



# Interventional therapies in stroke management: anaesthetic and critical care implications

J Redgrave MRCP DPhil<sup>1</sup>, Helen Ellis FRCA FFICM<sup>2</sup>, and G Eapen FRCA FFICM<sup>3,4,\*</sup>

<sup>1</sup>Clinical Lecturer in Neurology and Stroke, University of Sheffield, Sheffield, UK, <sup>2</sup>Speciality Trainee in Anaesthesia and Critical Care, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK, <sup>3</sup>Consultant in Anaesthesia and Neurocritical Care, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK, and <sup>4</sup>Department of Anaesthesia, C Floor, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF, UK

\*To whom correspondence should be addressed. Tel: +44 7730680408; Fax: +44 1142713894. E-mail: george.eapen@sth.nhs.uk

## Key points

- Advances in technology have increased therapeutic options for acute stroke management.
- Early mechanical thrombectomy should be considered for large vessel occlusion.
- Local critical care and anaesthesia protocols need to be developed for interventional stroke therapies.
- Arterial pressure therapy should be tailored to the type of stroke.
- Decompressive craniectomy should be considered for large hemispheric infarction.

Recent advances in stroke therapy have necessitated new multi-disciplinary care pathways. This article will cover interventions used in acute stroke management, including the role of imaging, thrombolysis, interventional radiology, arterial pressure (AP) management, carotid revascularization, haematoma evacuation, and decompressive hemicraniectomy (DHC). The anaesthetic and critical care implications of these interventions are described.

## Imaging in acute stroke

Computed tomography (CT) scanners have increased from a single-slice detector to advanced 320-slice scanners capable

of performing whole-head imaging in a single rotation. This allows multiple acquisitions during a single contrast injection such that non-contrast CT, angiogram, subtraction cerebral angiography, and perfusion imaging can be performed in a single sitting. With CT perfusion scans, the size of the infarcted core can be seen and also the hypoperfused area around it (the penumbra) which represents brain tissue that may be salvaged if blood flow is restored with reperfusion therapies.

Similar advances have been made with magnetic resonance imaging (MRI). MRI with diffusion-weighted imaging (DWI) can differentiate between recent infarction, intracranial masses, and inflammatory disease, and is more sensitive than CT for the detection of acute infarction. It does however have disadvantages in that acutely ill patients may not tolerate it as well and some may even have contra-indications for MRI. Furthermore, MRI may not be readily available in the emergency setting, the acquisition time is longer and MRI is more expensive than CT. Since the primary aim of imaging in acute stroke is to exclude intracranial haemorrhage (which CT is very well suited for), CT is still the most widely used imaging modality in the hyperacute stroke setting.

The National Institute for Health and Care Excellence (NICE) recommends that patients eligible for i.v. thrombolysis should have an urgent non-contrast CT head scan.<sup>1</sup> If the admitting centre has neuro-interventional services, a CT angiogram from the aortic arch to circle of Willis may also be performed to identify patients with large vessel occlusion as such patients may be suitable for mechanical thrombectomy (MT).

## Non-surgical options in acute stroke

### I.V. thrombolysis

NICE have recommended that i.v. thrombolysis with alteplase should be commenced for ischaemic stroke within 4.5 h of symptom onset.<sup>1</sup> However, the benefits of i.v. thrombolysis are offset by an increased risk of intracerebral haemorrhage. It is possible that a lower dose of alteplase than currently used might have a more favourable risk/benefit profile and a trial is underway to help determine this. Careful AP management in the hyperacute phase after thrombolysis is essential to minimize risk of haemorrhagic transformation of the cerebral infarct and this is discussed later.

### Intra-arterial therapy

Successful re-canalization of large arteries with thrombolysis occurs in <30% of cases, often resulting in a poor prognosis. Alternative ways of treating occlusions of large arteries (such as the middle cerebral or internal carotid) involve locally delivered thrombolytic agents (intra-arterial thrombolysis) and mechanical clot retrieval (thrombectomy).

