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### Management of Acute Ischaemic Stroke



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## Defining the Role of the Intensive Care Unit

This review article aims to alter the preconceived mindset that surrounds the intensive care unit (ICU) and the patient with an acute ischaemic stroke (AIS). A contemporary body of evidence is emerging that shows that specific interventions can improve outcomes, and this article highlights key evidence-based strategies in AIS management. More importantly, it focuses on the broader management facets such as the standards of AIS care, stroke care pathways and indications for ICU admission. When compared with other serious ICU diagnoses such as severe sepsis and long term ventilation, the outcome of AIS patients on ICU compares well. This comparison should shake the historical reluctance that surrounds admission of stroke patients to ICU.

Stroke is the second largest contributor to mortality worldwide. Its devastating consequences are also a major contributor to morbidity, especially in high-income countries, where it is a leading cause of years of life lived with disability (Lopez et al. 2006). Historically, acute ischaemic stroke (AIS) was largely seen as an irreversible condition with reports previously suggesting no significant reduction in morbidity and mortality following intensive care unit (ICU) admission (Drake et al. 1973; Kennedy et al. 1970). Modern-day paradigms have changed however with an established, contemporary body of evidence showing that specific interventions can improve outcomes. As a consequence, thresholds for admitting AIS patients to ICU to support these interventions, and their potential complications, are falling. A recent analysis of 31,301 AIS patients admitted to hospital in the eastern half of the United States showed that 26% required ICU admission at some stage (Golestanian et al. 2009). Despite this, there seems to be a lack of widely accepted indications for admission to the ICU and evidence for management thereafter.

### **Standards of Care and Stroke Care Pathways**

Management of acute stroke is complex. Interventions such as prompt diagnosis, consideration for thrombolysis, correction of deranged physiology and secondary prevention must be coordinated in a timely fashion. Care pathways assist healthcare professionals in making clinical decisions according to the best available evidence, thereby improving patient care and reducing variation in clinical practice. Their place in the acute management of AIS has therefore become commonplace. Some of the typical components of an AIS care pathway include (Intercollegiate Stroke Working Party 2012; National Collaborating Centre for Chronic Conditions (UK) 2008):

- If indicated, “immediate” brain imaging (ideally the next slot and definitely within one hour);
- If indicated, thrombolysis with alteplase within 4.5 hours;
- Direct admission to a specialist acute stroke unit;
- Antiplatelet treatment to start as soon as possible, and certainly within 24 hours.

The evaluation of care pathways in acute stroke is complicated however, given regional variability in content and delivery. A recent Cochrane review (Stroke Unit Trialists’ Collaboration 2013) looked at the use of care pathways in acute stroke management and rehabilitation. Of the 15 studies, which included more than 4,000 patients, only three were randomised. The primary outcome measures of death and dependency at discharge showed no clear benefit with the use of care pathways. Mindful that non-randomised studies are susceptible to biases and clinical studies of care pathways are open to confounding, this Cochrane review still suggests that the benefits of AIS care pathways are not proven.

If care pathways are to succeed, they are only likely to improve standards of care if implemented in specialised stroke units. Such units confer a clear morbidity and mortality benefit over general medical care and should form the standard of care. This benefit does not seem to be limited by age, sex, type or severity of stroke (Stroke Unit Trialists’ Collaboration 2013).

Where such units exist, cohesive multidisciplinary input ranging from paramedics and emergency physicians through to stroke specialists, interventional radiologists and surgeons are key to drive standards set in the care pathway. Intensivists are playing increasing roles within these teams, ensuring that provision of optimal organ support and specialised nursing care continue in parallel to other ongoing stroke management. The delay in transfer of critically ill stroke patients from the emergency department to the neurointensive care has been shown to be an independent indicator of poor outcome at hospital discharge (Rincon et al. 2010).

Appropriate training tools can also improve standards of acute stroke care. Simulation-based models have been used to improve utilisation of thrombolysis by helping to identify barriers along care pathways (for example picking up delays in ambulance transfers) and provide solutions for these (for example the scoop-and-run protocol) (Lahr et al. 2013). NavarreteNavarro et al. (2012) also showed that the introduction of a training model (e-learning course, lectures and workshops) focusing on therapeutic and organisational aspects of AIS management led to improved knowledge of emergency and critical care physicians and formed part of the regional strategy on stroke management, leading to increased uptake of thrombolysis in the region.

