Critical care management of the patient with an acute ischaemic stroke

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Abstract

Acute ischaemic stroke is a leading cause of morbidity and mortality worldwide. In the UK alone, there are more than 100000 strokes per year, causing 38000 deaths. While the incidence remains high, there has been significant medical progress in reducing mortality following a stroke. Admission of patients to specialised stroke units has led to an improvement in clinical outcomes, but the role of intensive care is less well defined. This article reviews the current critical care management and neuro-therapeutic options after an acute ischaemic stroke.

Key words: Acute ischaemic stroke; Anticoagulation; Critical care management; Decompressive craniectomy; Endovascular intervention; Ischaemic penumbra; Mechanical thrombectomy; Thrombolysis

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Introduction

There has been significant progress in the management of acute ischaemic stroke in the UK as a result of early recognition and management including thrombolysis and endovascular intervention. Thrombolysis and mechanical thrombectomy are discussed in more detail in the companion article (https://doi.org/10.12968/hmed.2020.0193). Managing patients who have had a stroke in centralised hyperacute stroke units, with resources in one place, has also led to improved outcomes. This hyperacute stroke unit model has gradually been adopted across the UK (Ramsay et al, 2015). While the majority of patients with acute ischaemic stroke are managed in a ward setting, some will require support on an intensive care unit. The management of acute ischaemic stroke on the intensive care unit is focused on minimising secondary brain injury such as propagation of cerebral oedema, avoiding tissue hypoxia and preventing further neuronal injury. Complications of reperfusion such as haemorrhagic transformation must also be anticipated and managed. Often, these patients may also require ventilatory or haemodynamic support during the acute phase. Historically, acute ischaemic stroke was seen as an irreversible condition with reports suggesting no significant improvement in outcomes following intensive care unit admission (Pitner and Mance, 1973). There is a growing body of evidence showing that specific interventions can lead to improved outcomes. This article discusses the current evidence and principles of managing acute ischaemic stroke in the intensive care unit.

Admission to the intensive care unit

Despite the availability of consensus guidance for the general management of acute ischaemic stroke by the European Stroke Organisation (European Stroke Organisation (ESO) Executive Committee and ESO Writing Committee, 2008), American Stroke Association (Powers et al, 2019) and the National Institute for Health and Care Excellence (2019), there is a lack of formal guidance on aspects of intensive care unit management.

The decision to admit to the intensive care unit should be based on comorbidities, functional status and previous wishes of the patient. Neurological prognostication is often difficult during the acute phase of acute ischaemic stroke and is more accurately determined through regular multidisciplinary assessments by experienced intensive care unit and stroke physicians. The management of the patient who has had an acute ischaemic stroke involves coordinated decision making with many other members of the multidisciplinary team (Kirkman et al, 2014).

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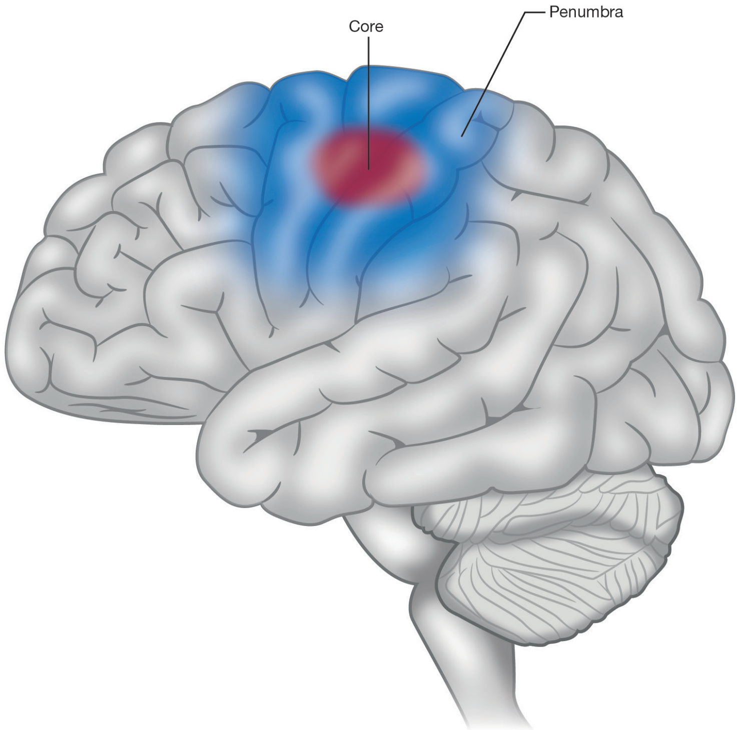

Figure 1. The ischaemic core and penumbra of a cerebral infarct.