Research has shown unequivocal benefit from intra-arterial therapy (IAT) in patients with stroke.<sup>2</sup> It is important to remember that IAT is not a replacement for i.v. thrombolysis and must not delay the delivery of i.v. alteplase where indicated. IAT may also be an option for patients in whom i.v. thrombolysis is contra-indicated. Intra-arterial thrombolytic therapies have been found to improve survival and minimize disability after stroke but have not as yet been compared directly with thrombolysis. In contrast, there is mounting evidence in favour of MT (with or without concurrent intra-arterial thrombolysis) over i.v. thrombolysis alone for selected patients and this is likely to be reflected in NICE guidance in the near future. Patients who may be considered for thrombectomy include those with a National Institutes of Health Stroke Scale (NIHSS)  $\geq 6$ , a large arterial occlusion, and an arrival time in hospital within 6 h of symptom onset.<sup>3</sup> The NIHSS is a well-validated assessment tool which quantifies the degree of impairment caused by stroke. It measures 11 separate domains including level of consciousness, motor scores, eye movements, and language ability, with each domain scoring 0–4 depending on the degree of impairment. The total score can be used to help guide treatment decisions or predict outcomes.

MT involves passing a guide wire and microcatheter through the femoral artery under image guidance to reach the occluding thrombus. Thromboembolic complications are minimized by balloon occlusion of the artery proximally and catheter aspiration. Several devices are available to remove the clot (Fig. 1). For example, aspiration catheters placed at the proximal surface of the clot enable its removal under constant negative pressure. Alternatively, a micro catheter with a retrieval device can be placed distal to the occlusion site, before being withdrawn to 'trap' the thrombus. Expanding stents can also be 'opened up' within the thrombus, thereby restoring blood flow to the ischaemic area.

NHS England is developing a framework for the delivery of IAT in the UK. However, providing a dedicated safe IAT service will have major implications on resources including anaesthetic staffing and critical care facilities. Anaesthetic considerations include:

- (i) delivery of a consultant-led service as these procedures are remote site, high risk, and time critical;
- (ii) minimizing patient movement to ensure good image quality and safe delivery of interventional therapy;
- (iii) provision of haemodynamic stability and maintenance of cerebral perfusion pressure (CPP);

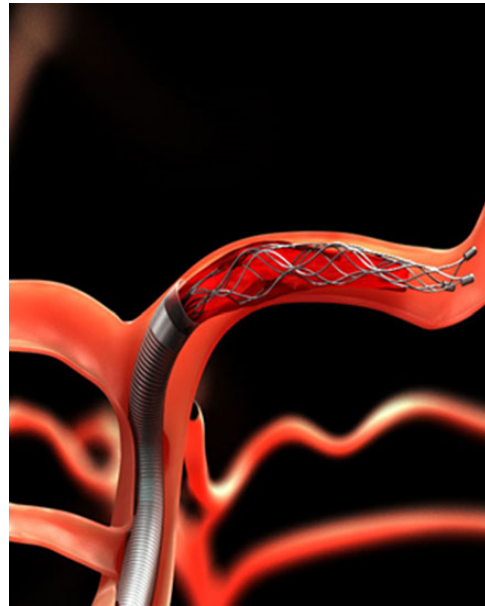


Fig 1 Schematic image of Solitaire™ MT device showing clot retrieval in the middle cerebral artery. (Image courtesy of Medtronic.)

- (iv) utilization of anaesthetic techniques that facilitate rapid recovery and allow early neurological assessment post-procedure.

MT can be performed under a local anaesthetic (LA) or conscious sedation (CS) technique for cooperative patients. This confers haemodynamic stability and allows early neurological assessment, but is not universally appropriate. A change in neurological status, oversedation, or agitation may require conversion to an emergency general anaesthetic (GA). GA is more likely to be appropriate for patients with severe deficits, airway compromise, or bulbar dysfunction. The risk of aspiration in emergency patients with full stomachs must also be considered. Our preferred GA method is a total i.v. technique using propofol and remifentanyl, given the cerebral uncoupling potentially caused by volatile agents. This should be used in conjunction with bispectral index and invasive AP monitoring. This technique has a rapid recovery profile which permits early neurological assessment.