### **Indications for ICU Admission**

The decision to admit an AIS patient to ICU is often to improve/support blood flow to the ischaemic penumbra. This is achieved through reperfusion therapies, optimisation of neuroprotective strategies and the support of other organs during neurological recovery. Other indications include prevention, early detection and treatment of complications and the need for close monitoring. Before making a final decision on appropriateness for admission, prior co-morbidity, cognitive and functional status and personal wishes should also be taken into consideration.

Accurate neurological prognostication is central to the decision to admit, but is notoriously difficult. Detailed history taking, thorough examination and appropriate imaging are key, but may not predict for all. Stroke mimics such as psychogenic disorders, hypoglycaemia, seizures, complicated migraine, encephalopathy, central nervous system mass lesions and drug toxicity need to be excluded. Neurological prognostication is near to impossible during the acute phase and is more accurately determined through repeated assessments temporally, involving regular discussion between ICU and stroke physicians (Kirkman et al. 2014). Therefore the American Stroke Association recommends aggressive treatment and postponement of “Do Not Attempt

Cardiopulmonary Resuscitation" (DNACPR) orders for at least the first 24 hours (Jauch et al. 2013). Kirkman et al. recently reviewed current AIS guidelines and produced recommendations on indications for ICU admission as shown in Table 1 (Kirkman et al. 2014). While patients with AIS, decreased level of consciousness and a National Institutes of Health Stroke Score (NIHSS) > 17 on admission are thought to have a poor prognosis, exceptions exist, such as the response seen by cerebellar infarcts to sub-occipital craniectomy (Kirkman et al. 2014; Wijdicks et al. 2014). The relationship between stroke severity and outcome should be observed with caution as patients with more severe deficits will inherently have the most to gain from treatment, especially when compared with mild strokes where death or severe disability have been used as the primary outcomes of research (Stroke Unit Trialists' Collaboration 2013).

□ The need for respiratory support is one of the more common causes for ICU admission in patients with AIS. While the literature is not clear, a few small trials indicate that patients who are intubated and ventilated for neurological deterioration (coma) and respiratory deterioration do not do as well as those who are intubated and ventilated for potentially reversible causes such as seizure management or prevention of aspiration pneumonia (Burtin et al. 1994; Leker and Ben-Hur 2000; Meyfroidt et al. 2014; Steiner et al. 1997; Wijdicks and Scott 1997).

### **Therapeutic Strategies in AIS Management**

The initial supportive management of AIS is not complex and should not intimidate the ICU practitioner. Even in ICU, the simple task of ensuring that all the small facets of stroke care are done well can have the greatest benefit to our patients by avoiding secondary brain damage. Supplemental oxygen therapy targeted to oxygen saturation (to avoid both hypoxia and hyperoxia), avoidance of fever and glucose control are paramount. Both high and low blood pressure during an AIS are independent poor prognostic factors for outcome (LeonardiBee et al. 2002). It is necessary to acutely lower blood pressure to less than 185/110mmHg to enable thrombolysis. If treatment does not include thrombolysis, only blood pressures greater than 220/120mmHg should be gently reduced by no more than 15% per 24 hours, except if co-morbidities such as severe cardiac failure, aortic dissection or hypertensive encephalopathy occur (European Stroke Organisation (ESO) Executive Committee and ESO Writing Committee 2008). AIS patients with very high or labile blood pressures, or patients who are being mechanically ventilated should have continuous invasive arterial blood pressure monitoring. Intravenous labetalol is most commonly recommended, but intravenous nicardopine or glycerine trinitrate may all be used to cautiously lower blood pressure. A recent trial has shown that more aggressive systolic blood pressure lowering to around 140mmHg is safe but confers no benefit (He et al. 2014).

Early 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). Aspirin therapy should not however be used 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 AIS patients are not therapeutically anticoagulated for at least the first two weeks after their stroke and preferably after liaison with a haematologist.

