Management of transient ischaemic attack

Transient ischaemic attack carries a high stroke risk. Accurate diagnosis requires careful clinical assessment and high-risk individuals can be identified by the ABCD2 score and the presence of large artery disease and brain infarction on imaging. Urgent secondary prevention improves early outcome.

Transient ischaemic attack is common, with an annual incidence of approximately 1.1 per thousand population. Because transient ischaemic attack services also manage patients with minor or non-disabling stroke and referrals with eventual non-neurovascular diagnoses, the 'burden' of transient ischaemic attack is 2–3 times higher, meaning that in 1 year an average-sized district general hospital serving a population of 330 000 may receive approximately 1000 referrals for 'suspected transient ischaemic attack' and a GP might expect to see three cases. The rate of transient ischaemic attack rises steeply with age with the majority of events occurring in those aged over 70 years, so an increase in overall rates is expected in the UK over the next two to four decades as a result of the ageing of the population (Rothwell et al, 2004; Giles and Rothwell, 2007a).

Over the last decade there have been considerable advances in the understanding of the pathology, prognosis and treatment of transient ischaemic attack, leading to changes in the proposed definition and management and, in the UK, recent reorganization of services. Doctors from a wide range of specialities including primary care, neurology, emergency medicine, geriatrics and ophthalmology are likely to encounter patients with suspected transient ischaemic attack, so the ability to make an accurate diagnosis followed by risk stratification and initiation of early management is important for many clinicians.

Diagnosis

The traditional, time-based definition of transient ischaemic attack is 'an acute loss of focal brain or monocular function with symptoms lasting less than 24 hours, of presumed vascular cause', while events lasting longer than 24 hours or leading to death are classified as stroke. There is no gold-standard investigation and diagnosis is based on careful history and examination; formulating a differential diagnosis and making an accurate diagnosis can be challenging and opinions sometimes differ on what is and is not a transient ischaemic attack, even among experts.

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The time-based distinction between transient ischaemic attack and stroke has been criticized on the grounds that it is inconsistent with current knowledge of pathophysiology and prognosis, and a tissue-based distinction between transient ischaemic attack and stroke has been proposed, based on the presence or absence of infarction on brain imaging (Easton et al, 2009). However, the 'traditional' or time-based definition is mainly used in the UK and has the advantage of a clear differential diagnosis which is informative when evaluating a patient presenting with transient, focal neurological symptoms.

Some conditions or 'mimics' are particularly frequently misdiagnosed as transient ischaemic attack (*Table 1*). Features in the history and examination are often helpful in distinguishing transient ischaemic attack from the most common mimics (*Table 2*).

Migraine with aura

Sometimes a migraine aura without subsequent headache can develop in an individual with no history of previous

Table 1. Causes of transient focal neurological symptoms

Transient ischaemic attack	
Migraine with aura	
Focal epileptic seizures	
Structural intracranial lesions	Tumour
	Subdural haematoma
	Vascular malformation
	Giant aneurysm
Multiple sclerosis	
Labyrinthine disorders	Ménière's disease
	Benign paroxysmal positional vertigo
Peripheral nerve or root lesion	
Metabolic derangement	Hypoglycaemia or hyperglycaemia
	Hypercalcaemia
	Hyponatraemia
Psychological	
Transient global amnesia	

migraine. In this situation, the slow intensification and fading of symptoms over time, often with spread from one domain to another (for example vision to speech) is suggestive of migraine as opposed to transient ischaemic attack (Dennis and Warlow, 1992).

Epilepsy

Focal seizures and post-ictal paralysis are often mistaken for transient ischaemic attack. Todd's paresis is a focal neurological deficit, typically unilateral motor weakness, which can follow both focal and generalized seizures and last for several hours (Gallmetzer et al, 2004). Partial sensory seizures tend to cause positive symptoms such as tingling which 'march' across a hand or foot, and up the limb in around a minute and may eventually be accompanied by focal motor seizures or secondary generalization.

Intracranial structural lesions

Occasionally intracranial structural lesions such as subdural haematoma or tumour cause transient neurological deficit although the mechanism is unclear. Additional features in the history such as headache or nausea, systemic symptoms and stuttering or gradual onset suggest non-transient ischaemic attack diagnoses.

