Management of Acute Ischaemic Stroke in the Acute Medical Unit

JM Atkinson, L Barton & CI Price

Key Learning Points
- Stroke is a common disease with devastating consequences for the patient, carers and wider society.
- Stroke must be viewed as a medical emergency.
- Urgent review of stroke patients in order to consider thrombolytic therapy has wider benefits. Stroke mimics will be identified and treated and early placement on specialist units will be facilitated.
- Providing a specialist stroke thrombolysis service is a challenge, particularly in smaller or more remote centres. Telemedicine is one option. Services must consider the best structure for their local needs.
- Provision of a stroke thrombolysis service requires coordination between primary care, the ambulance service, emergency medicine, acute medicine, the stroke team, radiology services and neurosurgery.
- Further research is needed to inform issues around the time frame for thrombolysis and the groups of patients this treatment should be offered to.
- Consent for thrombolysis is challenging given the urgency of the situation, risk-benefit analysis and communication difficulties associated with stroke. Physicians require specialist training in this area.

Abstract
Ischaemic stroke is a major cause of death and disability which costs the NHS £2.8 billion/year. Acute stroke care is developing rapidly in line with an increasing evidence base. Intravenous thrombolysis is now recommended by NICE. For this guidance to be effectively implemented stroke must be viewed as a medical emergency by both the public and professionals. Emergency medical services must work in partnership with stroke services to establish systems and protocols which offer high quality acute stroke care. This provides challenges, both in systems design and delivery of clinical care.

Keywords
Stroke, thrombolysis, telemedicine, emergency.

Introduction
Stroke is the third commonest cause of death in the UK. It affects 130,000 people each year, of which 28,000 are under 65 years old. It costs the NHS about £2.8 billion a year in direct care costs.[1] Around two thirds of patients survive their stroke but half of these are left with disabilities that require the assistance of others.[1] As a result stroke costs the wider economy £1.8 billion in disability and lost productivity and £2.4 billion in informal care costs, each year.[1] The National Stroke Strategy, has highlighted that urgent efforts are needed to improve the outcome of this medical emergency.[2] Stroke services are developing rapidly in the UK. In this article we aim to review current best practice for managing acute stroke including thrombolysis and implementation of a stroke thrombolysis service.

Consideration of patient for thrombolysis
Early imaging allows timely neuro-surgical referral or anti-platelet therapy
Admission to specialist stroke unit and access to multi-disciplinary team
Diagnosis and treatment of stroke mimics
Appropriate investigation of thrombo-embolic stroke and early consideration of carotid endarterectomy if appropriate

Table 1. Benefits of early stroke review.

Initial assessment and diagnosis
The early recognition of stroke has multiple benefits (Table 1). There is substantial evidence that early admission to a stroke unit can help limit early deterioration and reduce morbidity and mortality.[3,4] Since the publication of the National Institute for Clinical Excellence (NICE) guidance on the use of alteplase for the treatment of acute ischaemic stroke,[5] each patient presenting with suspected stroke should be considered for thrombolysis. Stroke mimics must be excluded as they often require their own specific treatments[6] (Table 2). The organisation of this is complicated, it requires public awareness of stroke and the co-operation between ambulance, emergency care, radiological and stroke medicine services.

Public campaigns aim to raise awareness of the symptoms of stroke and encourage a 999 response.[6] Changes in ambulance service provision and prioritisation are also being made. Ambulance

Dr JM Atkinson
MBChB, MRCP
ST trainee in Acute Medicine,
Northern Deanery

Dr L Barton
MBBS, MRCP
ST in Acute Medicine,
Northern Deanery

Dr CI Price
MD, FRCP, MClinEd
Consultant in Stroke Medicine and Clinical Senior Lecturer in Medicine,
Newcastle University

Correspondence:
Dr JM Atkinson
MBChB, MRCP
ST trainee in Acute Medicine
41 Regent Road
Gosforth, Newcastle,
NE3 1ED
Email: jane.atkinson@cddft.nhs.uk

Neurological	Seizure or post-ictal state Migraine Subdural haematoma Space occupying lesion Multiple sclerosis or other demyelinating process
Metabolic	Sepsis (especially if previous stroke or other longstanding neurological deficit) Hypo or hyperglycaemia Hyponatraemia Hepatic encephalopathy Drug overdose
Other	Syncope Functional disorders

