Stroke in the acute setting

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Abstract

Acute stroke and transient ischaemic attack (TIA) are focal neurological syndromes of vascular origin and should be treated as medical emergencies. Brain imaging with computed tomography or magnetic resonance imaging is required to distinguish ischaemic stroke from intracerebral haemorrhage, recognize non-stroke pathologies that mimic stroke and guide investigation into the underlying mechanism. Acute interventions of benefit in ischaemic stroke include intravenous thrombolysis with alteplase given within 4.5 hours of onset, endovascular thrombectomy within 6 hours of onset in selected patients, stroke unit care and aspirin. Decompressive hemicraniectomy reduces mortality in ischaemic stroke complicated by severe brain swelling. Intracerebral haemorrhage accounts for 10–15% of strokes, and while specific treatments are lacking at present, patients benefit from general measures, notably stroke unit care. TIA carries a high short-term risk of stroke, and immediate investigation and institution of secondary preventive treatment prevents a high proportion of this. Secondary prevention for ischaemic stroke and TIA should be tailored according to mechanism in individual patients.

Keywords

Acute treatment; cerebrovascular disease; intracerebral haemorrhage; stroke; thrombectomy; thrombolysis

Key points

- Acute ischaemic stroke is common and disabling
- Stroke unit care improves outcome, and all patients should be admitted to a specialist stroke service
- Prompt recognition of stroke requires awareness of clinical patterns and radiological features
- Treatment with intravenous thrombolytic drugs within 4.5 hours improves the odds of disability-free recovery; the earlier treatment is initiated, the greater the effect
- Additional endovascular mechanical thrombectomy using stent retrievers is highly effective in selected patients with occlusions of the intracranial internal carotid or middle cerebral artery
- In minor ischaemic stroke and transient ischaemic attack, early institution of secondary prevention reduces the incidence of recurrent stroke
- Intracerebral haemorrhage currently lacks evidence-based treatments beyond stroke unit care, but platelet transfusion is not helpful in antiplatelet-associated intracerebral haemorrhage

Definition

Stroke is a clinical syndrome defined by an acute focal neurological deficit with a vascular basis. Around 85–90% of strokes are ischaemic (caused by arterial occlusion), and 10–15% result from intracerebral haemorrhage (ICH). The 1976 World Health Organization definition also includes subarachnoid haemorrhage, but this is primarily of epidemiological interest. The term ‘transient ischaemic attack’ (TIA) conventionally denotes complete resolution of all symptoms within 24 hours, but this arbitrary time limit is probably an anachronism in light of modern imaging and reperfusion treatment.

Epidemiology

Stroke incidence increases with age, although a quarter occur in patients <65 years of age. Causes vary by age group. Ischaemic stroke is the most common, with TIA next and ICH least common. There are

approximately 150,000 incident strokes annually in the UK, and globally stroke is the third most common cause of death and most common disabling neurological disease.

Risk factors

Major predisposing factors for ICH and acute ischaemic stroke (AIS) are listed in Table 1. It is important to investigate the underlying mechanism in most individuals, regardless of risk factors.

Diagnosis and natural history

Presentations of AIS and ICH are similar, and the two cannot be distinguished without brain imaging. Symptoms are of sudden onset and usually maximal in severity at, or within minutes of, onset. Evolution of new neurological deficits or reduced level of consciousness is uncommon within the first few hours, but some deficits, notably lacunar strokes (‘capsular warning syndrome’) and incipient carotid occlusion, can fluctuate dramatically in severity.

Symptoms of TIA are identical to those of ischaemic stroke but can include transient monocular blindness. TIA is distinguished only by complete resolution, typically within 30–60 minutes: the longer the symptoms last, the higher the probability of brain infarction (30% of TIAs resolving within 24 hours have infarcts on diffusion-weighted magnetic resonance imaging (MRI) – DWI).

Clinical features

Common clinical patterns are summarized by the Oxfordshire Community Stroke Project (OCSP) classification (Figure 1). A more detailed approach to relevant clinical examination is provided by the National Institutes of Health Stroke Scale (NIHSS; Table 2), for which online training is available.

Contralateral hemiparesis can involve face, arm and leg equally (internal capsule, corticospinal tract) or be more focal (motor cortex), often face- and arm-predominant (typical of the distal middle cerebral artery (MCA) cortical territory) (Figure 2). Hemisensory disturbance is similarly distributed. Severity of weakness is not a reliable indication of stroke severity or prognosis: the presence of other neurological deficits and pattern of weakness are of more relevance.