MT performed under LA or CS technique may be associated with better clinical outcomes and is preferable to GA technique, but robust evidence for this is currently lacking.<sup>4,5</sup> Local protocols need to incorporate clinical status, anticipated procedural technique, and planned post-procedural care to decide on GA vs CS technique.<sup>4</sup>

### Carotid endarterectomy and stenting

While it is generally regarded as secondary preventive treatment, carotid endarterectomy (CEA) is increasingly being carried out for relevant patients during their first hospitalization with stroke. NICE guidance recommends that patients undergo surgery within 2 weeks of their symptomatic event.<sup>1</sup> CEA can also lower stroke risk for some patients with asymptomatic stenosis.<sup>6</sup>

The anaesthetic technique for CEA should be at the discretion of the team and patient, as research has shown no difference in surgical outcomes with GA vs LA.<sup>7</sup> A detailed review of anaesthetic management for CEA has been previously published in this journal.<sup>8</sup> Invasive AP monitoring in a critical care bed is usually

required in the postoperative phase to help prevent early hyperperfusion syndrome (usually resulting from >100% increase in cerebral blood flow compared with baseline) which causes headaches, seizures, and focal neurological deficits. If untreated, cerebral hyperperfusion can lead to intracerebral haemorrhage and oedema. AP should be kept <160/100 within the first few days to avoid this complication.

Carotid stenting is sometimes used as an alternative to CEA and is usually performed under sedation rather than GA.

## AP management

Optimum AP targets after stroke depend on whether the stroke is ischaemic or haemorrhagic.

### Ischaemic stroke

After ischaemic stroke, AP usually increases as a cerebral autoregulatory response and can help to maintain cerebral perfusion. However, in severe hypertension (systolic AP >220 mm Hg or diastolic AP >110 mm Hg), there is an increased risk of haemorrhagic transformation of the infarct. AP should therefore be reduced gradually unless the patient is a candidate for i.v. thrombolysis. In these cases, it should be lowered to <185/110 rapidly to allow timely delivery of alteplase.<sup>9</sup> Any antihypertensive agent can be used to lower AP in the acute phase with no evidence to favour one over another, but i.v. labetalol (bolus of 10–40 mg then infusion 2–8 mg min<sup>-1</sup>), i.v. nicardipine, or i.v. GTN are often used. During thrombolysis, AP should be kept <185/110 mm Hg and for the first 24 h after thrombolysis, AP should be kept <180/100 mm Hg to reduce the risk of haemorrhagic transformation.<sup>9</sup>

### Primary intracerebral haemorrhage

AP lowering in primary intracerebral haemorrhage (PICH) can help reduce growth of the haematoma.<sup>10</sup> American Heart Association guidelines currently recommend that AP be kept <180 mm Hg systolic, with mean arterial pressure (MAP) <130 mm Hg while maintaining CPP >70 mm Hg in the acute setting after ICH.<sup>11</sup>

In the hyperacute phase, resource implications preclude routine use of arterial lines to monitor AP. Patients are only referred to critical care if hypertension is not controlled with conventional therapy.

## Surgical interventions

### Intracerebral haemorrhage

Patients with a large lobar haematoma and a deteriorating conscious level, or those with a cerebellar haematoma and hydrocephalus should be considered for urgent surgical intervention. Currently, surgery is not thought to confer significant benefit for small or superficial haematomas and research is ongoing.

A promising new approach for treatment of PICH is minimally invasive surgery, which allows intermittent dosing of alteplase directly into the haematoma. Trials are currently underway to establish the benefits of this technique.

### Ischaemic stroke

Approximately 10% of ischaemic strokes are classified as 'malignant' infarcts because they are at high risk of causing cerebral herniation. Large hemispheric infarction (LHI) refers to an ischaemic stroke affecting the total or subtotal territory of the middle cerebral artery and involving the basal ganglia at least partially. Mortality after LHI without surgical intervention is reported to be as high as 80%.<sup>12</sup> DHC may be offered in these cases. NICE guidance recommends that patients meeting the following criteria should be considered for DHC:

- aged 60 yr or under,
- clinical deficits suggestive of infarction in the territory of the middle cerebral artery, with an NIHSS score above 15,
- decrease in level of consciousness so the patient can no longer be classified as 'alert' on the NIHSS,
- signs on CT of an infarct of at least 50% of the middle cerebral artery territory or infarct volume >145 cm<sup>3</sup> on diffusion-weighted MRI.

