Anaesthetic Management of the Patient With Acute Ischaemic Stroke
Z. H. Anastasian

Abstract and Introduction

Abstract

Anaesthetic management of the acute stroke patient demands consideration of the penumbra as the central focus. Recent studies have shown that patients who receive general anaesthesia for endovascular therapy for acute ischaemic stroke have worse outcomes than those who receive local anaesthesia. Although baseline condition of the patients in these studies differed, we should heed the warnings evident in the results. 'Time is brain': therapy should be quickly provided. Arterial pressure should be monitored carefully upon induction, avoiding a drastic reduction, and allowing for a reduction in arterial pressure upon recanalization. Keeping these factors in mind, anaesthetic technique (general, monitored anaesthesia care, or local) must be selected considering the individual patient's risks and benefits. Unfortunately, there are no proven neuroprotective strategies to date for use in acute ischaemic stroke.

Introduction

Acute stroke is the second leading cause of death worldwide and the leading cause of long-term disability.\textsuperscript{[1]} Ischaemic stroke is responsible for 87% of strokes.\textsuperscript{[2]} In acute ischaemic strokes, an embolus, thrombus, or stenosis can decrease brain perfusion. The goal of early therapy for acute ischaemic stroke is to restore perfusion. I.V. thrombolysis with recombinant tissue plasminogen activator (rtPA) is the only proven medical therapy shown to improve patient outcomes in acute ischaemic stroke, with better outcomes achieved with earlier administration.\textsuperscript{[3,4]} Patients who present within 4.5 h of stroke symptom onset and have no contraindications to therapy should be treated with i.v. rtPA.\textsuperscript{[5]} However, only 3–8.5% of all stroke patients are treated with i.v. rtPA.\textsuperscript{[6]} In addition, treatment with i.v. rtPA is unsuccessful in achieving recanalization in over half of patients with large-artery occlusions.\textsuperscript{[7]} Patients who are not eligible for i.v. rtPA due to delayed time to presentation, contraindications to i.v. rtPA therapy (recent surgery or coagulopathy), or failed i.v. rtPA can be considered for endovascular therapy. Although recent data from randomized clinical trials suggest that endovascular therapy was not superior to i.v. rtPA,\textsuperscript{[8,9]} studies show intraarterial thrombolysis or mechanical clot-removing devices to be efficacious for recanalization and restoration of cerebral blood flow.\textsuperscript{[10–12]}

This article reviews the current body of literature on the anaesthetic management of the acute ischaemic stroke patient, with a focus on the recent literature comparing outcomes after endovascular therapy performed with general compared with local anaesthesia, the importance of avoiding a time delay in treatment, the recent literature involving haemodynamic management of the acute stroke patient, and potentially neuroprotective strategies.

Anaesthetic Technique and Outcomes

There has recently been an increased interest in evaluating the relationship between type of anaesthesia a patient receives during endovascular therapy for stroke and outcomes. General anaesthesia can offer the benefits of immobility, pain control, and airway protection. The major disadvantages of general anaesthesia include haemodynamic changes with intubation, the possibility of delaying time to recanalization, pulmonary aspiration, and the requirement for additional workforce. Local anaesthesia or sedation (including monitored anaesthesia care) can maintain smoother haemodynamics due to the decreased administration of pharmacological vasodilators, and allow intra-procedural clinical neurological evaluation. But these approaches have the disadvantages of the lack of airway protection, continued patient movement, uncontrolled pain and agitation, and a prolonged procedure time. While the choice of anaesthetic technique can be individualized based on the needs of each patient, the anaesthesiologist
monitors and provides airway support to assure proper oxygenation, haemodynamic support to assure proper perfusion of the penumbra, and potentially immobility in the confused and agitated patient to provide better working conditions for revascularization.