Table 2. Common Mimics of Stroke.

services traditionally dispatched a category B ambulance (19 minutes target) for suspected stroke unless there was a reduced conscious level, but the National Stroke Strategy now recommends category A (8 minutes target).[2] The sentinel audit in 2006 found that only 12% of hospitals had protocols with their ambulance service to aid the rapid presentation of stroke patients.[4] This had improved to 49% in the 2008 audit; however some sites that admit stroke as a medical emergency had still not engaged with their ambulance service.[7]

Education for front line staff aims to promote clinical detection of stroke. Various assessment tools have been used to identify potential stroke patients in the emergency room. The current Department of Health 'actFAST' campaign and NICE recommend the use of the Face, Arm, Speech Test.[5,6] The Recognition of Stroke In the Emergency Room (ROSIER) scale, where a score of greater than zero suggests a high probability of stroke, is a little more complicated, but when used by medical staff allows correct identification of 90% of true strokes and 75% of stroke mimics (see Table 3).[8] The National Institutes of Health Stroke Scale (NIHSS) is a useful tool for research and quantification of neurological changes after thrombolysis but is too cumbersome to use as a screening test for stroke.[9]

After stroke recognition, the next priority is to assess the time scale of symptoms, comorbidities and witness accounts which could suggest alternative diagnoses. The initial observations should include Glasgow Coma Score, blood pressure, oxygen saturations and blood sugar. If the diagnosis of stroke is still suspected urgent referral for brain imaging and specialist medical assessment is mandatory.

Brain imaging

Patients with suspected stroke should not be admitted to a site without computerised tomography (CT) scanning. The main role of CT is exclusion of haemorrhage as changes associated with an acute infarct can be subtle. The sensitivity for ischaemia is only 7% within 3 hours, but for intracerebral haemorrhage the sensitivity is 89%, with

Has there been loss of consciousness or syncope?	Y (-1) N (0)
Has there been seizure activity?	Y (-1) N (0)
Is there a NEW ACUTE onset (or on awakening from sleep)	
• I. Asymmetric facial weakness	Y (+1) N (0)
• II. Asymmetric arm weakness	Y (+1) N (0)
• III. Asymmetric leg weakness	Y (+1) N (0)
• IV. Speech disturbance	Y (+1) N (0)
• V. Visual field defect	Y (+1) N (0)
	Total Score (-2 to +5)

Table 3. The ROSIER scale.

100% specificity.[10] CT will also exclude space occupying lesions, which occur in as many as 5% of patients with suspected stroke. Although MRI has a better sensitivity for demonstrating changes due to ischaemic stroke, it takes longer to perform, has more absolute contraindications and is available in fewer centres. A hospital providing stroke thrombolysis must be able to perform emergency brain imaging within one hour of request 24 hours a day, 7 days a week. Anti-coagulated or coagulopathic patients presenting with signs of a stroke should also have an urgent scan.

Specialist assessment

Patients with suspected stroke should be admitted directly to an acute stroke unit rather than a general admissions ward.[3,11] These are geographically defined units which provide:

- stroke physician led with ward rounds at least 5 times per week
- continuous physiological monitoring
- access to brain imaging within 3 hours
- a policy for direct admissions from A&E
- acute stroke protocols for medical and nursing staff[7]

These units have a multidisciplinary approach to acute care and rehabilitation including physiotherapy, occupational therapy, speech therapy and specialist nursing. Even before the definition of "acute" stroke units, a Cochrane review of 31 trials showed that the number needed to treat (NNT) in any stroke unit, compared to general ward care, to prevent one patient death and dependence was 24 patients.[3] The opinion of a specialist neurologist or stroke physician should be available in the emergency department, either in person or through a telemedicine arrangement. This facilitates identification of the 30-50% of patients, initially diagnosed with stroke, who actually have an alternative diagnosis and need other treatments (Table 2).[9] It is especially important to be wary of a diagnosing stroke in younger people with no risk factors, and patients with a reduced conscious level but few focal neurological signs.