DHC involves removal of a fronto-temporoparietal bone flap and incision of the dura on the affected side, allowing the swollen brain to herniate up through the cranial defect (Fig. 2). The Neuro Critical Care Society (NCS) recommends an incision diameter of 12 cm as an absolute minimum.<sup>13</sup> Although NICE and NCS guidelines both state patients should be operated on within 24–48 h after symptom onset, there is little evidence to support this. A pooled analysis of three European randomized controlled trials (DECIMAL, DESTINY, and HAMLET) in 2007 demonstrated that decompressive surgery undertaken within 48 h of stroke onset significantly reduced mortality.<sup>12</sup> The DESTINY II trial confirmed similar findings in patients over the age of 60 yr.<sup>14</sup> However, there was an



**Fig 2** CT scans taken before and after decompressive surgery, including a hemicraniectomy for acute middle cerebral artery (MCA) infarction. (A) Preoperative CT scan taken 1 day after stroke onset shows a large right MCA territory infarction with sulcal effacement. (B) On postoperative CT scan 1 day after decompressive surgery, the craniectomy covers the whole MCA territory. (C) On postoperative CT scan 2 weeks after decompressive surgery, the overlying scalp successfully accommodates the aggravated brain swelling and sulcal effacement has disappeared.

**Table 1** Critical care management guidelines for LHI

Intervention	Current guidance
Ventilation	Intubate immediately if signs of respiratory insufficiency or neurological deterioration. Mode of ventilation is at the clinicians discretion Aim for normocapnia ( $P_{aCO_2}$ 4.5–5.0 kPa) unless impending cerebral herniation
Sedation	No strong data to suggest a particular agent is superior Use of barbiturates is discouraged Sedation holds should be guided by ICP monitoring and clinical condition, blanket daily wake-up trials are not recommended
Thrombolysis	Still of benefit in this population if commenced within 4.5 h Impact on future plans for surgical decompression should be considered
Arterial pressure control	MAP should be maintained >85 mm Hg Systolic pressure should be kept <220 mm Hg to avoid haemorrhagic transformation and worsening oedema
Nutrition	Evidence is generally transferrable from the general critical care population SALT assessments are mandated before oral feeding is recommenced
Glycaemic control	Maintain blood glucose 7.8–10 mmol litre <sup>-1</sup>
Transfusion threshold	70 mg dl <sup>-1</sup> recommended until more evidence in this patient group is available
DVT prophylaxis	Use intermittent pneumatic compression rather than stockings Prophylactic LMWH should be instituted early and continued as long as the patient remains immobile Early mobilization for haemodynamically stable patients
Temperature control	Reserve therapeutic hypothermia for those unsuitable for surgery Initiate active cooling for pyrexial patients when core temperature reaches 37.5°C
Osmotherapy	Recommended in patients with clinical evidence of cerebral oedema Both mannitol and hypertonic saline are considered safe, choice should be based on renal function, serum sodium, and whether the patient will tolerate intravascular volume expansion Mannitol administration should be guided by osmolar gap
Patient position	Nurse at 30° head up
Seizure prophylaxis	Not recommended
Prophylactic antibiotics	Not recommended
Steroids	Not recommended

excess of moderate-to-severe disability (needing assistance to walk and attend to bodily needs) in survivors in the surgical arm.

Every effort should be made to determine whether survival with moderate to severe disability would be an acceptable outcome to the patient and their caregivers. Input from the multidisciplinary team is also vital before a decision is made to undertake aggressive surgical treatment, especially considering DHC can have potentially life-threatening complications. Despite the complexities involved in the decision-making process, follow-up studies suggest that the majority of DHC patients do not regret having undergone the surgery.<sup>15</sup>

There are limited data available on the impact of anaesthetic technique for DHC. The anaesthetist should focus on maintaining CPP until decompression has been achieved. Many patients will present to the anaesthetist having already been intubated for airway protection and control of ventilation, if not then this must be undertaken. A total i.v. technique using propofol reduces the cerebral metabolic rate without affecting autoregulation and the addition of a short-acting opioid such as remifentanyl helps prevent surges in intracranial pressure. Patients should be carefully positioned to avoid increases in central venous pressure. We prefer an armoured tracheal tube (TT) to prevent kinking during positioning. I.V. paracetamol, judicious use of longer acting opioids and antiemetics at the end of surgery, enhances the recovery profile. If prolonged postoperative ventilation is anticipated, the armoured TT should be exchanged for a high-volume-low-pressure tube. Critical care management guidelines for LHI are summarized in Table 1.