Vestibular dysfunction

Vertigo is common and should be distinguished from other less specific symptoms of 'unsteadiness' or 'lightheadedness'. Peripheral causes of vertigo (inner ear pathology, such as benign paroxysmal positional vertigo and acute labyrinthitis) are more common than central causes (brainstem or cerebellar disorders). Features suggestive of transient ischaemic attack mimics include retained ability to stand and walk, recurrent stereotypical episodes, presence of provoking factors (head position or movement), symptoms of middle ear disease (tinnitus, hearing loss) and absence of other focal brainstem symptoms (visual or speech disturbance, weakness or numbness). Features on examination which suggest a central cause of vertigo include nystagmus which is not suppressed by visual fixation, a normal head thrust test and other features of posterior circulation ischaemia including dysphagia, dysarthria, limb or facial weakness, gaze palsies or upgoing plantar responses.

Delirium or acute confusional state

Delirium or acute confusional state is a syndrome of acutely disordered cognition, associated abnormal attention and sometimes reduced conscious level. The differential diagnosis is long but the commonest causes are sepsis, metabolic derangement and adverse drug reaction (Francis et al, 1990). Delirium can be mistaken for transient ischaemic attack in cases which are mild and the predominant feature is interpreted as disorder of speech or language as opposed to confusion. Other features suggestive of delirium include the presence of a causative factor such as infection, inability of the patient to remember the event, fluctuating course and absence of a clearly sudden onset.

Table 2. Features of a patient's history which are less typical of transient ischaemic attack and alternative (mimic) diagnosis suggested

Symptom	Description	Non-neurovascular diagnosis suggested	Notes
Timing	Recurrent or stereotypical episodes	Anxiety related	Especially hemisensory loss
Onset	Stuttering	Tumour	Over hours or days
	Progressive	Migraine	Over minutes
	Ill defined	Delirium	
Symptoms	Prodrome	Aura	Migraine Seizure
	Non-focal	Syncope	Loss of consciousness
		Delirium	Reduced attention
		Labyrinthine dysfunction	Balance disturbance
	Positive	Seizure	Motor symptom
		Migraine	Visual spectra
	Additional symptoms	Migraine	Headache
		Labyrinthine dysfunction	Hearing loss or tinnitus
Course	Fluctuating	Tumour	
		Delirium	
Recall	Absent	Transient global amnesia	
		Generalized seizure	
	Patchy	Delirium	

Syncope and pre-syncope

Syncope is the abrupt loss of consciousness associated with loss of postural tone, usually followed by a rapid and complete recovery; pre-syncope is a premonitory sensation of syncope. The differential diagnosis of syncope is broad and rarely includes transient ischaemic attack. Infrequently, embolus to the tip of the basilar artery can present with acute coma but this is virtually never transient and other signs of brainstem dysfunction are present and obvious (Voetsch et al, 2004).

Risk and risk stratification

Once the diagnosis has been made, the importance of transient ischaemic attack lies in the early risk of stroke. Major stroke is often preceded by transient ischaemic attack although the symptoms may have neither alarmed the patient, nor have been reported to medical attention (Rothwell and Warlow, 2005).

Early studies underestimated the early risk of transient ischaemic attack by failing to recruit patients in the immediate phase after the event. However, more recent studies (Giles and Rothwell, 2007b) using different

methodologies and recruiting patients in the acute phase have reported the stroke risk immediately after transient ischaemic attack to be approximately 5% at 1 week and 10–15% at 3 months.

A systematic review and meta-analysis of these studies identified 18 cohorts, all published since 2000, reporting the early stroke risk in 10 126 transient ischaemic attack patients (Giles and Rothwell, 2007b). The pooled risks of stroke were 3.1% (95% confidence intervals 2.0–4.1) at 2 days and 5.2% (95% confidence intervals 3.9–6.5) at 7 days. Risks ranged from 0–12.8% at 7 days between the cohorts with significant heterogeneity between individual estimates. This heterogeneity was almost fully explained by study setting and method. The lowest risks were observed in studies in specialist stroke services offering emergency access and treatment, intermediate risks were observed in routine clinics and emergency departments and highest risks in population-based studies without urgent treatment.

Stroke risk after transient ischaemic attack poses a dilemma for patients, clinicians and service provision because although the majority of patients will have no acute sequelae, an important minority will go on to suffer a potentially disabling stroke which may be prevented with appropriate treatment. This has led to the development of risk stratification tools or scores to identify individuals at high (and low) risk.

Clinical features

The ABCD2 score was developed to predict the risk of stroke early after transient ischaemic attack using clinical features available at the time of initial patient assessment by a doctor in primary or emergency care. It was designed to facilitate triage to secondary care, focus public education and target secondary prevention. The score is based on five clinical features and is out of a total of seven (*Table 3*); patients with higher scores are at higher risk of early stroke (*Figure 1*) (Johnston et al, 2007). The score has been widely validated and was shown to have good prognostic value in a systematic review of twenty validation cohorts, reporting the performance of the ABCD2 score in 9808 subjects with 456 strokes at 7 days (Giles and Rothwell, 2010).

