Evidence-based treatment of acute stroke

Gillian Cluckie

Providing diagnosis and intervention is rapid, stroke is a treatable condition with a range of acute treatment options now available for different stroke types. This article provides a summary of the current evidence-based treatment of acute stroke including the emerging evidence for thrombectomy.

Stroke services have previously been described as the “Cinderella” services in the NHS; however, significant progress has been made following the launch of the National Stroke Strategy in 2007.1,2 This strategy set out standards for improved services such as direct access to specialist stroke units for all patients and improving the availability of thrombolysis across the UK, and has been followed and supported by a range of clinical evidence such as that from NICE and from the Royal College of Physicians (RCP) stroke programme.3-5 Improvements in UK stroke care have been regularly audited by the RCP stroke programme, currently conducted via an ongoing prospective clinical audit in England and Wales, the Stroke Sentinel National Audit Programme (SSSNAP). This audit produces publicly available reports for CCGs and individual hospitals.

Stroke is defined as “rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin”.6 While there has been recent debate that this definition requires updating, given the advances in diagnostics and imaging, the sudden onset of focal neurological symptoms remains an important feature of stroke.7

Presentation and diagnosis

As stroke presents with a sudden onset of focal neurological deficits, much effort has been made to raise public awareness and recognition of stroke. The FAST (Face, Arms, Speech, Time) test has been used to aid public recognition of stroke using a range of media including television advertisements. This easy to apply test of facial weakness, arm weakness and speech disturbance has been proven to have a positive predictive value of 78 per cent and good applicability in the prehospital setting.8,9 Public awareness of the individual signs of stroke based on the FAST test is high (facial weakness 89 per cent, arm weakness 83 per cent and speech problems 91 per cent).10 Public awareness is crucial to timely access to specialist emergency treatments for stroke such as thrombolysis and thrombectomy.

<table>
<thead>
<tr>
<th>Indications</th>
<th>Contraindications</th>
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<tbody>
<tr>
<td>• Ischaemic stroke</td>
<td>• Intracerebral haemorrhage</td>
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<tr>
<td>• CT confirms no haemorrhage or other nonvascular cause for symptoms</td>
<td>• Anticoagulation with warfarin and International Normalised Ratio (INR) &gt;1.7</td>
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<tr>
<td>• Age &gt;18 years</td>
<td>• Patient on new oral anticoagulant</td>
</tr>
<tr>
<td>• Confirmed onset time &lt;4.5 hours</td>
<td>• Recent surgery of noncompressible site</td>
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<tr>
<td></td>
<td>• Diabetes and prior stroke</td>
</tr>
<tr>
<td></td>
<td>• Platelets &lt;100 x 10^9 per litre</td>
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<tr>
<td></td>
<td>• Seizure at onset</td>
</tr>
<tr>
<td></td>
<td>• Hypo- or hyperglycaemia</td>
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<tr>
<td></td>
<td>• Systolic BP &gt;185mmHg or diastolic BP &gt;110mmHg</td>
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</tbody>
</table>

Table 1. Thrombolysis indications and contraindications
Acute stroke treatments

Thrombolysis

Thrombolysis trials in stroke began in the 1990s and thrombolysis for acute ischaemic stroke has been licensed in the UK since 2007. A European-wide monitoring study confirmed the safety and efficacy of thrombolysis compared to pooled clinical trials and reported a symptomatic intracerebral haemorrhage rate of 1.7 per cent. A recent investigation by the Medicines and Healthcare products Regulatory Agency (MHRA) into thrombolysis has also supported the safety and efficacy of the treatment. Thrombolysis has become increasingly available in the UK with thrombolysis rates in England and Wales reported as 9.1 per cent of all stroke admissions.

Thrombolysis is currently licensed for use up to 4.5 hours from stroke onset using alteplase. The time of onset is required to ensure treatment is provided as quickly as possible to improve the likelihood of a good outcome. Thrombolysis has also been shown to be as safe and effective in those aged over 80 years as in those below this age, with the critical element for outcome being time to treatment. Many stroke services have a rapid response stroke team to meet the patient in the emergency department, ensure rapid assessment and minimise the door-to-needle time. In order to provide thrombolysis treatment, clinicians will confirm the clinical diagnosis of stroke, confirm the onset time, and exclude haemorrhage or other diagnosis with a CT brain scan. Clinicians will also confirm there are no exclusions or contraindications to its use (see Table 1).

Alteplase is then provided on a weight-based calculation of 0.9mg per kg body weight with an initial 10 per cent bolus followed by the remainder by infusion over one hour. Patients require careful monitoring and nursing care throughout the first 24 hours to rapidly identify and treat any complications (see Table 2).

While thrombolysis is an important element of stroke services, many patients will not be suitable and others will have a proximal cerebral artery thrombus for which thrombectomy is a new and emerging treatment.

