]

Cholesterol lowering agent

Together with dietary advice, a statin should be considered in all patients following a TIA.[34]

Blood pressure lowering

Evidence suggests that all patients should receive blood pressure lowering treatment after a TIA unless contraindicated by symptomatic hypotension.[35] Angiotensin converting enzyme inhibitors (ACEIs) and diuretics separately and together, have the most evidence and in one study were shown to decrease vascular events, with treatment recommended within the first week after a TIA.[36] However, most antihypertensives have been found to be effective and choices should be tailored to the patient's comorbidities. The addition of an angiotensin receptor blocker has not shown any further benefit.[37]

Carotid surgery

Carotid endarterectomy has been found to reduce the risk of disabling stroke or death for patients with stenosis exceeding 70%, in surgically fit patients operated on by surgeons with low complication rates (less than 6%).[38]

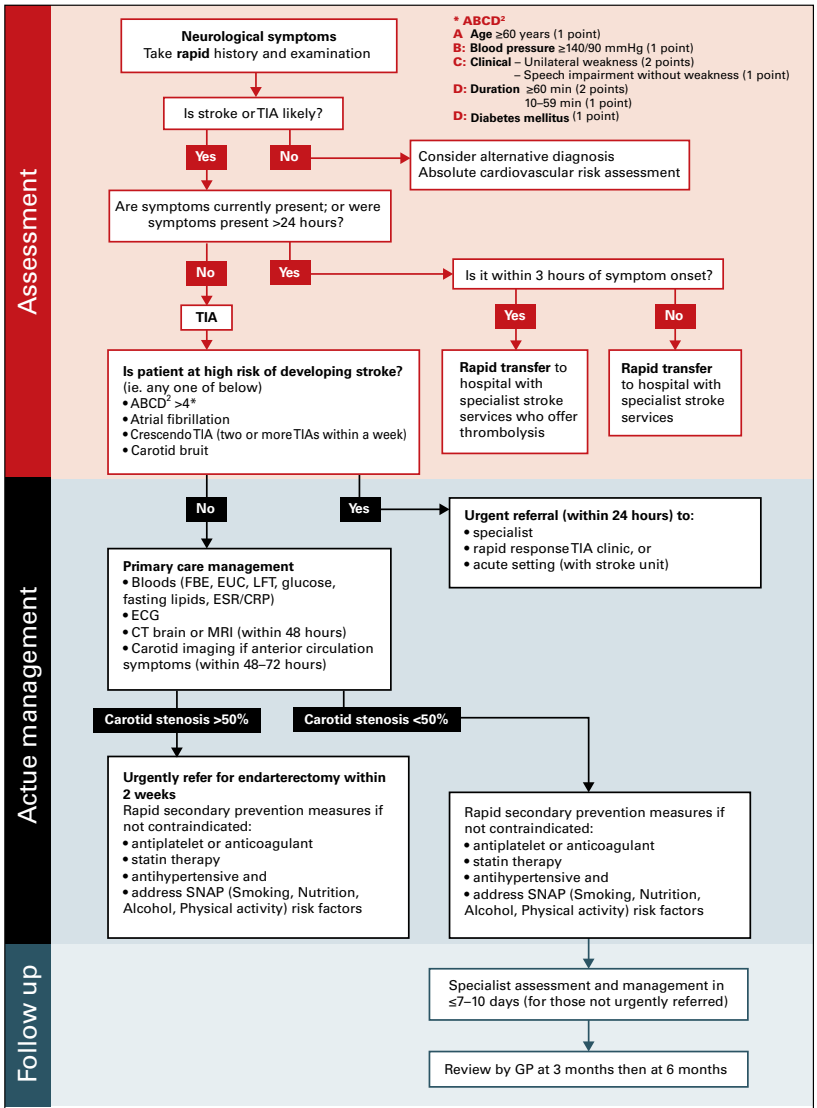

Figure 1. Transient ischaemic attack pathway[39]

Diabetes care

Blood glucose should be monitored in all patients following a TIA as it is an independent risk factor for stroke, while patients with diabetes or glucose intolerance should aim for good control.[23]

Hormone therapy

There may be a risk of increased stroke associated with hormone therapy,[40] and following a TIA patients should be individually counselled regarding the risks and benefits.[23]

Conclusion

Transient ischaemic attacks can be a trap for the unwary, given the difficulty in diagnosis and the limited evidence on the best location for assessment and management. Given the significant risk of subsequent stroke, GPs play a highly important role in the initial assessment and subsequent longer term secondary prevention. Early assessment and initiation of treatment, which may be in general practice for lower risk patients, could lower the risk of stroke and potentially lower healthcare costs significantly, although more research is needed in this area. But any doubts about either the diagnosis or the risk of stroke should result in an immediate referral to hospital. Liaising with regional stroke units is required to establish an optimal pathway of care.