Principles of intensive care unit management

Intensive care unit management of the patient who has had an acute ischaemic stroke is focused on preventing secondary brain injury. After an acute ischaemic stroke, there are two zones of injury in the brain: the ischaemic core and the penumbra (Figure 1). The core represents the zone of tissue that has already infarcted or is going to infarct regardless of reperfusion. The ischaemic penumbra denotes the tissue that is at risk of progression to infarction but remains salvageable if rapidly reperfused. It is vital to maintain blood flow to this ischaemic penumbra. This is achieved through reperfusion therapies, optimisation of neuroprotective strategies and the support of other organs during neurological recovery.

Airway and ventilatory support

Endotracheal intubation

The clinical indications for intubating a patient with an acute ischaemic stroke are listed in Table 1.

Mechanical ventilation

The need for respiratory support is one of the more common causes of intensive care unit admission. The need for mechanical ventilation is related to the location of the stroke. Involvement of areas of the brain that regulate conscious level (thalami, limbic system, reticular formation), breathing (respiratory centres in the cortex, pons and medulla) and swallowing (medulla and brainstem) increase the risk of respiratory failure (Bösel, 2017). Mechanical ventilation should maintain adequate oxygenation and control of carbon dioxide levels while avoiding lung damage.

Management of aspiration

Aspiration pneumonia occurs frequently after stroke and is related to a decreased level of consciousness with impaired swallowing and dysphagia. Techniques to reduce the risk of aspiration include elevation of the head of the bed, vigilance with the absorption of enteral feed and avoidance of excessive sedation. The incidence of pneumonia in stroke patients is higher than in other groups of patients who suffer dysphagia or a compromised conscious

Table 1. Reasons for intubation in patients who have had a stroke
Reduced conscious level (Glasgow Coma Score <8)
Failure of oxygenation
Inability to protect the airway, eg reduced gag and cough reflexes
Dysphagia
Seizures
Sedative medication suppressing respiratory drive
Need for intracranial pressure management

level. This suggests that other mechanisms such as immune activation and alteration in lung injury pathogenesis may be involved (Hoffman et al, 2017).

Extubation or tracheostomy?

Prediction of successful extubation is critical since both premature and delayed extubation increase complication rates, need for tracheostomy, duration of intensive care unit stay and mortality (Kutchak et al, 2015). Traditional parameters used to predict successful extubation (such as tidal volume, respiratory rate and forced vital capacity) are often unreliable because of the stroke (Savi et al, 2012). New parameters have been evaluated in patients with severe brain injury. On the basis of these, the VISAGE score (age <40, visual pursuit, swallowing, Glasgow Coma Score >10) was constructed. If three or more items are positive, an extubation success rate of 90% can be expected (Asehnoune et al, 2017).

Up to 45% of patients admitted to the intensive care unit for stroke require tracheostomy vs 10–15% of the general intensive care unit population (Robba et al, 2019). In patients who fail extubation or who are not expected to recover oropharyngeal function for a prolonged period, tracheostomy may be an appropriate bridge to allow for rehabilitation. The SETPOINT trial assessing the role of early tracheostomy vs prolonged orotracheal intubation in acute ischaemic stroke and haemorrhagic stroke showed no difference in the primary outcome of length of stay on the intensive care unit. However, secondary outcomes including intensive care unit mortality and 6-month mortality were lower in the early group than in the standard group (Bösel et al, 2013). Results of the larger SETPOINT 2 trial are awaited.

Haemodynamic management

The majority of patients who have had an acute ischaemic stroke are hypertensive at presentation with systolic blood pressure >140 mmHg. The reasons for this are multifactorial and include pre-existing hypertension, raised intracranial pressure and a sympathetic response. American Stroke Association guidelines (Powers et al, 2019) recommend that, if a patient is not being thrombolysed, then only blood pressure above 220/120 mmHg should be actively managed with antihypertensives. Blood pressure should be reduced by no more than 15% per 24 hours, unless there are comorbidities such as cardiac failure, aortic dissection or hypertensive encephalopathy. Before thrombolysis it is necessary to acutely lower blood pressure to 185/110 mmHg. After thrombolysis the blood pressure target is ≤180/105 mmHg to minimise the risk of haemorrhagic conversion. Intravenous labetalol is the most recommended antihypertensive agent but other drugs such as intravenous glycerine trinitrate may also be used. Continuous invasive arterial blood pressure monitoring is used to guide treatment.