Table 1. General anaesthesia or local anaesthesia forendovascular therapy after acute ischaemic stroke

<table>
<thead>
<tr>
<th>General anaesthesia</th>
<th>Local anaesthesia</th>
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<tr>
<td><strong>Pros</strong></td>
<td><strong>Pros</strong></td>
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<tr>
<td>Immobility</td>
<td>Smoother haemodynamics</td>
</tr>
<tr>
<td>Pain control</td>
<td>Intra-procedural neurological evaluation</td>
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<tr>
<td>Airway protection</td>
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<tr>
<td><strong>Cons</strong></td>
<td><strong>Cons</strong></td>
</tr>
<tr>
<td>Haemodynamic changes</td>
<td>Lack of airway protection</td>
</tr>
<tr>
<td>Additional workforce</td>
<td>Patient movement possible</td>
</tr>
<tr>
<td>Potential of time delay before start of procedure</td>
<td>Uncontrolled pain and agitation</td>
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</table>

In 2010, three studies\textsuperscript{[13–15]} and multiple editorials\textsuperscript{[16–18]} were published, evaluating outcomes and anaesthetic technique. Jumaa and colleagues performed a retrospective, single-centre study of 126 patients undergoing endovascular procedures for acute ischaemic stroke. They reported that intubated patients had longer intensive care unit stays, increased in-hospital mortality, worse clinical outcome, and larger final infarct volume size. However, the clinical conditions of the intubated patients differed from those not intubated before endovascular therapy in having significantly higher baseline National Institutes of Health Stroke Scale (NIHSS) scores.\textsuperscript{[13]} Nichols and colleagues reviewed the anaesthetic management of 75 patients in the Interventional Management of Stroke (IMS) II trial with anterior circulation stroke who underwent angiography with or without intra-arterial treatment. They categorized the anaesthetic management into four levels (no sedation, mild sedation, heavy sedation, and pharmacological paralysis). They found that the group of patients who received no sedation had relatively good outcome (modified Rankin score of 0–2), lower death rates, and higher reperfusion rates. Patients who received more sedation also had higher baseline NIHSS scores.\textsuperscript{[14]} Abou-Chebi and colleagues performed a large (980 patients) retrospective multicentre (12 centres) study, which found that general anaesthesia during an endovascular procedure for anterior circulation ischaemic stroke was an independent predictor for poor outcome. Similarly, patients who received a general anaesthetic had higher baseline NIHSS scores and were more likely to have carotid terminus occlusions.\textsuperscript{[15]}

More recently, studies have included arterial pressure measurements in evaluating the relationship between general anaesthesia and poor outcomes after endovascular therapy for acute ischaemic stroke. Davis and colleagues performed a retrospective single-centre study of 96 patients undergoing endovascular therapy for acute ischaemic stroke and also found an association between general anaesthesia and poor outcomes (15% probability of good outcomes compared with 60% in the local anaesthesia group). Patients who underwent general anaesthesia had higher baseline NIHSS scores than those given local anaesthesia. However, the investigators also found an association of good outcomes with systolic arterial pressure (SAP) >140 mm Hg. There was a correlation between low arterial pressure (defined as the minimum pressure recorded) and general anaesthesia.\textsuperscript{[19]} Abou-Chebi and colleagues reviewed the North American SOLITAIRE Stent-Retriever Acute Stroke (NASA) Registry to compare the outcomes of patients receiving general anaesthesia with those receiving sedation.\textsuperscript{[20]} They included data from 281 patients from 18 sites that described anaesthesia type, and grouped patients into general anaesthesia (if they were intubated) or local anaesthesia (if they were not intubated, regardless of whether or not they received sedation). Patients who received general anaesthesia had higher baseline NIHSS score and lower baseline arterial pressures. In a multivariate analysis, hypertension, NIHSS score, unsuccessful revascularization, non-utilization of balloon guide
catheter, and general anaesthesia were associated with mortality. The relationship between general anaesthesia and worse outcomes persisted when they excluded patients who arrived intubated (and were intubated emergently) and those who had posterior circulation strokes.[20] More recently, Rai and colleagues published an abstract that showed that although general anaesthesia was associated with higher patient mortality, it was not an independent predictor of outcome when baseline NIHSS score, age, and recanalization were taken into account. In addition, the interval between arrival and groin puncture was higher in patients with general anaesthesia. They also found a higher difference in pre- and post-SAP was associated with a worse outcome in patients with general anaesthesia[21].