Authors

Elaine S Leung MBBS, BSc(Med), DCH, FRACGP, is a general practitioner and PhD candidate, Discipline of Medicine, University of Adelaide, Queen Elizabeth Hospital, Adelaide, South Australia. elaine.leung@optusnet.com.au

M Anne Hamilton-Bruce BSc, MSc, MBA, PhD, AFCHSE, CBiol, MSB, CSci, FIBMS, is Principal Medical Scientist and Management Coordinator, Neurology, and Centre for Inflammatory Diseases Research, Basil Hetzel Institute for Medical Research, Co-director, Stroke Research Programme, The Queen Elizabeth Hospital, South Australia, and Affiliate Lecturer, School of Medicine, University of Adelaide, South Australia

Simon A Koblar BMBS, PhD, FRACP, is Associate Professor, University of Adelaide, School of Medicine, Queen Elizabeth Hospital, Director, Stroke Research Programme, University of Adelaide, Schools of Medicine, Medical Science and Molecular Biomedical Science, and Basil Hetzel Institute for Medical Research, Senior Consultant Neurologist, Stroke Physician, Queen Elizabeth Hospital Neurology Unit, Stroke Unit, and Clinical Adviser, Centre for Stem Cell Research, Robinson Institute, University of Adelaide, South Australia.

Conflict of interest: none declared.

References

1. Johnston SC, Gress DR, Browner WS, et al. Short-term prognosis after emergency department diagnosis of TIA. JAMA 2000;284:2901–6.
2. Australian Institute of Health and Welfare. Senes S. How we manage stroke in Australia. AIHW cat. no. CVD 31. Canberra: Australian Institute of Health and Welfare, 2006.
3. Thrift AG, Dewey H, Macdonell RAL, et al. Stroke incidence on the east coast of Australia: The North East Melbourne Stroke Incidence Study (NEMESIS). Stroke 2000;31:2087–92.
4. Hankey GJ, Jamrozik K, Broadhurst RJ, et al. Long-term disability after first-ever stroke and related prognostic factors in the Perth Community Stroke Study, 1989–1990. Stroke 2002;33:1034–40.
5. Giles MF, Flossman E, Rothwell PM. Patient behaviour immediately after transient ischemic attack according to clinical characteristics, perception of the event, and predicted risk of stroke. Stroke 2006;37:1254–60.
6. Kleindorfer D, Panagos P, Pancioli A, et al. Incidence and short-term prognosis of transient ischemic attack in a population-based study. Stroke 2005;36:720–3.
7. Rothwell PM, Giles MF, Chandratheva A, et al. Effect of urgent treatment of transient ischaemic attack and minor stroke on early recurrent stroke (EXPRESS study): A prospective population-based sequential comparison. Lancet 2007;370:1432–42.
8. Albers GW, Caplan LR, Easton JD, et al. Transient ischaemic attack- proposal