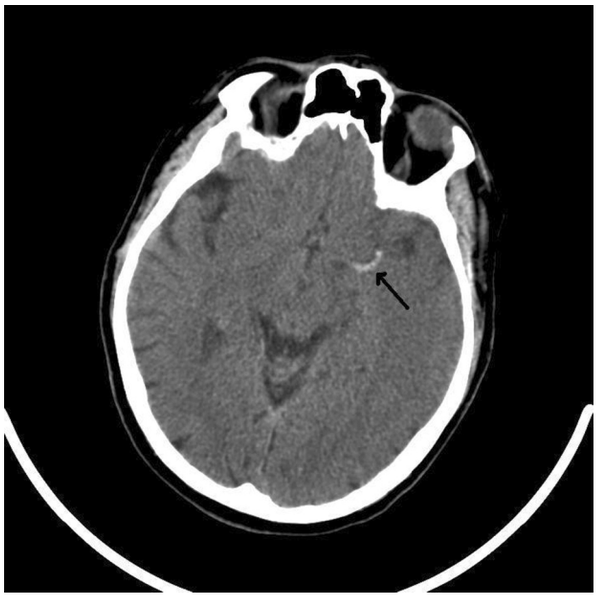

Figure 1. Hyperdense artery on CT scan. (arrow)

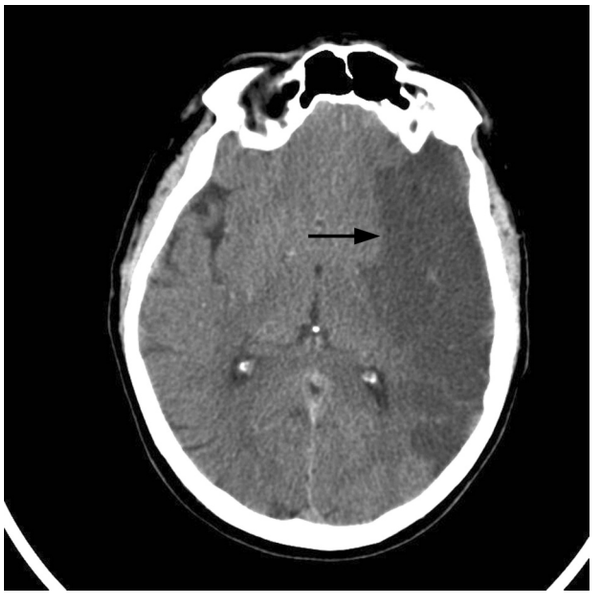

Figure 2. Established cerebral infarct. (arrow)

Methods of treatment

Ischaemic stroke often occurs due to thrombosis occluding the blood supply to an area of the brain. This is commonly triggered by atherosclerotic plaques, either locally or in the carotid or vertebral arteries but can also be cardio-embolic due to atrial fibrillation or mural thrombus following myocardial infarction. Rarer causes of ischaemia are arterial dissection, arterial spasm, hypoperfusion, hypoxia and air or fat embolus after trauma.

Early CT changes are minimal but can sometimes show a hyperdense artery indicative of clot (Figure 1). Later, more obvious changes will occur (Figure 2).

Stroke Thrombolysis

There is good evidence that thrombolysis in acute stroke is an effective treatment.[3,12] Use of thrombolytic agents for acute stroke has been permissible in the United States since 1996 and under a provisional license within the European Union since 2001.[4,12] In 2007 NICE approved alteplase for use in the NHS as long as a specialist with sufficient expertise is involved in the treatment decision.[5] A number of thrombolytic agents were originally trialed, including streptokinase and urokinase, but recombinant tissue plasminogen activator (rTPA - alteplase) was associated with lower complication rates due to its shorter half life. New cerebral infarcts are prone to bleeding, so the haemorrhagic complication rate exceeds that experienced by trials of coronary thrombolysis. Although the NICE guidance follows the European marketing authority for Alteplase which licenses treatment up until 3 hours, the ECASS III trial has now shown that thrombolysis given within 4.5 hours reduces disability.[3]

In 2006 less than 1% of stroke patients in the UK received thrombolysis, and only 40 (18%) trusts in the UK provided the service, many on an opportunistic basis.[4] By 2008 this had improved to 42%, treating a median number of 6 patients each per year.[7] This reflects the complexity of the rapid assessment process, delays in presentation to specialist services and inexperience with the therapy. Although it has been estimated that it would cost £9.9 million a year to thrombolyse 9% of stroke patients, this would save around £26.4 million a year due to a reduction in disability.[12] Since 2007, regional networks established by the Department of Health Stroke Improvement Program have been assessing local circumstances in order to increase the thrombolysis capacity of stroke services in response to the National Stroke Strategy.