Although the score has been shown to work, the mechanism by which it does so is uncertain. It does have a diagnostic component, and discriminates those with genuine transient ischaemic attack from others with mimics or non-transient ischaemic attack diagnoses in 'mixed' cohorts (Quinn et al, 2009). However, its prognostic power is maintained in cohorts containing only transient ischaemic attack patients and even in cohorts of transient ischaemic attack patients with brain infarction on imaging.

Use of the ABCD2 score has been recommended by the National Institute for Health and Clinical Excellence (2008) and other national guidelines for triage between primary or emergency care and specialist care services (see below) (Department of Health, 2007).

Table 3. Clinical features and scoring for ABCD2 score

	Element	Category	Score
A	Age	Age ≥60 years	1
B	Blood pressure*	Systolic blood pressure >140 mmHg or diastolic blood pressure ≥90 mmHg	1
C	Clinical features	Unilateral weakness or speech disturbance (no weakness)	2 or 1
D	Duration	≥60 minutes or 10–59 minutes	2 or 1
D	Diabetes	Present	1
	Total		7

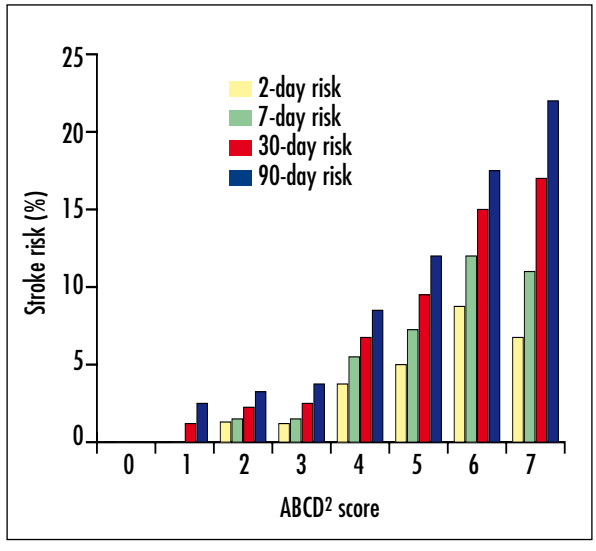
*measured at time of earliest assessment after transient ischaemic attack. From Johnston et al (2007)

Aetiology

Common causes of transient ischaemic attack include cardioembolism, most frequently as a result of atrial fibrillation, thrombus formation and embolism from an unstable plaque in a stenosed internal carotid artery (large artery atherosclerosis) and thrombosis of a deep penetrating cerebral artery causing a lacunar infarction.

Early stroke risk is particularly high after transient ischaemic attack caused by large artery atherosclerosis. Although this association has been mostly studied in stroke patients, in two large prospective cohorts of transient ischaemic attack patients, the mechanism has now been studied in relation to outcome at 3 months (Purroy et al, 2007; Calvet et al, 2009). Results were consistent, with highest stroke risk observed among those with large

Figure 1. Increasing stroke risk observed with increasing ABCD2 score after transient ischaemic attack. Observed stroke risk at 2, 7, 30 and 90 days after transient ischaemic attack stratified by ABCD2 score pooled from six validation cohorts. Individual bars refer to risk observed at different intervals from initial transient ischaemic attack. From Johnston et al (2007).



artery atherosclerosis, lowest risk in those with lacunar or small vessel disease, and intermediate risk in those with cardioembolic or undetermined cause of transient ischaemic attack.

Imaging

There is considerable interest in the role of diffusion weighted imaging on magnetic resonance imaging in predicting stroke risk after transient ischaemic attack. Diffusion weighted imaging measures the diffusion of water molecules in different tissues in the body and is very sensitive to the early phase of cerebral infarction. Diffusion weighted imaging is positive in approximately 30% of transient ischaemic attacks, but this proportion depends on the aetiology and clinical characteristics of the event itself and the delay to imaging (Redgrave et al, 2007). It has been proposed that diffusion weighted imaging may identify transient ischaemic attack patients with an active 'vascular process' such as a source of emboli or large artery atherosclerosis disease, signifying a high risk of further thromboembolism and so recurrent stroke.