AIS patients are at high risk of deep vein thrombosis (DVT) and pulmonary embolus (Jauch et al. 2013). This risk may be reduced through hydration and early mobilisation. However, the use of prophylactic subcutaneous low molecular weight heparin should be avoided for at least 24 hours after thrombolysis, and is commonly withheld for 2 weeks following an AIS for fear of potentiating a haemorrhagic transformation. The exact timing of initiating low molecular weight heparins is unclear and further research in this area is underway. The use of intermittent pneumatic compression is an effective method of reducing DVTs and shows a trend to reduced mortality, while graduated compression stockings do not reduce thromboembolic events and may cause skin tears and are therefore best avoided (CLOTS (Clots in Legs Or sTockings after Stroke) Trials Collaboration et al. 2013).

Two interventions that alter the natural course of AIS, which are both backed by level 1 evidence, are worthy of discussion and should be actively facilitated and supported where necessary with ICU admission. First, thrombolysis with intravenous recombinant tissue plasminogen activator (rTPA), after clinical and radiographic diagnosis of AIS. This should be given within a four-and-a-half-hour window and be instituted as soon as possible. Endovascular alternatives (e.g. clot retrieval, stenting) are gaining in popularity. New evidence suggests that some patients with AIS and moderate to severe neurological impairment, with very proximal occlusions, benefit from clot retrieval and stenting, demonstrated by improved outcomes beyond that possible by thrombolysis alone (Prabhakaran et al. 2015). Time to reperfusion seems to be the most crucial factor, irrespective of the method used. However, this field is moving fast and indications and preferences are likely to change.

Secondly, patients with large infarctions who are at risk of malignant cerebral oedema should be monitored closely, and early referral to a unit with neurosurgical capabilities should be discussed as soon as possible. Patients under the age of 60 with malignant MCA infarcts and cerebral oedema have improved outcome if decompressive craniectomy is achieved within 48 hours (Vahedi et al. 2007). The recent Decompressive

Surgery for the Treatment of Malignant Infarction of the Middle Cerebral Artery (DESTINY) II trial has illustrated increased survival, but some survivors are often left with substantial disability (Jüttler et al. 2014) and surgery should be considered with caution especially in advancing age.

### **Comparing Outcomes - Is it Worth it?**

One of the main reasons for refusing an AIS patient admission to the ICU is the perceived futility of the admission. Navarrete-Navarro et al. conducted a multicentre, prospective observational study in 28 Spanish hospitals that recorded the mortality and disability of 132 ICU-admitted severe stroke patients. Patients with AIS had the highest inpatient survival rate of 78%, but this decreased to 34% after one year and only 25% of patients had minimal or no disability at one year (Navarrete-Navarro et al. 2003). This data is similar to critical care outcomes at one of the largest acute stroke units in London, which followed up 144 patients over two years and found an ICU survival rate of 62% and a one-year survival rate of 30% in patients with AIS. Importantly over 60% of these survivors had a favourable neurological outcome (unpublished data).

These outcomes are not markedly different from other groups of critically ill patients. A recent prospective analysis of severe sepsis survivors showed comparable mortality outcomes as well as cognitive and functional disability rates. This large nationally representative cohort of more than 1,194 patients over the age of 50 revealed a 90-day mortality after severe sepsis of 41%. The odds of acquiring a moderate to severe cognitive impairment were 3.3 times more likely following sepsis when compared with a general hospital admission. Furthermore, there was a mean increase of 1.5 new functional limitations following sepsis (Iwashyna et al. 2010). Similarly, studies have shown that only 9% of long-term (median of 27 days) ventilated patients reach independent functioning at one year (Unroe et al. 2010).

Stroke should therefore be viewed in the same light as other severe conditions requiring ICU admission, including severe sepsis and longterm ventilation. Rapidly evolving strategies that aggressively alter the natural course of stroke hope to further improve stroke outcomes in the near future.

### **Conclusion**

Stroke is a major contributor to mortality and morbidity worldwide. Modern-day attitudes and paradigms are shifting as a rapidly growing body of evidence emerges. As a result, there is generally less reluctance to admit AIS patients to ICU, and outcomes compare well with other serious ICU conditions. Effective management of the critically ill stroke patient requires proactive, rapid and coordinated decision-making by a multidisciplinary team, including stroke physicians and nurses, intensivists and radiologists. This teamwork does not always come naturally; education, regular training, systems and support need to be put in place to ensure that the correct resources are rapidly brought to bear on one of the most time-critical medical emergencies. It is hoped that future trials will identify further medical interventions and better ways to structure stroke units to facilitate better outcomes.

See Also: [ICU-Related Dysphagia](#)

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