Conjugate gaze deviation (away from the affected limbs) results from involvement of the frontal eye field, a bilaterally represented centre that directs voluntary gaze. Often incorrectly attributed to visuospatial ‘neglect’, this usually resolves over days. Occasionally, pontine lesions cause gaze deviation towards the affected side.

Higher cortical dysfunction is represented by language disorders (dysphasia) in dominant (usually left) hemisphere strokes, or visuospatial neglect, usually in non-dominant (right) hemisphere strokes. Dysphasia can conform to Broca's syndrome (characterized by non-fluent speech, recognized to be difficult and generally frustrating for the patient, with words omitted or substituted) or Wernicke's syndrome (fluent speech of abnormal content including word or phonemic substitution, the patient generally appearing unconcerned or unaware of the problem); the pattern is, however, often mixed. Broca's pattern dysphasia is usually accompanied by brachiofacial weakness because the relevant brain regions are anatomically close, whereas Wernicke-pattern dysphasia is usually not accompanied by motor deficits, and thus can be incorrectly described as ‘confusion’. Visuospatial neglect is identified by a failure to recognize bilateral simultaneous tactile or visual stimuli when a unilateral stimulus is perceived, and can also manifest as an apraxia of eye opening, unawareness of the neurological deficit (anosognosia) and inability to recognize the affected side.

Contralateral homonymous hemianopia can occur in MCA strokes involving the optic radiation or in isolation with posterior cerebral artery strokes, when late presentation is common because the deficit is commonly asymptomatic or non-specific. Transient monocular blindness is a symptom of retinal ischaemia in ocular TIA.

Differential diagnosis

Common stroke mimics include:

- intercurrent illness including infection, particularly in the elderly
- hypoglycaemia
- migraine aura
- focal seizure or post-ictal state (Todd's paresis)
- brain tumours
- subdural haematoma

•metabolic disturbance (including hypoxia and drug overdose)
•hypotension.

Reduced conscious level is the most important predictor of non-stroke pathology. Stroke rarely causes reduction of conscious level in the first few hours, exceptions being rapidly expanding supratentorial ICH or bilateral thalamic ischaemia ('top of the basilar' syndrome). In occlusion of the basilar artery (the main blood supply to the brainstem), a patient can be 'locked in' rather than truly unconscious. The Glasgow Coma Scale may not accurately reflect level of consciousness in acute stroke because of confounding by dysphasia in dominant hemisphere stroke, and apraxia of eye opening in non-dominant hemisphere stroke. Reduced consciousness in ischaemic stroke otherwise typically occurs 2–5 days after onset with large infarcts as a result of brain swelling ('malignant MCA syndrome').

In someone with previous stroke, decompensation of an existing deficit can be caused by intercurrent illness, alcohol or sedative medication, stress or infection.

Prognosis

Outcome of acute stroke is predicted most strongly by the severity of the initial stroke (NIHSS score), together with age and blood glucose concentration. Compared with ischaemic stroke, ICH carries higher mortality (50% by day 30, compared with 17%). Outcome is a function of haematoma volume and is worse with early expansion and intraventricular extension of bleeding.

Urgent evaluation of TIA is required as the 30-day stroke risk is around 10%, mainly within the first 7 days. Prognostic scores based on duration, symptoms, age and premorbid conditions can help risk stratification, and imaging findings including the presence of recent brain ischaemia on diffusion-weighted MRI, intracranial vessel occlusion and extracranial carotid stenosis also predict individuals at highest risk of early stroke.

Immediate investigation

Because acute reperfusion treatment is critically time-dependent, clinical assessment in acute stroke presenting within a potential time window for treatment should be focused and include only key information to inform treatment decisions. Blood pressure, NIHSS, history to define the time last known to be well (corroborated by witnesses if possible) and relevant medical history (other illnesses, medication history) are required. Minimum laboratory tests include blood glucose, platelet count and coagulation screen.

Brain imaging

Imaging is required to confirm the diagnosis and gives insight into mechanism and prognosis. Computed tomography (CT) is sensitive and specific for acute ICH (high attenuation on unenhanced CT).
In AIS of moderate severity, CT has around 66% sensitivity in the first 5 hours after onset, but radiological signs are subtle. Typical changes associated with acute MCA occlusion are illustrated (Figure 3). Training and a systematic approach to CT review improve recognition.

Patient selection for endovascular thrombectomy requires additional vascular imaging – usually CT angiography – to confirm the presence of large artery occlusion of relevant target intracranial vessels (ICA or M1 segment of MCA), adequate vascular access via the extracranial vessels and the status of intracranial leptomeningeal collateral vessels. The extent of any hypodensity on initial CT should be carefully reviewed because benefit of endovascular treatment is not clearly established in very extensive ischaemia. CT perfusion imaging may provide additional selection value and has been used in several recent trials.