The association between diffusion weighted imaging and early stroke risk has been addressed in a number of studies, although these have been hampered by small size, and sometimes retrospective design. In a recent systematic review of 3206 transient ischaemic attack patients receiving acute brain imaging with diffusion weighted imaging from 12 independent cohorts, 884 (27.6%) were found to have infarction and 72 (2.2%) had a stroke within 7 days (Giles et al, 2011). Among those with infarction on diffusion weighted imaging, pooled rates of recurrent stroke at 7 days were 7.1% (95% confidence intervals 5.5–9.1), compared to 0.4% (95% confidence intervals 0.2–0.7) in those without (P<0.0001), an eighteen-fold difference.

Although the associations between stroke risk after transient ischaemic attack and clinical features, aetiology and brain infarction are well established, the interaction between these different prognostic elements is less clear. For example, some components of the ABCD2 score (motor weakness, speech disturbance and longer symptom duration) are associated with diffusion weighted imaging lesions, while diffusion weighted imaging positivity is more common in patients with large artery atherosclerosis. There has therefore been uncertainty about whether these different elements might be combined to give prognostic information. However, in a cohort of 2654 transient ischaemic attack patients from different centres with detailed clinical features, phenotyping and brain imaging, it was found that these different elements could be combined into a unified predictive tool, the ABCD3-I score, which yielded additional prognostic information to any of the elements individually (*Table 4*) (Merwick et al, 2010).

Although this score still requires further validation, its strength is in defining and encouraging a systematic approach to the evaluation of a transient ischaemic attack patient, incorporating information on diagnosis, aetiology and subsequent injury. Risk stratification begins at the time of initial assessment in either primary or emergency care using core clinical information, and is then refined with results of vascular and brain imaging following assessment in specialist care.

Urgent treatment

The evidence base for secondary prevention of stroke is well established in the long term after transient ischaemic attack but, until recently, data on acute treatment were lacking. It has been argued that the benefit of secondary prevention in the long term could be observed in the acute period and that the combined effect of individual treatments such as antiplatelet agents, antihypertensives and carotid artery endarterectomy may be additive (Hackam and Spence, 2007). This argument formed the basis of two studies conducted in specialist units of the effect of combined preventive treatments started urgently on stroke risk after transient ischaemic attack (Lavallée et al, 2007; Rothwell et al, 2007).

The EXPRESS study

The Early Use of Existing Preventive Strategies for Stroke (EXPRESS) study aimed to determine the effect of urgent treatment after transient ischaemic attack or minor stroke in an outpatient setting (Rothwell et al, 2007). In a prospective population-based study (Oxford Vascular Study; OXVASC), the investigators determined the effect of urgent assessment and immediate treatment (phase 2) compared to appointment-based assessment and GP-initiated treatment (phase 1) in a daily transient ischaemic attack clinic. The primary outcome was the 90-day stroke risk. Treatment and imaging regimens were the same in both phases and all outcome events were independently adjudicated, blinded to study period.

Of all 1278 patients in the OXVASC study population with transient ischaemic attack or stroke over the 5-year study period (634 in phase 1 and 644 in phase 2), 620 with transient ischaemic attack or minor stroke were referred for outpatient assessment, while the remainder were treated as inpatients in hospital or at home. Of all

Table 4. Clinical features, investigation results and scoring for ABCD3-I score

	Element	Category	
	ABCD2	ABCD2 score as in *Table 3*	0–7
D	Dual transient ischaemic attack	Preceding transient ischaemic attack within 1 week of index transient ischaemic attack	1
I	Carotid stenosis	Ipsilateral carotid stenosis ≥50%	2
I	Infarction	Presence of brain infarction on diffusion weighted imaging, consistent with clinical syndrome	2
	Total		13

From Merwick et al (2010)

outpatient referrals 591/620 (95%) were to the EXPRESS study clinic. Baseline characteristics were similar in the two phases, but median delay to assessment in the study clinic fell from 3 days in phase 1 to <1 day in phase 2 (P<0.0001), and the median delay to first prescription of treatment fell from 20 days to 1 day (P<0.0001). The 90-day risk of recurrent stroke in the patients referred to the study clinic was 10.3% (32/310) in phase 1 *vs* 2.1% (6/281) in phase 2 (P=0.0001) (*Figure 2*). There was no significant change in risk among patients treated elsewhere. The reduction in risk was independent of age and sex, and early treatment did not increase the risk of haemorrhage.