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### Thrombolysis

<table>
<thead>
<tr>
<th>Complication</th>
<th>Monitoring required</th>
</tr>
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| Intracerebral haemorrhage     | Regular neurological monitoring at set intervals including Glasgow Coma scale, vital signs and limb assessment:  
Every 15min for first 2 hours  
Every 30min for 2 hours  
Every 60min up to 24 hours post-treatment |
| National Institutes of Health Stroke Scale (NIHSS) assessment of stroke-related disability at 2 hours |
| Monitoring for new headache, nausea or vomiting, which may indicate intracerebral haemorrhage |
| Angioedema                    | Oral inspection prior to treatment and during every set of neurological observations |
| Observation for signs of tongue, palate or lip swelling or upper airway obstruction |
| Patient monitoring for reports of new dysphagia, oral irritation/swelling or difficulty breathing |
| Extracranial haemorrhage      | Regular vital signs monitoring as part of neurological observations                   |
| Observation for signs of major extracranial haemorrhage such as haematemesis, malena or haemoptysis |
| Observation of signs such as pallor, sweating, ecchymosis, haematoma development, abdominal pain or discomfort, which may indicate significant extracranial haemorrhage |
| Avoidance of invasive procedures for initial 24 hours such as urinary catheterisation, cannulation, arterial blood gases (unless clinically urgent) |
| Monitoring for signs of minor extracranial haemorrhage such as oral mucosal bleeding, bleeding around cannula sites or minor bruising |

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### Thrombectomy

Thrombectomy is an acute clot retrieval procedure that has very recently come to prominence. The procedure is performed by interventional neuroradiologists using a range of devices for suction, intra-arterial thrombolysis and stent removal of the thrombus inside the cerebral arteries. A series of clinical trials reported in 2014 and 2015 demonstrated the safety and efficacy of the treatment – see Table 3 for a summary of the trials. A recent meta-analysis has combined these five trials with three earlier thrombectomy trials and has confirmed that thrombectomy improves functional independence without a significant increase in the rate of symptomatic intracerebral haemorrhage or mortality at 90 days.

In the UK, the operation of thrombectomy services is currently being considered and is likely to require regional solutions to ensure equitable access throughout a 24-hour period for suitable patients.
While a proportion of patients may be suitable for thrombolysis or thrombectomy, others will present with intracerebral haemorrhage requiring treatment.

Management of intracerebral haemorrhage
For patients with an intracerebral haemorrhage, haematoma expansion can continue for the first 24 hours. However, in lobar intracerebral haemorrhages there is no benefit to early surgery versus conservative management. Tranexamic acid is currently being studied for its potential benefit in limiting haematoma expansion. There is clinical benefit of early intensive blood pressure lowering in intracerebral haemorrhage with a target systolic blood pressure of 140mmHg. Patients will typically continue on their usual antihypertensive treatments initially, which can then be optimised during admission.

While there is no evidence for early surgery in lobar intracerebral haemorrhages, there are a few clinical indications for neurosurgery.

Indications for neurosurgery in acute stroke
There are a couple of situations in which neurosurgery is indicated in acute stroke – malignant middle cerebral artery (MCA) syndrome and intraventricular haemorrhage:
- Malignant MCA syndrome – this is characterised by significant cerebral oedema and raised intracranial pressure usually as a result of a middle cerebral artery or carotid territory infarct. If left untreated, there is a risk this will result in brainstem herniation. A decompensatory hemi-cranieotomy is currently recommended for patients under the age of 60 years with a nondominant hemisphere stroke.
- Intraventricular haemorrhage – if left untreated, this can lead to obstructive hydrocephalus requiring neurosurgical treatment such as the insertion of an extraventricular drain. Serial CT scans and careful clinical observations are usually indicated to monitor the extent of the intraventricular haemorrhage and any symptomatic hydrocephalus.

For patients with posterior fossa haemorrhage such as in the cerebellum, in some cases surgery may be indicated to avoid brainstem herniation but careful clinical observation is indicated initially. There have been no proven benefits of performing neurosurgery in any other stroke types.

Of the whole population of stroke patients, a proportion will be suitable for thrombolysis, thrombectomy or treatment for intracerebral haemorrhage. However, all stroke patients have been shown to benefit from care in specialist stroke units.

Evidence-based stroke unit care
Stroke units have been proven to improve morbidity and mortality compared to either general medical ward care or mobile stroke team care in general wards. Stroke units have been shown to reduce mortality by the prevention of complications such as aspiration pneumonia and deep vein thrombosis. A recent study based on the SSNAP national audit data has identified key factors that have an impact on mortality on stroke units:
- review by a consultant in less than 24 hours
- adequate nutrition and hydration
- swallow screening to detect impaired swallowing
- early antiplatelet treatment.

These elements have a cumulative effect, reducing the odds of mortality by 26 per cent at 30 days post-stroke, even with adjustment for case mix. It is clear that relatively simple treatments when applied consistently have a significant impact in stroke care. Additionally there are areas of service organisation that have a relationship with morbidity and mortality such as nurse staffing ratios and early specialist assessments.

The need for rapid access to thrombolysis and specialist stroke care available at all times has prompted some CCGs to consider stroke reorganisation in order to improve the speed of treatment for all patients. However, this solution depends upon local services, geography and travel times, and in some areas access to technology such as telemedicine may also improve specialist care where centralisation is not appropriate. It is clear that there are a range of specific treatments, assessments and investigations that are necessary in acute stroke and that can have a significant impact on morbidity and mortality.

Conclusion
This article has summarised the current evidence-based treatments for acute stroke including thrombolysis, thrombectomy, intracerebral haemorrhage and specialist stroke unit care. It is clear that stroke is now a treatable condition with a range of acute treatments depending on the stroke type and aetiology. All patients should have direct access to a specialist stroke unit regardless of the time or day of their attendance with the provision of evidence-based treatment such as swallow screening and early transition to stroke unit care.
antiplatelet treatment. The development of thrombolysis and emerging treatments such as thrombectomy are exciting steps forward in stroke care but these may also require service reorganisation to ensure equitable access for all patients.

References

17. IST3 Collaborative Group. The benefits and harms of intravenous thrombolysis with recombinant tissue plasminogen activator within 6 h of acute ischaemic stroke (the third international stroke trial [IST-3]): a randomised controlled trial. The Lancet 2012;379(9834):2352–63.

Declaration of interests
None to declare.

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