For patients who do not undergo surgery and for whom the outlook is poor, palliative care and issues surrounding withdrawal

of life-sustaining treatments should be discussed with the team, patient, and caregivers.

### Non-neurological surgery after stroke

It has been previously suggested that elective surgical procedures should be deferred for at least 6 months in acute stroke patients.<sup>16</sup> This is based on observational data showing an increased risk of death, major cardiac events, and recurrent stroke in patients operated on sooner. Urgent surgical cases should be managed on a balance of risks, and the advice of a neurologist sought.

In summary, the emergence of new medical technologies and availability of high quality evidence from randomized trials has seen an increase in therapeutic options for patients with acute stroke. A coordinated response by all stakeholders and a significant increase in resource allocation will be needed to develop regional pathways that deliver tailored therapy to achieve the best possible outcomes for individual patients.

### Declaration of interest

None declared.

### MCQs

The associated MCQs (to support CME/CPD activity) can be accessed at <https://access.oxfordjournals.org> by subscribers to BJA Education.



## References

1. National Institute for Health and Clinical Excellence. Stroke and transient ischaemic attack in over 16s: diagnosis and initial management. NICE guideline (CG68), 2008
2. Berkhemer OA, Fransen PSS, Beumer D *et al.* A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med* 2015; **372**: 11–20
3. Grotta JC, Hacke W. Stroke neurologist's perspective on the new endovascular trials. *Stroke* 2015; **46**: 1447–52
4. Froehler MT, Fifi JT, Majid A *et al.* Anesthesia for endovascular treatment of acute ischemic stroke. *Neurology* 2012; **79**: 167–73
5. Schönenberger S, Möhlenbruch M, Pfaff J *et al.* Sedation vs. Intubation for Endovascular Stroke Treatment (SIESTA)—a randomized monocentric trial. *Int J Stroke* 2015; **10**: 969–78
6. Halliday A, Mansfield A, Marro J *et al.* Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. *Lancet* 2004; **363**: 1491–502
7. Lewis SC, Warlow CP, Bodenham AR *et al.* General anaesthesia versus local anaesthesia for carotid surgery (GALA): a multicentre, randomised controlled trial. *Lancet* 2008; **372**: 2132–42
8. Howell SJ. Carotid endarterectomy. *Br J Anaesth* 2007; **99**: 119–31
9. Adams HP, del Zoppo G, Alberts MJ *et al.* Guidelines for the early management of adults with ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atheros. *Stroke* 2007; **38**: 1655–711
10. Ohwaki K, Yano E, Nagashima H *et al.* Blood pressure management in acute intracerebral hemorrhage: relationship between elevated blood pressure and hematoma enlargement. *Stroke* 2004; **35**: 1364–7
11. Broderick J, Connolly S, Feldmann E *et al.* Guidelines for the management of spontaneous intracerebral hemorrhage in adults: 2007 update: a guideline from the American Heart Association/American Stroke Association Stroke Council, High Blood Pressure Research Council, and the Quality of Care and Out. *Stroke* 2007; **38**: 2001–23
12. Vahedi K, Hofmeijer J, Juettler E *et al.* Early decompressive surgery in malignant infarction of the middle cerebral artery: a pooled analysis of three randomised controlled trials. *Lancet Neurol* 2007; **6**: 215–22
13. Torbey MT, Bösel J, Rhoney DH *et al.* Evidence-based guidelines for the management of large hemispheric infarction: a statement for health care professionals from the Neurocritical Care Society and the German Society for Neuro-intensive Care and Emergency Medicine. *Neurocrit Care* 2015; **22**: 146–64
14. Jüttler E, Unterberg A, Woitzik J *et al.* Hemispherectomy in older patients with extensive middle-cerebral-artery stroke. *N Engl J Med* 2014; **370**: 1091–100
15. Rahme R, Zuccarello M, Kleindorfer D *et al.* Decompressive hemispherectomy for malignant middle cerebral artery territory infarction: is life worth living? *J Neurosurg* 2012; **117**: 749–54
16. Sanders RD, Jørgensen ME, Mashour GA. Perioperative stroke: a question of timing? *Br J Anaesth* 2015; **115**: 11–3