SOS-TIA study

The good prognosis associated with urgent, intensive treatment was confirmed in the observational SOS-TIA study (Lavallée et al, 2007). An emergency transient ischaemic attack clinic was set up in a university hospital in Paris and local clinicians were invited to refer all transient ischaemic attack patients to the service which offered round the clock availability and urgent treatment and investigation. In all 629 consecutive patients with definite transient ischaemic attack seen over 3 years from January 2003, there were only two strokes within 7 days and 12 strokes within 3 months, resulting in risks of 0.3% and 1.9% respectively. These rates were much lower than those expected from prognostic scores and were attributed to the urgent intervention offered in the study. However, this study only assessed stroke risk among patients referred to the service and not all those within the population and did not have a control arm.

The interpretation of these two studies is that urgent specialist assessment, investigation and initiation of secondary prevention substantially reduces stroke risk in the acute phase after transient ischaemic attack.

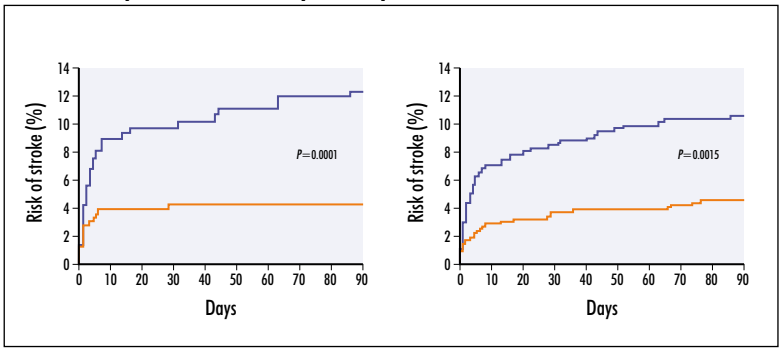
National guidance

In response to this evidence on risk stratification and the benefit of acute treatment and partly in recognition that transient ischaemic attack services in some parts of the UK were under-performing, National Institute for Health and Clinical Excellence and the National Stroke Strategy issued guidance on the acute management of transient ischaemic attack (Department of Health, 2007; National Institute for Health and Clinical Excellence, 2008).

It is recommended that all patients with suspected transient ischaemic attack in primary or emergency care are treated immediately with aspirin 300 mg and assessed for early stroke risk with the ABCD2 score. Those at high risk, defined as ABCD2 ≥4 or other high-risk features such as 'crescendo transient ischaemic attack', should receive specialist assessment and treatment in secondary care within 24 hours while others should be assessed within 7 days.

It goes on to recommend that magnetic resonance imaging with diffusion weighted imaging is the brain imaging modality of choice, especially in those with uncertain pathology or vascular territory, that those with symptomatic carotid stenosis should receive carotid artery endarterectomy within 2 weeks and that patients should receive specialist follow up at 1 month for lifestyle advice and risk factor control. Clearly, these are challenging recommendations and acute hospital trusts and commissioners have struggled to achieve them.

Figure 2. Reduction in stroke following urgent management of transient ischaemic attack. a. The 90-day risk of recurrent stroke after first seeking medical attention in all patients with transient ischaemic attack and (b) in all patients with transient ischaemic attack or stroke in the entire OXVASC study population. The blue line represents phase 1 of the EXPRESS study and the red line represents phase 2. From Rothwell et al (2007).



Secondary prevention and investigation

Both the EXPRESS and the SOS-TIA studies used standardized 'black box' approaches to secondary prevention, incorporating regimens of combined antiplatelet agents, antihypertensives and statins, and in selected cases, anticoagulation and carotid artery endarterectomy. Neither study demonstrated the extent of benefit provided by individual agents within the regimen. National Institute for Health and Clinical Excellence guidance recommends that 'measures for secondary prevention be introduced as soon as the diagnosis of TIA [transient ischaemic attack] is confirmed', but does not further specify the nature of the secondary prevention. Secondary prevention treatment should be started as soon as possible after the diagnosis has been reached and should be tailored according to the aetiology of the transient ischaemic attack (cardioembolic, large artery atherosclerosis, lacunar or other mechanism) and an individual's risk factors.

The choice of antiplatelet agents immediately after transient ischaemic attack is controversial and is covered below. Antihypertensive agents are recommended in patients with elevated blood pressure after transient ischaemic attack and in selected cases where blood pressure is normal, although the choice of agent is unclear. The PROGRESS trial demonstrated benefit of the combination of angiotensin-converting enzyme inhibitor and thiazide diuretic following either ischaemic stroke or transient ischaemic attack in both hypertensive and normotensive subjects compared to placebo (PROGRESS Collaborative Group, 2001). There has been interest in the potential additional benefit of control of blood pres-

sure variability with calcium-channel blockers compared to the more standard approach of 'average blood pressure' control (Webb et al, 2010). This approach has yet to be tested prospectively in randomized controlled trials. Cholesterol lowering after transient ischaemic attack with statins provided moderate benefit in vascular outcomes compared with placebo in the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial (Amarenco et al, 2006).