Table 2. Studies on general compared with regional anaesthesia for endovascular therapy for acute stroke. ICH, intracranial haemorrhage

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Anaesthetic management</th>
<th>Outcomes</th>
<th>Limitations</th>
</tr>
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<tbody>
<tr>
<td>Jumaa and colleagues[13]</td>
<td>Retrospective, single centre, 126 patients with acute ischaemic stroke</td>
<td>Intubated or not intubated</td>
<td>Intubated patients had longer ICU stays, increased in-hospital mortality, worse clinical outcome, larger final infarct size</td>
<td>Intubated patients had higher baseline NIHSS scores</td>
</tr>
<tr>
<td>Nichols and colleagues[14]</td>
<td>Retrospective, 75 patients enrolled in IMS II trial with anterior circulation stroke</td>
<td>No sedation, mild sedation, heavy sedation, pharmacological paralysis</td>
<td>Lower sedation was associated with good outcome (modified Rankin score of 0–2), lower mortality and higher successful reperfusion rates</td>
<td>Patients with more sedation had higher baseline NIHSS scores and had less successful angiography reperfusion rates</td>
</tr>
<tr>
<td>Abou-Chebl and colleagues[15]</td>
<td>Retrospective, multicentre, 980 patients</td>
<td>General anaesthesia or conscious sedation</td>
<td>Independent predictors of poor outcome and mortality: age, NIHSS, general anaesthesia, recanalization, ICH, carotid terminus occlusion. Predictors of poor outcome: no stent placed</td>
<td>Patients with general anaesthesia had higher baseline NIHSS scores and were more likely to have carotid terminus occlusions</td>
</tr>
<tr>
<td>Davis and colleagues[19]</td>
<td>Retrospective, single centre, 96 patients</td>
<td>General anaesthesia or local anaesthesia (local anaesthesia includes light sedation with midazolam and fentanyl, if needed, provided by the stroke neurologist)</td>
<td>Independent predictors for good outcomes are: local anaesthesia, low baseline stroke scores, and systolic pressure &gt;140 mm Hg. General anaesthesia is correlated with low arterial pressures</td>
<td>Patients with general anaesthesia had higher baseline NIHSS scores and Good outcomes were associated high higher arterial pressures</td>
</tr>
<tr>
<td>Abou-Chebl and colleagues[20]</td>
<td>Retrospective, multicentre (18 sites), 281 patients</td>
<td>General anaesthesia (intubated) or local anaesthesia (not intubated, but unknown if sedated)</td>
<td>Independent predictors of mortality: hypertension, NIHSS, unsuccessful revascularization, non-utilization of balloon guide catheter, and general anaesthesia</td>
<td>Patients who received general anaesthesia had higher baseline NIHSS and lower baseline arterial pressures</td>
</tr>
</tbody>
</table>
Unfortunately, to date, there are no randomized controlled clinical trials and no prospectively collected data specific to anaesthetic management of endovascular treatment of acute ischaemic stroke. Studies that have been published include patients who have different baseline characteristics. In addition, in most studies, the types of anaesthesia often are classified as 'general anaesthesia' or 'intubated' vs 'local anaesthesia' or 'not intubated'. This binary stratification excludes haemodynamic management, depth of sedation, and the presence of anaesthesiologist.

The topic and study results are important and more data are necessary: the induction of general anaesthesia in each individual patient has individual risks and benefits, and as Molina and Selim\textsuperscript{[16]} summarized can become a choice of general anaesthesia, 'sailing quietly in the darkness', or local anaesthesia, sailing 'fast under a daylight storm'.

The results of these studies and the differences between the groups that received general anaesthesia, sedation, or local anaesthesia suggest several hypotheses as to why patients who have general anaesthesia have worse outcomes. First, patients who have general anaesthesia in every study are 'sicker' at baseline by NIHSS scores. Even after correcting for this 'sicker' patient status, selection bias is inherent in any retrospective study. In addition, patients who received general anaesthesia had, in certain centres, longer time from arrival to groin puncture.\textsuperscript{[21]}

Finally, patients who received general anaesthesia had lower arterial pressures recorded, including baseline\textsuperscript{[20]} and lowest recorded,\textsuperscript{[19]} and had greater arterial pressure fluctuations.\textsuperscript{[21]}