MRI offers improved sensitivity for both acute ischaemia and chronic haemorrhage compared with CT, but acquisition times are longer and MRI has more contraindications. DWI is highly sensitive to acute ischaemia and is more sensitive than CT for small lesions associated with minor or transient deficits. Susceptibility-weighted or gradient-echo MRI sequences are sensitive to haemoglobin degradation products and have similar sensitivity to CT for acute ICH; however, they also identify old haemorrhage, which cannot be distinguished from old ischaemic lesions by CT. The significance of small focal areas of old haemorrhage (cerebral microbleeds) on MRI is under investigation.

Investigation for stroke mechanism

Identifying the stroke mechanism is essential for optimal selection of secondary prevention. Initiation of secondary preventive treatment is urgent in many patients, particularly those with TIA or minor stroke where reperfusion therapy is not relevant. Most ischaemic strokes result from thromboembolism originating in the extracranial vessels or heart (Figure 4). Intracerebral small vessel disease can give rise to ischaemic strokes or ICH. Investigation should therefore include extracranial vascular imaging and cardiac rhythm monitoring, and in some cases intracranial vessel and heart imaging. 'Embolic stroke of uncertain source' is a proposed operational definition for strokes of embolic brain imaging appearances but lack of clear cardiac, extracranial or intracranial vascular disease. Subsequent investigation may identify paroxysmal atrial fibrillation in a proportion of patients initially in sinus rhythm.

In ICH, haematoma location and patient age offer clues to the aetiology (Figure 4), but these associations overlap. Cerebral amyloid angiopathy (CAA) may give rise to repeated bleeding episodes. Arteriovenous malformation can underlie ICH, particularly in young or normotensive patients and may require intracranial vascular imaging.

Treatment

Stroke unit care benefits both ICH and AIS patients. Attendance to basic investigation and management (brain imaging, stroke unit admission, swallowing screening, aspirin prescription) improves outcomes and avoids complications.[1] Very early aggressive mobilization is not beneficial,[2] and early multidisciplinary team management is essential. Stroke patients are vulnerable to pneumonia, deep vein thrombosis, urinary tract infection, aspiration, depression, falls and shoulder subluxation; deterioration should therefore prompt a review for systemic causes.

Intracerebral haemorrhage

Neither haemostatic treatment nor aggressive blood-pressure-lowering has been established to improve outcome, and some trials are ongoing. Platelet transfusion in ICH among patients on antiplatelet therapy was associated with poorer outcome in a recent trial. Evidence for acute surgical interventions (evacuation via craniotomy, drainage via a burr hole or stereotaxy, external ventricular drainage of intraventricular blood) is limited. A strategy of ICH evacuation within 48 hours was no better than initial conservative management, but few studies have evaluated intervention within the first few hours, when deterioration usually occurs.

Ischaemic stroke

Intravenous thrombolysis with alteplase, a recombinant tissue plasminogen activator, improves the proportion of patients with complete neurological recovery when given within 4.5 hours of symptom onset. Earlier treatment is associated with greater likelihood of benefit.[3] The number-needed-to-treat (NNT) for excellent recovery is 5 for patients treated within 90 minutes, 9 if treated within 91–180 minutes and 14 if treated within 191–270 minutes of onset. The absolute excess risk of ICH with significant neurological deterioration is related primarily to stroke severity and rises from 1.5% in very mild stroke to 3.7% in very severe stroke. There is a slightly higher early mortality with treatment, and it is important to consider the balance of risk and benefit in individuals; however, there is net benefit across almost all subgroups of age and severity.[4] Treatment of 15–20% of AIS is possible, systems should be organized to minimize door-to-needle times. Rapid assessment and scanning of all patients has general benefits.

Intravenous alteplase recanalizes occluded arteries in around 56% of patients, and is least effective with the largest clots (and most severe strokes), with <10% recanalization in intracranial ICA occlusion. Endovascular mechanical thrombectomy improved clinical outcomes significantly in patients with ICA and MCA M1 segment occlusion in a series of recent trials. Pooled analysis of the five trials published in 2015[5] showed an absolute increase in disability-free survival of 19.5% (NNT 5).and NNT of 3 to move upwards to a more favourable disability level. In 90% of cases in all trials, thrombectomy was undertaken in patients treated early with intravenous recombinant tissue plasminogen activator (rtPA) and in the setting of highly organized specialist services. Benefit of thrombectomy also declines steeply with time. Very few patients were randomized beyond 6 hours after onset, and reperfusion (i.e. the end of the procedure) beyond 7 hours was not beneficial. Relative treatment effects were consistent across major age groups and stroke severities.