Carotid artery endarterectomy performed rapidly (within 14 days) after transient ischaemic attack or non-disabling stroke in those with symptomatic 70–99% carotid stenosis provides considerable benefit in terms of reducing the risk of stroke or death compared to medical treatment alone (Rerkasem and Rothwell, 2011). Although carotid artery stenting has been compared to carotid artery endarterectomy in a number of randomized controlled trials, it has not been shown to be clearly superior to surgery and, in the UK, carotid artery endarterectomy remains the treatment of choice for symptomatic carotid stenosis except in selected cases.

Figure 3 shows a simplified schema for the investigation of a patient with transient ischaemic attack.

Areas of uncertainty: antiplatelet agents

Data are lacking on the optimal combination or duration of antiplatelet agents in the acute phase after transient ischaemic attack. For instance, although aspirin reduces long-term vascular risk after transient ischaemic attack or stroke, and the risk of early recurrent stroke in the acute phase after ischaemic stroke (International Stroke Trial, 1997), its use specifically in the acute phase after transient ischaemic attack has not been studied. The combination of aspirin and dipyridamole is as effective as aspirin alone when started immediately after transient ischaemic attack or ischaemic stroke in preventing a combined vascular end point (Dengler et al, 2010) and the combination is superior in the prevention of stroke and cardiovascular events when started within 6 months of transient ischaemic attack or minor stroke (ESPRIT Study Group, 2006).

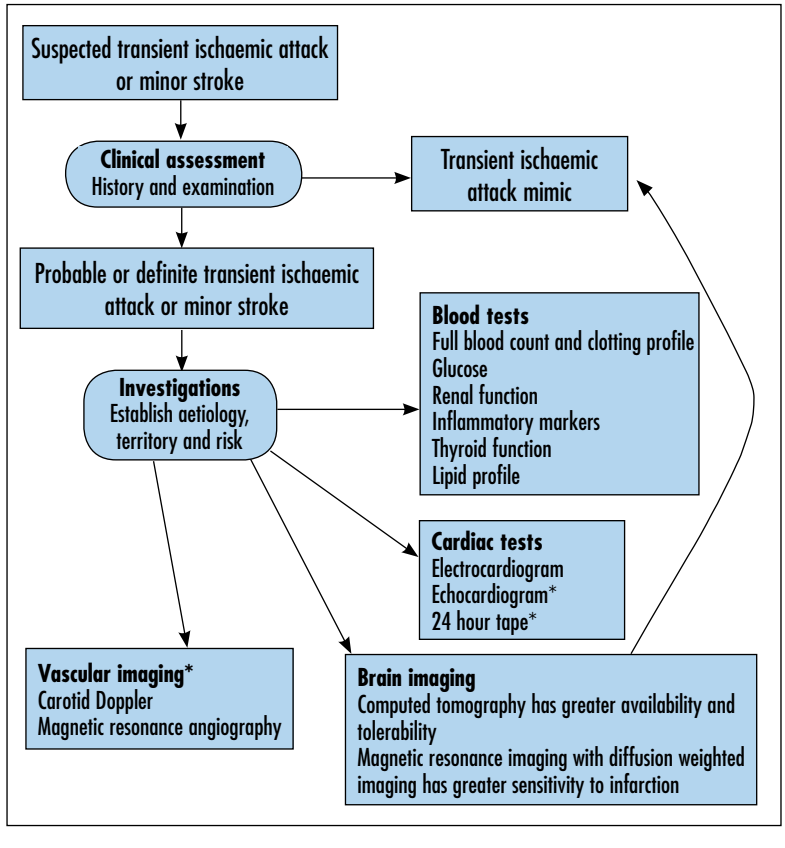
Two studies have suggested the benefit of the combination of aspirin and clopidogrel in the acute phase after transient ischaemic attack. The pilot Fast Assessment of Stroke and Transient ischemic attack to prevent Early Recurrence (FASTER) Trial (Kennedy et al, 2007) was a randomized controlled trial comparing this combination to aspirin alone acutely after transient ischaemic attack or minor ischaemic stroke. It found a trend towards lower rates of recurrent stroke at 90 days in the combination arm, but at the expense of a higher rate of intracranial haemorrhage. The CARESS trial compared the combination of aspirin and clopidogrel to aspirin alone in patients with recent transient ischaemic attack or stroke and symptomatic carotid stenosis (Markus et al, 2005). A reduction was observed in the primary end point (rate of asymptomatic microemboli detected by transcranial Doppler) in the combination group, as was a trend towards reduced stroke rate at 90 days.