**Time is Brain**

A survey of members of the Society for Vascular and Interventional Neurology (SVIN) found that interventional surgeons felt the most important limitation of general anaesthesia and the main reason for not preferring it for all cases was time delay.\textsuperscript{[22]} Time delay to therapy is indeed a major concern in therapy for the patient with acute ischaemic stroke. The target of therapy in acute ischaemic stroke is the ischaemic penumbra, which is the threatened but salvageable tissue surrounding the infarct core. The ischaemic penumbra is short-lived, lasting only for a few hours in human patients.\textsuperscript{[23]} The typical ischaemic stroke patient loses 1.9 million neurones for each minute they are untreated. Compared with the normal rate of neurone loss in brain ageing, the ischaemic brain ages 3.6 yr each hour without treatment.\textsuperscript{[24]} Recanalization of occluded arteries is a necessary, but not sufficient, condition for achieving good clinical outcomes with endovascular therapy. If the entire tissue at risk has already progressed to irreversible infarction, reperfusion will be futile, and can even cause harm by increasing the risk of haemorrhagic transformation.

Although induction of general anaesthesia and the involvement of an anaesthesia care team could conceivably delay endovascular treatment of acute ischaemic stroke, most studies show no difference in time from patient arrival to treatment for patients receiving general anaesthesia or local anaesthesia.\textsuperscript{[14,15,19,20]} A single institutional study did find a significantly longer arrival to groin puncture time in patients who received general anaesthesia.\textsuperscript{[21]} In contrast, interventional procedure time has been noted to be less for patients who receive general anaesthesia.\textsuperscript{[13]} Although this is true in reported studies, there can be substantial variability between institutions. It is critical to remember the race to save the penumbra and avoid delay of therapy.

**Haemodynamic Management**
More than 60% of patients who present with ischaemic stroke have elevated arterial pressures.\textsuperscript{[25,26]} The elevated systemic arterial pressures are due, in part, to baseline hypertension. In addition to baseline hypertension, there exists a superimposed early hypertensive response to brain ischaemia. Potential mechanisms behind this response include the Cushing response to a mass effect of oedema,\textsuperscript{[27]} autoregulation response in a hypertensive patient,\textsuperscript{[28]} and neuroendocrine response to physiological stress.\textsuperscript{[29]} Within the first 24 h after stroke, arterial pressure declines by about 25% in most patients.\textsuperscript{[30]} Presentation with high systemic arterial pressure at the time on ischaemic stroke is associated with poor outcome.\textsuperscript{[31]} In addition, presentation with low systemic arterial pressure at the time of ischaemic stroke is also associated with poor outcome. Data from the International Stroke Trial suggest that the relationship between arterial pressure at the time of acute ischaemic stroke and outcomes is a U-shaped curve, with both low arterial pressure and high arterial pressure increasing death and dependency, with the lowest risk of death or dependency at a systolic arterial pressure of 150 mm Hg.\textsuperscript{[32]}

Optimal management of the acute ischaemic stroke patient with hypertension is unclear. Lowering arterial pressure should reduce cerebral oedema and decrease probability of haemorrhagic transformation of the infarct. However, lowering arterial pressure might potentially decrease collateral flow in the penumbral area, especially in the setting of ischaemia and impaired autoregulation.\textsuperscript{[25]} Animal data show that hypertension induced upon cerebral artery occlusion improves local cerebral blood flow\textsuperscript{[33]} and decreases infarct volume.\textsuperscript{[34]} In an animal model of chronic hypertension, maintaining arterial pressure resulted in animals with increased regional blood flow, decreased oedema, decreased stroke volume, and improved neurological scores.\textsuperscript{[35]} In humans, arterial pressure elevation during carotid occlusion during a carotid endarterectomy has been shown to improve postoperative cognitive function.\textsuperscript{[36]} A Cochrane meta-analysis through 2008 identified 12 randomized trials that included 1153 patients with stroke, and concluded there was insufficient evidence to evaluate the effect of altering arterial pressure on patient outcomes.\textsuperscript{[37]}