The management of hypotension after stroke has not been widely studied. While symptomatic hypotension should be treated, there are no data to support the routine use of induced hypertension.

Fluid balance should be carefully individualised with the aim of maintaining euvolaemia. The use of hypotonic glucose containing solutions and albumin is not recommended (Oddo et al, 2018).

Thrombolysis, anticoagulation and antithrombotic therapy

Thrombolysis with intravenous tissue plasminogen activator and endovascular intervention can alter the natural course of acute ischaemic stroke. They are both backed by high level evidence and should be actively facilitated then supported with intensive care unit admission as necessary. Thrombolysis should be given within a 4.5-hour window and ideally be instituted as soon as possible (Lees et al, 2010). Endovascular intervention results in favourable functional independence, health-related quality of life, and cognitive function at long-term follow up compared to thrombolysis alone (McCarthy et al, 2019).

Aspirin therapy within 48 hours seems to confer a small benefit with fewer deaths and less stroke recurrence without an increase in haemorrhagic complications (CAST (Chinese Acute Stroke Trial) Collaborative Group, 1997). However, aspirin should not be given within 24 hours of thrombolysis (Jauch et al, 2013). Although immediate treatment with subcutaneous heparin is associated with less recurrent ischaemic strokes, it is associated with more haemorrhagic strokes and therefore patients with acute ischaemic stroke are not therapeutically anticoagulated for at least the first 2 weeks.

Patients who have had an acute ischaemic stroke are at high risk of deep vein thrombosis and pulmonary embolism (Jauch et al, 2013). However, the use of prophylactic subcutaneous low molecular weight heparin should be avoided for at least 24 hours after thrombolysis and is sometimes withheld for even longer because of concerns relating to haemorrhagic transformation. The exact timing of initiating low molecular weight heparin is unclear and further research in this area is underway. Intermittent pneumatic compression is an effective method of reducing deep vein thrombosis and shows a trend towards reduced mortality. Graduated compression stockings do not reduce thromboembolic events and may cause skin tears, so should be avoided (Dennis et al, 2013a,b).

Management of cerebral oedema and decompressive craniectomy

Patients with large hemispheric infarctions are at risk of malignant middle cerebral artery infarction and should be monitored closely, ideally in the intensive care unit. Patients younger than 60 years of age with middle cerebral artery infarction and cerebral oedema have improved outcomes if decompressive craniectomy is achieved within 48 hours (Vahedi et al, 2007). However, the role of decompressive craniectomy in elderly stroke patients is more controversial and should be considered with caution. The Decompressive Surgery for the Treatment of Malignant Infarction of the Middle Cerebral Artery (DESTINY) II trial showed increased survival but with severe disability in patients older than 60 years (Jüttler et al, 2014) (**Table 2**, **Figure 2**).

Ventriculostomy to relieve acute hydrocephalus and suboccipital decompressive craniectomy are potential options after cerebellar infarction. As for malignant middle cerebral artery infarction, clinical deterioration and imaging are key to determining the need for surgical intervention.

Table 2. Criteria for decompressive craniectomy in malignant middle cerebral artery infarction

Consider decompressive craniectomy within 48 hours in patients who meet all of the following criteria:	Clinical deficits that suggest infarction in the territory of the middle cerebral artery, with a score above 15 on the National Institutes of Health Stroke Scale	
	Decreased level of consciousness, with a score of one or more on item 1a of the National Institutes of Health Stroke Scale	
	Signs on computed tomography of an infarct of at least 50% of the middle cerebral artery territory:	With or without additional infarction in the territory of the anterior or posterior cerebral artery on the same side
		With infarct volume greater than 145 cm^3, as shown on diffusion-weighted magnetic resonance imaging scan