Two ongoing trials will provide further data on antiplatelet agent choice. The Triple Antiplatelets for Reducing Dependency after Ischaemic Stroke (TARDIS) Trial (www.tardistrial.org/) is studying the addition of clopidogrel to aspirin and dipyridamole during the acute phase after transient ischaemic attack or ischaemic stroke. The CHANCE trial will compare the effect of the combination of aspirin and clopidogrel with aspirin alone on stroke reduction in the acute phase after transient ischaemic attack or minor stroke (Wang and Johnston, 2010).

Conclusions

Management of patients with suspected transient ischaemic attack should follow a structured approach, starting with confirming the diagnosis and excluding mimics, followed by establishing the aetiology and identifying an individual's risk factors. Formulating a differential diagnosis in suspected transient ischaemic attack is challenging and requires careful clinical assessment. In those with confirmed transient ischaemic attack, early stroke risk is high. This risk can be quantified using clinical data (ABCD2 score) and aetiology and imaging results (ABCD3-I score). Early stroke risk is reduced considerably with urgent specialist management with the initiation of secondary prevention and carotid artery endarterectomy in selected cases. BJHM

Figure 3. Schema for the investigation of a patient with suspected transient ischaemic attack or minor stroke. * = selected patients.



Conflict of interest: none.

Amarenco P, Bogousslavsky J, Callahan A 3rd et al (2006) High-dose atorvastatin after stroke or transient ischemic attack. *N Engl J Med* **355**(6): 549–59

Calvet D, Touzé E, Oppenheim C et al (2009) DWI lesions and TIA etiology improve the prediction of stroke after TIA. *Stroke* **40**(1): 187–92

Dengler R, Diener HC, Schwartz A et al; EARLY Investigators (2010) Early treatment with aspirin plus extended-release dipyridamole for transient ischaemic attack or ischaemic stroke within 24 h of symptom onset (EARLY trial): a randomised, open-label, blinded-endpoint trial. *Lancet Neurol* **9**(2): 159–66

Dennis M, Warlow C (1992) Migraine aura without headache: transient ischaemic attack or not? *J Neurol Neurosurg Psychiatry* **55**(6): 437–40

Department of Health (2007) *National Stroke Strategy.* Department of Health, London

Easton JD, Saver JL, Albers GW et al (2009) 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. *Stroke* **40**(6): 2276–93

ESPRIT Study Group, Halkes PH, van Gijn J, Kappelle LJ et al (2006) Aspirin plus dipyridamole versus aspirin alone after cerebral ischaemia of arterial origin (ESPRIT): randomised controlled trial. *Lancet* **367**(9523): 1665–73

Francis J, Martin D, Kapoor WN (1990) A prospective study of delirium in hospitalized elderly. *JAMA* **263**(8): 1097

Gallmetzer P, Leutmezer F, Serles W et al (2004) Postictal paresis in focal epilepsies - incidence, duration, and causes: a video-EEG monitoring study. *Neurology* **62**(12): 2160–4

Giles MF, Rothwell PM (2007a) Substantial underestimation of the need for outpatient services for TIA and minor stroke. *Age Ageing* **36**(6): 676–80

Giles MF, Rothwell PM (2007b) Risk of stroke early after transient ischaemic attack: a systematic review and meta-analysis. *Lancet Neurol* **6**(12): 1063–72

Giles MF, Rothwell PM (2010) Systematic review and pooled analysis of published and unpublished validations of the ABCD and ABCD2 transient ischemic attack risk scores. *Stroke* **41**(4): 667–73

Giles MF, Albers GW, Amarenco P et al (2011) Stroke risk & ABCD2 score performance in 'tissue' versus 'time' defined TIA: a multicentre study. *Neurology* (in press)

Hackam DG, Spence JD (2007) Combining multiple approaches for the secondary prevention of vascular events after stroke: a quantitative modelling study. *Stroke* **38**(6): 1881–5

International Stroke Trial (IST) (1997) A randomised trial of aspirin, subcutaneous heparin, both, or neither among 19435 patients with acute ischaemic stroke. International Stroke Trial Collaborative Group. *Lancet* **349**(9065): 1569–81

Johnston SC, Rothwell PM, Nguyen-Huynh MN et al (2007) Validation and refinement of scores to predict very early stroke risk after transient ischaemic attack. *Lancet* **369**(9558): 283–92