Three large, prospective trials focused on arterial pressure management in the time interval after stroke. The COSSACS trial randomized 763 patients who presented within 48 h of stroke (only 5% haemorrhagic) to either continue their chronic pre-stroke antihypertensive therapy or to temporarily discontinue antihypertensive medications for the first 2 weeks after stroke. There was no difference at 2 weeks in the rate of death or dependency. The study was stopped before target recruitment due to slow recruitment and lack of funding, and therefore the study was potentially underpowered.\textsuperscript{[38]} The SCAST trial randomized 2029 patients within 30 h of stroke (\textless{}85% ischaemic, 15% haemorrhagic) and a SAP >140 mm Hg to receive an angiotensin receptor blocker (ARB) or placebo for 7 days. Additional antihypertensive medications were received by more than one-quarter of enrolled patients. The study showed that there was no indication that ARB therapy was beneficial to the endpoints death, myocardial infarction, or recurrent stroke at a 6 month time point. In fact, there was a higher risk of poor functional outcome in patients who received an ARB.\textsuperscript{[39]} The CATIS trial randomized 4071 patients who presented within 48 h of ischaemic stroke and had elevated SAP. Two thousand and thirty-eight patients assigned to the intervention group received antihypertensive therapy to decrease SAP by 10–25% within the first 24 h after randomization, and achieved arterial pressure <140/90 mm Hg within 7 days, maintaining this during hospitalization. Two thousand and thirty-three were assigned to the control group that had all antihypertensive medication discontinued. Patients who received thrombolysis were excluded. There was no significant difference in death or major disability at 14 days or discharge, or in composite death and major disability at 3 months post-treatment. Subgroup analysis showed that time to treatment did affect the primary outcome, with patients who were enrolled more than 24 h after stroke having significantly better outcomes in the treatment arm. These data favour the use of lowering arterial pressure after 24 h, when the impact of arterial pressure on the penumbra is decreased. Limitations of the study include an open-label intervention that can introduce rater bias, exclusion of cervicocerebral disease, an ethnically Chinese population, and a median time to randomization of 15 h.\textsuperscript{[40]}

Recently, the Efficacy of Nitric Oxide trial (ENOS) finished recruitment of 4011 patients with a new onset motor deficit, SAP between 140 and 220 mm Hg, and presenting within 48 h of onset of symptoms. Patients were randomized to treatment with transdermal glyceryl trinitrate (GTN) (5 mg for 1 h daily) for 7 days or no GTN. Patients with a history of prior antihypertensive treatment were randomized independently into continuing their treatment or stopping it. The primary outcome measure was combined death and dependency. Secondary outcome measures
were arterial pressure over 7 days of treatment, death/impairment, recurrence, quality of life, and cognition. Results were presented at the 23rd European Stroke Conference. There was no significant change in primary outcome for patients who continued or stopped their antihypertensive medication. However, some secondary outcomes were better in patients who stopped taking their antihypertensive medication for the week after the stroke. In addition, there appeared to be a benefit in patients who were treated with GTN in the very early (<6 h) time frame.\cite{41,42}

The ENCHANTED trial is an ongoing interventional, international, randomized trial started in 2012 designed to enrol 3300 patients presenting with acute ischaemic stroke confirmed by imaging within 4.5 h of onset of symptoms, and with SAP<185 mm Hg. Patients will be randomized to two arms: a low dose (0.6 mg kg\textsuperscript{-1}) rtPA compared with standard dose (0.9 mg kg\textsuperscript{-1}) rtPA arm, and an intensive (target systolic pressure 140–150 mm Hg) lowering compared with standard guideline (target systolic pressure 180 mm Hg) arterial pressure management arm. The primary outcome will be measured in terms of combined death and disability 90 days after discharge. The secondary outcome measures will be occurrence of secondary intra-cerebral haemorrhage within 36 h of administration of rtPA, death and disability as separate measures at the end of 90 days, neurological deterioration, quality of life, and admission to residential care\cite{43}.