Decompressive hemicraniectomy reduces mortality in patients with 'malignant' brain swelling after a large infarction, but a high proportion of survivors remain disabled.

Aspirin started within 48 hours (300 mg/day for up to 14 days) reduces death or dependence, probably acting as acute secondary prevention. If intravenous thrombolysis is given, aspirin should be withheld for 24 hours as it increases the risk of haemorrhage.

Secondary prevention

Preventive treatment should be informed by the mechanism of stroke in each individual, and can include antiplatelet, antihypertensive or anticoagulant therapy, statins and surgical carotid endarterectomy.

In non-randomized comparisons, significantly fewer strokes occurred when secondary preventive treatments were started within 24 hours of symptoms in patients with TIA, compared with delayed institution of treatment.

Major risk factors for stroke

Modifiable	Unmodifiable
ICH	
Hypertension Alcohol excess Drug treatments – thrombolytic agents, anticoagulants, antiplatelet agents Diabetes mellitus Cigarette smoking	Age Apolipoprotein E ε2 or ε4 carriage (CAA) Race (probably higher in South-East Asian populations)
Ischaemic stroke	
Hypertension	Age
Diabetes mellitus (or elevated HbA1c)	
Ischaemic heart disease	
Atrial fibrillation	
Valvular heart disease	
Cigarette smoking	
Dietary Risks (high sodium, low fruit and vegetables) Low physical activity	

Table 1

NIHSS items

Item	Score range
•LOC – LOC questions – LOC commands	0–3 0–2 0–2
•Best gaze	0–2
•Visual fields	0–3
•Facial weakness	0–3
•Motor, arm	0–4 (right and left)
•Motor, leg	0–4 (right and left)
•Limb ataxia	0–2
•Sensory loss	0–2
•Best language	0–3
•Dysarthria	0–2
•Extinction and inattention	0–2

Table 2
LOC, level of consciousness.

Oxfordshire Community Stroke Project (OCSP) classification: syndromes and imaging examples

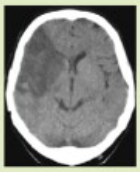
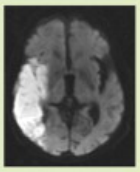
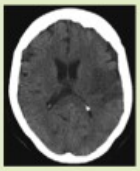
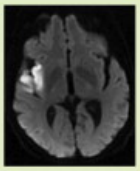
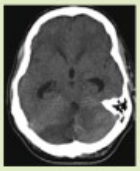
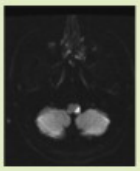
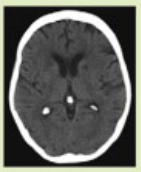
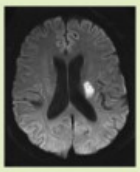
OCSP term	Clinical features	Vascular basis	Example CT	Example MRI
Total Anterior Circulation Syndrome (TACS)	• Hemiparesis **AND** • Higher cortical dysfunction (dysphasia or visuospatial neglect) **AND** • Homonymous hemianopia	Usually proximal middle cerebral artery (MCA) or ICA occlusion		
Partial Anterior Circulation Syndrome (PACS)	• Isolated higher cortical dysfunction **OR** • Any two of hemiparesis, higher cortical dysfunction, hemianopia	Usually branch MCA occlusion		
Posterior Circulation Syndrome (POCS)	• Isolated hemianopia (posterior cerebral artery (PCA)) brainstem or cerebellar syndromes	Occlusion of vertebral, basilar, cerebellar or PCA vessels		
Lacunar Syndrome (LACS)	• Pure motor stroke **OR** • Pure sensory stroke **OR** • Sensorimotor stroke **OR** • Ataxic hemiparesis **OR** • Clumsy hand-dysarthria	Small penetrating artery occlusion, usually in lenticulostriate branches of MCA, or supply to brainstem or deep white matter		

Figure 1
OCSP classification: syndromes and imaging examples.
ICA, internal carotid artery.