Patient Selection

Selecting the correct patients for thrombolysis is key. Benefits and risks for the individual must be considered by a clinician with training in stroke thrombolysis. Patients with a high bleeding risk or minimal and improving symptoms should not be thrombolysed (Table 4). There still remains some concern about the value of the treatment in patients older than 80 years, but sub-group analysis of the CASES study found no increased mortality. The 3rd International Stroke Trial should provide further clarification.[13]

Consent for thrombolysis

If thrombolysis is indicated the benefits and risks need to be explained to the patient in a manner they can understand, in the context of possible immediate and longer term prognosis according to current stroke severity. It is good practice to explain that harm may include a deterioration in neurological function and even death as a result of unpredictable intracerebral haemorrhage. Mental capacity may be impaired in the acute setting because of emotional distress, aphasia and other cognitive impairments.[14] In this situation, if the benefits outweigh the potential risks, treatment may be given in the best interest of the patient.

Presentation	Seizure activity Low conscious level
History	Stroke within last 6 weeks Any previous sub-arachnoid haemorrhage Any major gastrointestinal or urinary bleeding in last 3 weeks Major trauma or surgery in last 6 weeks Poor previous functional status (immobile)
Examination	Rapidly resolving symptoms Very mild deficit (e.g.just facial weakness) Blood pressure >180/105 on repeated readings
Laboratory results	Platelets $< 100 \times 109$ INR >1.7 Glucose <2.8 or >22.2 mmol/L Positive pregnancy test

Table 4. Contraindications to Thrombolysis

Risks and Benefits

The main risk of thrombolysis is intracranial haemorrhage which occurs in 4.6% of cases.[15] Analysis of the thrombolysis trials data suggests that the number needed to treat (NNT) for benefit is 3, whereas the NNT to harm is 30.[16] Therefore the ratio of benefit to harm is 10:1. There is a non-linear incidence of complications as such those with the most severe strokes are more likely to suffer haemorrhage but also have the most to gain in terms of disability reduction.[9] Other side effects are significant systemic bleeding (0.4%), orolingual angioedema (1.3%) and acute hypotension (0.4%).[9]

Thrombolysis can proceed as long as the whole assessment process remains within 4.5 hours of onset, but will be of maximum benefit if given as soon as possible.[12,14,16] An American trial found the commonest reasons for delay was uncertainty regarding time of onset (24%), patients delayed presentation (29%) and travel time to appropriate hospital (6%). Of those presenting within the timeframe, a further 27% were excluded due to very mild symptoms, improving symptoms, perceived protocol exclusions, referral delay and co-morbidities.[17]

Thrombolysis administration

The dose of Alteplase is 0.9mg/kg (up to a maximum of 90mg) with 10% as an intravenous bolus and the remainder infused over 1hr.[9] Heparin and anti-platelet agents should not be given within the first 24 hours.

Once treated, patients need to be monitored closely with observations every 15 minutes for the first two hours, reducing to every 30 minutes for 4 hours and hourly thereafter.[9] This should be on an acute stroke unit or in a high dependency setting which has awareness of the additional needs of acute stroke patients. If conscious level decreases or neurological symptoms clearly worsen then the thrombolysis must be stopped and an immediate repeat CT head scan ordered. If intracerebral haemorrhage is identified, patients should be discussed with a neurosurgical team. There are currently no clear guidelines on what surgical management is appropriate. A repeat CT is indicated at 24 hours post thrombolysis in all patients to exclude asymptomatic haemorrhage before aspirin and other anti-platelet agents can be started.[9]

Implementation of thrombolysis

Providing a safe stroke thrombolysis service outside a neuroscience centre is challenging. According to NICE guidelines, thrombolytic therapy should only be given under the supervision of a physician who has expertise in the diagnosis of stroke.[5] Some patients may need to be transported extra distances to a regional hub but this could delay treatment. This is particularly challenging out of hours in small or geographically remote centres.