Table 3. Haemodynamic management trials in acute stroke

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leonardi-Bee and colleagues\textsuperscript{32}</td>
<td>17 398 patients from the international stroke trial with ischaemic stroke</td>
<td>Analysis of data from patients in the randomized international stroke trial designed to evaluate aspirin and heparin use in acute stroke</td>
<td>A U-shaped relationship was found between baseline arterial pressure and both early death and late death or dependency: both high arterial pressure and low arterial pressure were independent prognostic factors for poor outcome</td>
</tr>
<tr>
<td>COSSACS Robinson and colleagues\textsuperscript{38}</td>
<td>763 patients within 48 h of stroke</td>
<td>Randomized to: Continue pre-stroke antihypertensive medications for 2 weeks; Stop pre-stroke antihypertensive medications for 2 weeks</td>
<td>Primary outcome: no difference at 2 weeks in rate of death or dependency. Study stopped early due to slow recruitment and lack of funding</td>
</tr>
<tr>
<td>SCAST Sandset and colleagues\textsuperscript{39}</td>
<td>2029 patients within 30 h of stroke with systolic arterial pressure &gt;140 mm Hg</td>
<td>Randomized to: Receive ARB for 7 days; Receive placebo for 7 days</td>
<td>Primary outcome: ARB therapy not beneficial to composite vascular endpoint; Secondary outcome: Higher risk of poor functional outcome in patients who received ARB</td>
</tr>
<tr>
<td>CATIS He and colleagues\textsuperscript{40}</td>
<td>4071 patients within 48 h of ischaemic stroke and had elevated systolic arterial pressure</td>
<td>Randomized to: Decrease arterial pressure by 10–25% within 24 h, achieve arterial pressure &lt;140/90 within 7 days, and maintaining it during</td>
<td>Primary outcome: no significant difference in death and major disability at 14 days or discharge, or in composite death and major disability at 3 months post-treatment; Subgroup analysis: time to treatment did affect the primary outcome, with patients who were enrolled more than 24 h after stroke having significantly better</td>
</tr>
<tr>
<td>ENOS (recently completed)</td>
<td>Hospitalization Discontinue antihypertensives</td>
<td>outcomes in the treatment arm</td>
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<tr>
<td>4011 patients with a new onset motor deficit, systolic arterial pressure between 140 and 220 mm Hg and presenting within 48 h of onset of symptoms</td>
<td>Randomized to: Treatment with transdermal GTN for 7 days No GTN Patients with a history of prior antihypertensive treatment were randomized independently into continuing their treatment or stopping it</td>
<td>Primary outcome: death and dependency: no significant change for patients who continued vs stopped their antihypertensive medication. Secondary outcomes: arterial pressure over 7 days of treatment, death/impairment, recurrence, quality of life, and cognition better in patients who stopped taking their antihypertensive medication for the week of the stroke Subgroup analysis: potential benefit in patients who were treated with GTN in the very early (&lt;6 h) time frame</td>
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</table>

| ENCHANTED (ongoing) | Patients will be randomized in two arms: Low dose (0.6 mg kg⁻¹) rtPA arm Standard dose (0.9 mg kg⁻¹) rtPA arm Intensive (target systolic arterial pressure 140–150 mm Hg) lowering arm Standard guideline (target systolic arterial pressure 180 mm Hg) management arm | Primary outcome: death and disability 90 days after discharge. Secondary outcome: secondary intra-cerebral haemorrhage within 36 h of administration of rtPA, death and disability as separate measures at the end of 90 days, neurological deterioration, quality of life, and admission to residential care |

The question of how arterial pressure should be managed in early ischaemic stroke, especially when there is still substantial penumbra, tissue at-risk remains unanswered by the current body of literature. A potential strategy for management supported by current literature is to avoid lowering arterial pressure dramatically during the first 12 h after stroke onset, when collateral circulation compromise is still a concern. This time period likely includes the period in which an endovascular procedure might be attempted. The Society for Neuroscience in Anesthesia and Critical Care (SNACC) has recommended that systolic arterial pressure should be maintained >140 mm Hg (fluids and vasopressors) and <180 mm Hg (with or without i.v. rtPA), and diastolic arterial pressure <105 mm Hg (class IIA, level of evidence B). After successful recanalization, arterial pressure targets should be adjusted to avoid potential haemorrhagic conversion.⁴⁴

**Future Directions: Neuroprotective Strategies**

A considerable amount of research has been invested into the development of potential neuroprotective agents: ideally one that would be administered in the field immediately after stroke to get maximum penetration into ischaemic tissue and the penumbra. Multiple neuroprotective treatments have been identified that show great promise
in animal models of stroke. Unfortunately, nearly all have failed to provide protection in human trials. In a study of 178 acute stroke trials performed in the 20th century, 49 involved promising neuroprotective agents that emerged from preclinical stroke studies and entered human testing. One hundred and fourteen clinical trials were performed with more than 21 000 patients. Every agent tested failed.[45]