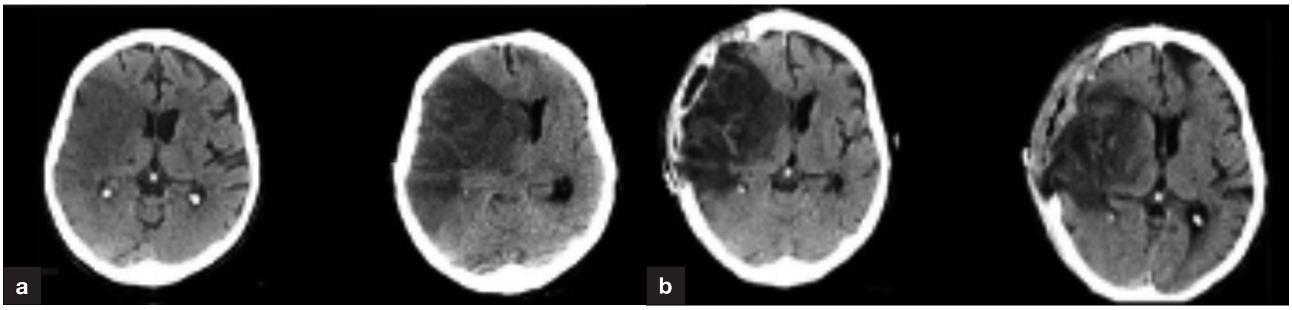

Figure 2. a. Malignant right-sided middle cerebral artery infarction as seen on computed tomography scan. b. Cerebral oedema and midline shift resolving after decompressive craniectomy.

In the presence of raised intracranial pressure, medical treatment includes the administration of mannitol and hypertonic saline. There is no robust evidence to show that their use improves outcome after acute ischaemic stroke, and they should only be used as a temporising measure without delaying planned surgical intervention. Steroids are of no benefit in the management of cerebral oedema after acute ischaemic stroke (Sandercock and Soane, 2011).

Preventing haemorrhagic transformation of infarct

Haemorrhagic transformation is a complication of acute ischaemic stroke and can significantly worsen prognosis. It is thought that approximately half of all cerebral infarcts develop a haemorrhagic component at some stage. The majority are petechial haemorrhages (89%) with the rest (11%) being haematomas. The European Cooperative Acute Stroke Study (ECASS) classification system (Hacke et al, 1995) is used to describe the type of haemorrhage (Table 3). Classification of the haemorrhage type is important because it determines the subsequent plan of management. Large bleeds might require treatment of coagulopathy whereas petechial haemorrhages can be observed.

Although haemorrhagic transformation can occur spontaneously, it is more common after anticoagulant therapy or in patients undergoing thrombolysis. The incidence of symptomatic haemorrhagic transformation is approximately 6% in patients given intravenous tissue plasminogen activator (Jauch et al, 2013). In untreated patients, haemorrhagic transformation usually develops within the first few days after infarction. In patients who have been given thrombolysis, haemorrhage occurs mainly within the first 24 hours of starting treatment. No robust evidence exists to guide treatment, but a combination of different clotting products may be used, ideally with input from the haematology team. Any ongoing infusions of tissue plasminogen activator should of course be stopped.

There are no definitive data from clinical trials about the role of surgery following haemorrhagic transformation, and the decision to proceed to surgical evacuation is determined by the size and location of the haemorrhage as well as the patient's overall clinical condition.

Glycaemic control

Hyperglycaemia during acute ischaemic stroke is common and can occur even in those patients without a previous diagnosis of diabetes mellitus. Hyperglycaemia causes neuronal

Table 3. Types of haemorrhagic transformation

Type of haemorrhage	Definition
Haemorrhagic infarction 1 (HI1)	Small petechiae
Haemorrhagic infarction 2 (HI2)	More confluent petechiae
Parenchymal haematoma 1 (PH1)	<30% of the infarcted area with mild space-occupying effect
Parenchymal haematoma 2 (PH2)	>30% of the infarcted area with significant space-occupying effect

From European Cooperative Acute Stroke Study (ECASS) (Hacke et al, 1995) damage secondary to anaerobic metabolism and associated lactic acidosis within brain tissue. It is independently associated with worse clinical outcomes including infarct growth and haemorrhagic transformation (Capes et al, 2001). Hypoglycaemia should also be avoided as this has been associated with an increased risk of stroke. The mechanism is thought to involve sympathetic associated changes in blood flow affecting the cerebral vascular system which then leads to an increased risk of cerebral ischaemia (Yun et al, 2019).

Regular blood glucose monitoring and careful glycaemic control is required in all patients who have had an acute ischaemic stroke, but treatment targets vary between guidelines. The SHINE trial randomised patients who had had an acute ischaemic stroke to either intensive (4.4–7.2 mmol/litre) or standard (4.4–9.9 mmol/litre) glucose control for up to 72 hours and showed no significant difference in favourable functional outcome at 90 days (Bruno et al, 2014). In the absence of benefit from intensive insulin therapy and considering its attendant risks of hypoglycaemia, our practice is to aim for a maximum upper blood glucose value of 10 mmol/litre. This is based on findings from the NICE-SUGAR trial which investigated management of blood glucose in general critically ill patients (Finfer et al, 2009). Referral to the diabetic team should be considered for patients whose blood sugar level is difficult to control.