Kennedy J, Hill MD, Ryckborst KJ et al; FASTER Investigators (2007) Fast assessment of stroke and transient ischaemic attack to prevent early recurrence (FASTER): a randomised controlled pilot trial. *Lancet Neurol* **6**(11): 961–9

Lavallée PC, Meseguer E, Abboud H et al (2007) A transient ischaemic attack clinic with round-the-clock access (SOS-TIA): feasibility and effects. *Lancet Neurol* **6**(11): 953–60

Markus HS, Droste DW, Kaps M et al (2005) Dual antiplatelet therapy with clopidogrel and aspirin in symptomatic carotid stenosis evaluated using doppler embolic signal detection: the Clopidogrel and Aspirin for Reduction of Emboli in Symptomatic Carotid Stenosis (CARESS) trial. *Circulation* **111**(17): 2233–40

Merwick A, Albers GW, Amarenco P et al (2010) Addition of brain and carotid imaging to the ABCD² score to identify patients at early risk of stroke after transient ischaemic attack: a multicentre observational study. *Lancet Neurol* **9**(11): 1060–9

National Institute for Health and Clinical Excellence (2008) *Stroke. Diagnosis and initial management of acute stroke and transient ischaemic attack (TIA)* NICE Clinical Guidelines 68. National Institute for Health and Clinical Excellence, London

PROGRESS Collaborative Group (2001) Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. *Lancet* **358**(9287): 1033–41

Purroy F, Montaner J, Molina CA et al (2007) Patterns and predictors of early risk of recurrence after transient ischemic attack with respect to etiologic subtypes. *Stroke* **38**(12): 3225–9

Quinn TJ, Cameron AC, Dawson J, Lees KR, Walters MR (2009) ABCD2 scores and prediction of noncerebrovascular diagnoses in an outpatient population: a case-control study. *Stroke* **40**(3): 749–53

Redgrave JN, Coutts SB, Schulz UG et al (2007) Systematic review of associations between the presence of acute ischemic lesions on diffusion-weighted imaging and clinical predictors of early stroke risk after transient ischemic attack. *Stroke* **38**(5): 1482–8

Rerkasem K, Rothwell PM (2011) Carotid endarterectomy for symptomatic carotid stenosis. *Cochrane Database Syst Rev* **13**(4): CD001081

Rothwell PM, Warlow CP (2005) Timing of transient ischaemic attacks preceding ischaemic stroke. *Neurology* **64**(5): 817–20

Rothwell PM, Coull AJ, Giles MF et al; Oxford Vascular Study (2004) Change in stroke incidence, mortality, case-fatality, severity, and risk factors in Oxfordshire, UK from 1981 to 2004 (Oxford Vascular Study). *Lancet* **363**(9425): 1925–33

Rothwell PM, Giles MF, Chandratheva A et al (2007) Major reduction in risk of early recurrent stroke by urgent treatment of TIA and minor stroke: EXPRESS Study. *Lancet* **370**(9596): 1432–42

Voetsch B, DeWitt LD, Pessin MS et al (2004) Basilar artery occlusive disease in the New England Medical Center Posterior Circulation Registry. *Arch Neurol* **61**(4): 496–504

Wang Y, Johnston SC; CHANCE Investigators (2010) Rationale and design of a randomized, double-blind trial comparing the effects of a 3-month clopidogrel-aspirin regimen versus aspirin alone for the treatment of high-risk patients with acute nondisabling cerebrovascular event. *Am Heart J* **160**(3): 380–6.e1

Webb AJ, Fischer U, Mehta Z, Rothwell PM (2010) Effects of antihypertensive-drug class on interindividual variation in blood pressure and risk of stroke: a systematic review and meta-analysis. *Lancet* **375**(9718): 906–15

KEY POINTS

- Doctors from a range of specialties, including primary care, acute medicine, neurology, accident and emergency, geriatrics and ophthalmology, are likely to encounter patients with suspected transient ischaemic attack.
- Several mimics are frequently misdiagnosed as transient ischaemic attack, and accurate diagnosis requires careful history and examination.
- The early risk of recurrent stroke following minor stroke or transient ischaemic attack is in the region of 10% at 1 week and 15% at 1 month.
- Early stroke risk can be stratified by prognostic scores at initial assessment (ABCD2 score) and following specialist investigation (ABCD3-I score).
- Systematic evaluation is required after transient ischaemic attack to identify aetiology and territory.
- Urgent secondary prevention is essential to reduce early stroke risk.
- The National Stroke Strategy and National Institute for Health and Clinical Excellence have set demanding targets for management of transient ischaemic attack patients in specialist care.