Anaesthetic agents, including thiopental, isoflurane, sevoflurane, and xenon, have also been investigated for their neuroprotective effects.[46] While animal data[47,48] and human data for cardiopulmonary bypass[49] have shown promise, and studies are ongoing to evaluate the possibility of neuroprotection,[50] there is no human evidence for the neuroprotective effects of anaesthesia in focal ischaemia.[46]

Magnesium has shown promise for neuroprotection during carotid endarterectomy[51] and cardiac bypass surgery.[52] The potential use of magnesium in acute stroke is being investigated in the recently completed FAST-MAG Phase 3 trial. The goal of the trial was to enrol patients at an early time period to administer magnesium while it could have an effect on the penumbra. Patients were enrolled in the field within 2 h of onset of symptoms, received a 4 g bolus of magnesium sulphate i.v. over 15 min, followed by a 16 g maintenance infusion in hospital over 24 h.[53]

Hypothermia has been shown to be neuroprotective in experimental and focal hypoxic brain injury models.[54] Hypothermia decreases cerebral metabolism, suppresses glutamate release, reduces neuroinflammatory response, disrupts apoptotic pathways, reduces free radical generation, and minimizes oedema formation.[55] Mild to moderate hypothermia is associated with improved neurological outcome among patients with cardiac arrest, which resulted in hypothermia becoming the first neuroprotective strategy to be recommended by the American Heart Association in comatose patients after cardiac arrest.[56,57] In addition, hypothermia has been shown to reduce mortality without increasing major disability in term and late preterm newborns with hypoxic–ischaemic encephalopathy. In 2010, the International Liaison Committee on Resuscitation recommended therapeutic hypothermia be offered to term or near-term infants with moderate to severe encephalopathy.[58,59] However, in the investigation of mild hypothermia in the setting of potential focal ischaemia, the IHAST trial, a multicentre clinical trial, found that mild hypothermia administered during surgery for treatment of a ruptured intracranial aneurysm did not improve outcome after neurosurgical aneurysm clipping.[60]

Pilot clinical trials to date have been designed to establish the safety and feasibility of various cooling techniques in stroke patients. No study has had sufficient sample size to provide results.[61,62] Two ongoing clinical trials are assessing the efficacy of therapeutic hypothermia in acute ischaemic stroke. The Intravascular Cooling in the Treatment of Stroke (iCTuS) 2/3 study was designed to compare the safety and clinical benefit of endovascular hypothermia and thrombolysis compared with thrombolysis alone. The projected enrolment is 1600 patients in multiple centres presenting within 3 h of stroke who are eligible to receive tPA.[63] The EuroHYP-1 trial is targeted to enrol 1500 patients presenting within 6 h of stroke symptoms and will randomize them to hypothermia and best medical treatment or best medical treatment alone.[64]

Without conclusive evidence that hypothermia is beneficial in acute ischaemic stroke in adults, current recommendations are to maintain normothermia and to treat patients with antipyretics if febrile.[44]

Conclusions

In a patient with acute ischaemic stroke, time is of the essence to save the vulnerable penumbra. With the current evidence, the decision between general anaesthesia, monitored anaesthesia care, or local anaesthesia for endovascular procedures should be made with the individual risks and benefits of each patient considered. Arterial pressure should be monitored carefully upon induction of anaesthesia and induction should be expedient to allow for timely endovascular intervention if possible. Target arterial pressures should be systolic readings of 140–180 mm Hg with a reduction in pressure upon recanalization. Unfortunately, there are no proven neuroprotective strategies to date for ischaemic stroke.
Sidebar

Editor's Key Points

- Anaesthetic management for endovascular treatment of acute ischaemic stroke has been shown to affect outcome.

- General anaesthesia can result in worse outcomes compared to local anaesthesia, although technique must be tailored to patient-specific variables.

- Time to reperfusion and arterial pressure are critical in maximizing survival of the ischaemic penumbra.

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