Temperature management

Hyperthermia following acute ischaemic stroke is associated with increased mortality secondary to increased metabolic demand. The Paracetamol (Acetaminophen) in Stroke 2 (PAIS 2) trial assessed whether early treatment with paracetamol led to improved functional outcome in patients with acute ischaemic stroke and a body temperature ≥36.5°C. It was halted prematurely because of slow recruitment and lack of funding (de Ridder et al, 2015). A pragmatic approach is to avoid pyrexia and to treat any identified infectious causes of fever. Ibuprofen does not appear to reliably reduce body temperature after stroke (Dippel et al, 2003).

Although many preclinical studies support the neuro-protective role of therapeutic hypothermia in acute ischaemic stroke, definitive evidence for benefit is currently lacking. EuroHYP-1 was planned to be the largest ever prospective clinical trial on therapeutic hypothermia for stroke patients in Europe. At the end of the 52-month recruitment period, with 98 patients included, the trial was underpowered to demonstrate the impact of therapeutic hypothermia on functional outcomes (van der Worp et al, 2014).

Management of anaemia

Analysis of UK Regional Registry Data by Barlas et al (2016) showed that a significant proportion of stroke patients had anaemia at stroke presentation and that this was associated with increased mortality up to 1 year. Anaemia was defined according to World Health Organisation standards as a haemoglobin <12 g/dl in women and <13 g/dl in men. Anaemia is associated with worsening of infarct size, larger final infarct volume and faster infarct growth, although the relationship between haemoglobin level and outcome might not be a simple one. Elevated haemoglobin (>15.5 g/dl in women and >17.0 g/dl in men) is also associated with increased mortality. The threshold level of haemoglobin at which transfusion should occur in a patient with an acute ischaemic stroke is currently unclear. The sensitivity of the brain to oxygen deprivation suggests that haemoglobin optimisation might improve oxygenation in the penumbral region but robust evidence to this effect is lacking. Although anaemia should be avoided, aggressive transfusion approaches are not recommended. There is marked variability in transfusion strategies in these patients and further research in this area is needed.

Seizure control

Convulsive and non-convulsive seizures can occur after stroke. They are less common after acute ischaemic stroke than after haemorrhagic stroke so prophylactic anticonvulsants are not routinely recommended. Seizures should be treated aggressively when they do occur. The first-line anticonvulsant is phenytoin because of the paucity of studies of other agents

Key points

- Acute ischaemic stroke is a medical emergency.
- Increasing numbers of patients are being admitted to the intensive care unit.
- Intensive care management initially aims to minimise secondary brain injury by optimising blood flow to the ischaemic penumbra.
- Repeat clinical examination and imaging are vital to assess progress of the patient.
- Further large-scale patient trials are needed to add to the growing body of evidence in this area of intensive care management.

but newer generation drugs such as levetiracetam are now used. Electroencephalography should be used in all acute ischaemic stroke patients with unexplained and/or persistently altered consciousness.

Neuromonitoring

Clinical and radiological monitoring are key to identifying deterioration after acute ischaemic stroke. Routine intracranial pressure monitoring is not recommended but can be considered in those with large infarct volumes or haemorrhagic conversion with mass effect. Measured intracranial pressure values are often normal even in the presence of large infarct volumes (Poca et al, 2010).

The risks of using invasive neuromonitoring tools such as intracranial pressure bolts in those undergoing thrombolysis are currently poorly quantified. Transcranial Doppler ultrasonography is a non-invasive monitor that can assess cerebral blood flow velocity and is a promising neuromonitor in acute ischaemic stroke (Kirkman and Smith, 2012). Optic nerve ultrasonography has also been used as a non-invasive alternative to invasive intracranial pressure monitoring (Rajajee et al, 2011). Brain tissue oxygen tension monitoring and near-infrared spectroscopy both require further research before their routine bedside use can be recommended.

Conclusions

In the past, one of the main reasons for refusing intensive care unit admission to a patient who had had an acute ischaemic stroke was the perceived futility of the admission. A rapidly growing body of evidence has challenged this mindset and there is generally less reluctance to admit patients who have had an acute ischaemic stroke to the intensive care unit. Stroke is a medical emergency with a limited time window for early intervention. Specialised care in the intensive care unit should be offered promptly to those patients who require it.

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Conflicts of interest

The authors declare no conflicts of interest.

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