Use of Telemedicine

One approach is to use telemedicine to improve administration of thrombolysis in district general hospitals. A web-based telestroke tool has been used successfully to deliver a stroke thrombolysis service in rural community hospitals in Georgia, USA.[18] The local hospital activates the system if a patient with suspected stroke presents within 4 hours of onset of symptoms. An on-call stroke specialist uses a broadband internet connection with video, audio and scan review functions to assess the patient before relaying a treatment decision. Over a two year period this telemedicine service provided 194 acute stroke consultations and 30 patients received thrombolysis. Sixty percent were treated within 2 hours of stroke onset. Sixty percent of patients showed a rapid improvement (drop of > 4 points on NIHSS at 24hrs) and there were no symptomatic intracerebral haemorrhages.

A similar model is used in Bavaria, but employs 24 hour video-conferencing technology to allow remote assessment of patients with any acute neurological disorder.[19] Introduction of this service raised thrombolysis rates by about ten fold. Thrombolysis rates were initially lower than the regional neuroscience centre, and there were more symptomatic haemorrhages in the community group but this was not statistically significant. No significant differences were found in rates of mortality. A follow study found similar longer term mortality and functional outcomes for patients thrombolysed in community and specialist hospitals.[20]

These studies demonstrate that thrombolysis can be delivered safely outside a stroke centre by using telemedicine. Patients still require urgent CT scanning facilities and the ongoing care of an on site multidisciplinary stroke unit to recognise other complications and implement appropriate secondary prevention treatments. Development of a thrombolysis service should only be encouraged where there is already a good standard for acute stroke care, otherwise any benefit of thrombolysis will quickly be lost. Thrombolysis services should closely monitor any protocol violations and complication rates.[9]

Anti-platelet therapy

There is strong evidence to support the administration of aspirin 150 – 300mg to all ischaemic stroke patients who have not received thrombolysis as soon as haemorrhage is excluded.[21] If the patient has received thrombolysis aspirin

can only be instigated after a CT scan at 24hours has excluded asymptomatic haemorrhage. Although anti-platelet therapy risks a higher rate of haemorrhagic transformation, it is associated with a significant reduction overall in the number of patients who die or are dependent due to prevention of early recurrence and pulmonary embolism. There is little evidence looking at the acute effects of other anti – platelet therapies and NICE guidance suggests a Proton Pump Inhibitor for those who experience dyspepsia with aspirin.[22] Anti-coagulants such as heparin should not be used routinely in the acute treatment of ischaemic stroke, unless there are exceptional individual circumstances such as a prosthetic heart valve.[9]

Physiological monitoring

Even in the most established centres, approximately 90% of patients with ischaemic stroke are unsuitable for thrombolytic treatment, but they still benefit from monitoring.[3] If patients are hypoxic (oxygen saturations under 95%) supplemental oxygen therapy should be prescribed. It is important to monitor blood glucose control, aiming for readings of 4-11 mmol/l whilst avoiding hypoglycaemia. Current guidance indicates that blood pressure should not be manipulated acutely unless very high, but research is on-going.

Ongoing care

Stroke patients benefit from the early input of a specialist multi-disciplinary team. Early mobilisation is important and improves outcome.[3] Swallowing assessment should be completed by trained nursing staff before the patient receives any oral intake. Involvement of speech and language specialists will be vital for some patients. Functional assessment and rehabilitation needs should be rapidly identified. Patients and carers may need psychological support and depression is common.

Thromboprophylaxis should be considered on an individual patient basis. Assessment of vascular risk factors and sources of emboli should be considered and investigated appropriately.

Conclusion

Stroke has a devastating effect on people's lives and the economy, but needs to increase its profile as a medical emergency with "brain attack" being akin to "heart attack". As public awareness of stroke symptoms increases, patients will seek prompt treatment and if this is available then outcomes will improve. Increasing access to acute stroke units reduces morbidity and mortality. Studies show that the benefits of thrombolysis extends up to 4.5 hours after onset of symptoms. The role of the emergency medical services is to ensure that patients are given the opportunity to access this treatment as quickly as possible for maximum benefit.

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