for a new definition. New Engl J Med 2002;347:1713–6.
9. Hatano S. Experience from a multicentre stroke register: a preliminary report. Bull WHO 1976;54:541–53.
10. Kidwell CS, Alger JR, Di Salle F, et al. Diffusion MRI in patients with transient ischaemic attacks. Stroke 1999;6:1174–80.
11. Lansberg M, Bluhmki E, Thijs V. Efficacy and safety of tissue plasminogen activator 3 to 4.5 hours after acute ischemic stroke: a meta-analysis. Stroke 2009;40:2438–41.
12. 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;40:2276–93.
13. Castle J, Mlynash M, Lee K, et al. Agreement regarding diagnosis of transient ischemic attack fairly low among stroke-trained neurologists. Stroke 2010;41:1367–70.
14. Prabhakaran S, Silver AJ, Warrior L, et al. Misdiagnosis of transient ischemic attacks in the emergency room. Cerebrovasc Dis 2008;26:630–5.
15. Kleindorfer DO, Miller R, Moomaw CJ, et al. Designing a message for public education regarding stroke: does FAST capture enough stroke? Stroke 2007;38:2864–8.
16. Cucchiara BL, Messe SR, Sansing L, et al. Lipoprotein-associated phospholipase A2 and C-reactive protein for risk-stratification of patients with TIA. Stroke 2009;40:2332–6.
17. Dichgans M, Hegele RA. Update on the genetics of stroke and cerebrovascular disease 2008. Stroke 2009;40:e289–91.
18 Jannes J, Hamilton-Bruce MA, Pilotto L, et al. Tissue plasminogen activator -7351C/T enhancer polymorphism is a risk factor for lacunar stroke. Stroke 2004;35:1090–4.
19. Lovett JK, Dennis MS, Sandercock PA, et al. Very early risk of stroke after a first transient ischaemic attack. Stroke 2003;34:e138–40.
20. 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;369:283–92.
21. Fallon C, Noone I, Ryan J, et al. Assessment and management of transient ischaemic attack: The role of the TIA clinic. Irish Journal of Medical Science 2006;175:24–7.
22. Price CJ, Blacker DJ, Grimley RS, et al. National survey of management of transient ischaemic attack in Australia: Take immediate action. Med J Aust 2009;191:17–20.
23. National Stroke Foundation. Clinical guidelines for acute stroke management 2010. Available at www.strokefoundation.com.au/health-professionals [Accessed 22 September 2010].
24. Lavallee PC, Meseguer E, Abboud H, et al. A transient ischaemic attack clinic with round-the-clock access (SOS-TIA): Feasibility and effects. Lancet Neurol 2007;6:953–60.
25. Luengo-Fernandez R, Gray AM, Rothwell PM. Effect of urgent treatment for transient ischaemic attack and minor stroke on disability and hospital costs (EXPRESS study): a prospective population-based sequential comparison. Lancet Neurol 2009;8:235–43.
26. Wu CM, Manns BJ, Hill MD, et al. Rapid evaluation after high-risk TIA is associated with lower stroke risk. Can J Neurol Sci 2009;36:450–5.
27. Central Northern Adelaide Health Service. Ethics of Human Research Committee Approval number 2009123. COMBAT Stroke Pilot Study: Community-Based Rapid Access Transient Ischaemic Attack (TIA) Management, 2009.
28. Kerr E, Arulraj N, Scott M, et al. A telephone hotline for transient ischaemic attack and stroke: prospective audit of a model to improve rapid access to specialist stroke care. BMJ 2010;341:c3265.
29. National Stroke Foundation. Clinical guidelines for stroke and TIA management: a quick guide for general practitioners 2008. Available at www.strokefoundation.com.au/component/option,com_docman/Itemid,174/task,doc_view/gid,169 [Accessed 22 September 2010].
30. Antithrombotic Trialists Collaboration. Collaborative meta-analysis of randomised trial of antiplatelet therapy for prevention of patients death, myocardial infarction, and stroke in high risk patients. BMJ 2002;324:71–86.
31. ESPRIT Study Group, Halkes PH, van Gijn J, Kappelle LJ, et al. Aspirin plus dipyridamole versus aspirin alone after cerebral ischaemia of arterial origin (ESPRIT): randomised controlled trial. Lancet 2006;367:1665–73.
32. Sacco RL, Diener H-C, Yusuf S, et al. Aspirin and extended-release dipyridamole versus clopidogrel for recurrent stroke. New Engl J Med 2008;359:1238–51.
33. Saxena R, Koudstaal PJ. Anticoagulants for preventing stroke in patients with nonrheumatic atrial fibrillation and a history of stroke or transient ischaemic attack. Cochrane Database Syst Rev 2004;2:CD000185. Available at www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD000185/frame.html [Accessed 22 September 2010].
34. Manktelow B, Potter J. Interventions in the management of serum lipids for preventing stroke recurrence. Cochrane Database Syst Rev 2009;3:CD002091. Available at http://onlinelibrary.wiley.com/o/cochrane/clsysrev/articles/CD002091/frame.html [Accessed 22 September 2010].
35. Rashid P, Leonardi-Bee J, Bath P. Blood pressure reduction and secondary prevention of stroke and other vascular events: a systematic review. Stroke 2003;34:2741–9.
36. Nazir FS, Overell JR, Bolster A, et al. Effect of perindopril on cerebral and renal perfusion on normotensives in mild early ischaemic stroke: a randomized controlled trial. Cerebrovasc Dis 2005;19:77–83.
37. Yusuf S, Diener H-C, Sacco RL, et al. Telmisartan to prevent recurrent stroke and cardiovascular events. New Engl J Med 2008;359:1225–37.
38. Cina CS, Clase CM, Hayes RB. Carotid endarterectomy for symptomatic carotid stenosis. Cochrane Database Syst Rev 1999;3:CD001081. Available at http://onlinelibrary.wiley.com/o/cochrane/clsysrev/articles/CD001081/frame.html [Accessed 21 September 2010].
39. The Royal Australian College of General Practitioners. check Program: stroke. Issue 454/455. South Melbourne: The RACGP, 2010.
40. Bath PMW, Gray LJ. Association between hormone replacement therapy and subsequent stroke: a meta-analysis. BMJ 2005;12:342.

correspondence **afp@racgp.org.au**