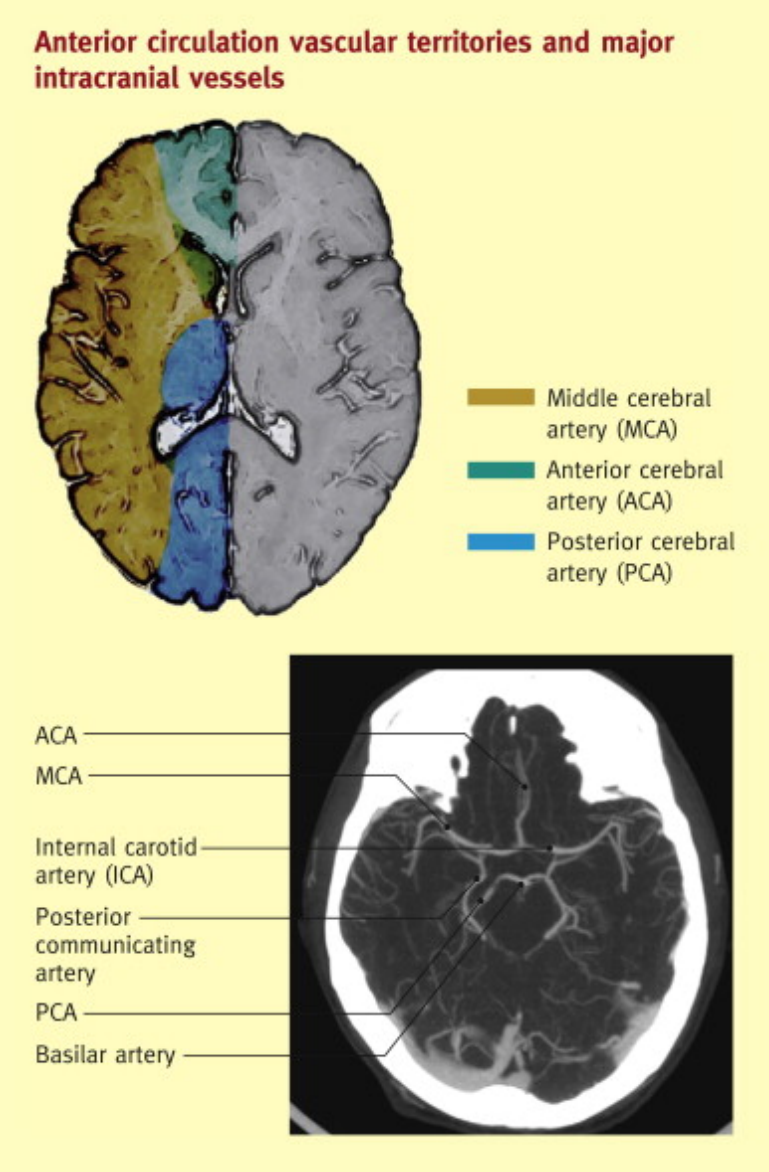


Figure 2
Anterior circulation vascular territories and major intracranial vessels.

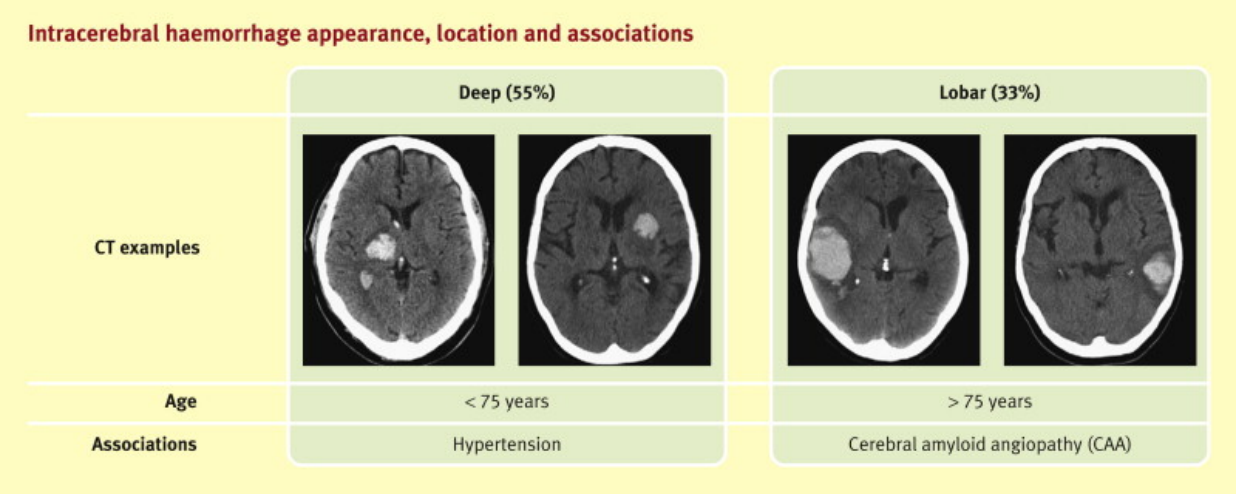


Figure 4
ICH appearance, location and associations.

Figure 3
Early radiological features of AIS due to MCA M1 segment occlusion.

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