How Do I Manage Cerebral Vasospasm and Delayed Cerebral Ischemia?

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Abstract

Delayed cerebral ischemia (DCI) is the leading cause of mortality and disability in patients who survived the initial bleed of subarachnoid hemorrhage. Currently available guidelines are based on expert opinions derived from small observational studies due to the lack of randomized controlled trials. In this review, we will review some of the available literature and describe our local protocols for prophylaxis, risk stratification, monitoring in patients at risk, including multimodal invasive monitoring, and interventions measures in patients with DCI. These protocols are largely in line with the current guidelines but are deemed to evolve as ongoing and future trials provide stronger evidence to support interventions.
Introduction

Delayed cerebral ischemia (DCI) is the leading cause of mortality and disability in patients who survived the initial bleed of subarachnoid hemorrhage (SAH).\(^1\) It occurs in approximately 30% of patients. Therefore, one of the main goals of critical care of patients with SAH is to prevent DCI. Cerebral vasospasm, the narrowing of intracranial arteries that occurs in up to 70% patients after SAH, used to be considered the main cause of neurological deterioration and long-term deficits, but animal and human studies have challenged this view in the recent past.\(^2\) As DCI can occur independently from vasospasm, the two concepts should not be considered synonymous anymore. This view is emphasized in the consensus definitions and operational criteria that have been recently proposed (Table 1)\(^3\), primarily to homogenize clinical research but which can be used in clinical practice as well. These definitions show excellent inter-rater reproducibility.\(^4\)

Management of DCI entails the identification of patients at higher risk of DCI, prophylactic measures, close monitoring to detect early signs of DCI and prompt intervention to prevent impeding ischemia to cause irreversible infarction, brain injury and long-term disability.\(^5\)

Pathophysiology

A comprehensive review of the mechanisms leading to vasospasm and DCI is beyond the scope of this article, and has been reviewed in depth recently.\(^2\) But some knowledge of the pathophysiology is useful to understand how to manage these complications. Delayed ischemia can occur prior to, remotely from, or in the absence of visible vasoconstriction, clearly challenging the simplistic view that the narrowing of the large intracranial arteries is the sole cause of decreased perfusion and indicating.\(^6\) Further, interventions aiming at reducing vasoconstriction, either mechanically or pharmacologically, do not necessarily protect against DCI and unfavorable outcome.\(^2\) On the other hand, systemic nimodipine, the only Class I, Level of Evidence A prophylactic agent recommended by the American Heart Association/American Stroke Association improves outcome, decreases the risk of DCI but has no measurable effect on vasospasm.\(^7\) Animal and human studies over the last decade have clearly demonstrated that other events also contribute to ischemia.\(^2\) These include early vascular dysfunction and loss of neurovascular coupling at the arterial level and vasoconstriction of the microvasculature, endothelial injury and platelet activation at the arteriolar and capillary levels leading to a hypercoagulable state. More recently, intracranial
EEG recording with electrocorticography (ECOG) have revealed the occurrence of cortical spreading depolarizations and depressions (CSD) in up to 84% of patients with SAH. Normally, as observed in migraine, these waves of massive neuronal depolarization trigger a strong positive hemodynamic response, to ensure adequate blood flow and metabolic supply in support of the highly energy-dependent repolarization process. In SAH, however, CSD induce biphasic or even negative responses, leading to hypoperfusion and subsequent ischemia. Known triggers of vascular dysfunction, vasospasm and CSD include hemoglobin and byproducts of its degradation, potassium, and endothelin-1 (ET-1).

**Risk factors**

Predisposing risk factors for DCI include smoking, diabetes, younger age, and genetic polymorphisms in various genes. The strongest determinant of the risk of DCI is the severity of the initial hemorrhage. Poor neurological status upon initial resuscitation and large amount of blood in the subarachnoid space and ventricles are the main independent risk factors for DCI. The presence of substantial alteration of consciousness (lethargy or worse; and corresponding to Glasgow Coma Scale [GCS] score <12, Hunt-Hess grade III-V or World Federation of Neurosurgical Societies [WFNS] grade 4-5) is associated with greater odds of DCI. Similarly, several radiological scales exist to predict the risk of vasospasm or DCI. These scales are useful to identify patients at higher risk of DCI and who should receive closer monitoring. Alteration of consciousness also limits the usefulness of the clinical examination and should prompt clinicians to recourse to other monitoring tools, including invasive multimodality invasive monitoring (MIIM). We use the WFNS and the modified Fisher scale to tailor the level of monitoring according to their predicted risk of DCI (Table 2).

**Prophylactic measures**

Briefly, we follow the general measures recommended or suggested to prevent secondary brain injury in SAH (Table 3), including IV nimodipine, anti-seizure prophylaxis and control of systemic factors, as well as of intracranial pressure. We think that other prophylactic measures, including statins, endothelin receptor antagonists, magnesium sulfate, cilostazol, currently have no achieved a sufficient level of evidence to be included in our practice.
**Monitoring for DCI**

The first step in DCI management is to monitor the patient for early changes suggestive of DCI. Monitoring can be achieved with a variety of modalities and should be in essence multimodal, given the multifaceted process underlying DCI.\(^5\)\(^12\)

**Clinical examination**

Clinical features of DCI mostly consist of new focal neurological deficits or a decrease in the level of consciousness. Deficits typically have a gradual and fluctuating onset over several hours or days. Bedside neurological examination should thus be performed several times daily. In conscious patients, it should include testing for both global cerebral dysfunction (encephalopathy)\(^13\) and focal signs, such as weakness (including facial palsy), gaze deviation, sensory loss, visual field defect, tactile or visual neglect, apraxia, asymmetry in tonus or reflexes, and frontal release signs. In unconscious patients, the examination should be tailored to quantify the degree of alteration of consciousness, using a suitable scale\(^14\), and to uncover changes or asymmetry in tonus or reflexes, spontaneous gaze deviation, and asymmetry in facial grimace and motor response upon noxious stimulation. The neurological examination becomes less informative as coma deepens or if sedation increases and is useless once the patient requires neuromuscular blockade. In addition to the neurological examination, general signs are associated with DCI, including the systemic inflammatory response and hyponatremia.\(^9\)

**Transcranial Doppler ultrasonography**

Transcranial Doppler (TCD) is non-invasive and can be performed at the bedside.\(^15\) However, it assesses large proximal intracranial arteries and does not inform on the distal microvasculature. Further, it provides only an indirect estimate of the caliber of intracranial vessels through measurement of blood flow velocity (FV). The presence of vasoconstriction is thus inferred from increased FV, provided blood flow remains constant. Systemic factors, such as PaCO\(_2\), blood viscosity, red blood cell count, and cardiac output, and changes in intracranial pressure (ICP) may alter FV and interfere with the assessment of vasospasm. The Lindegaard ratio, defined as the ratio between FV in the middle cerebral artery (MCA) and the mean FV in the distal extracranial internal carotid artery, is thought to be less sensitive to systemic hemodynamic factors. Ideally, TCD studies for vasospasm should include the
measure of FV, pulsatility index (defined as \([\text{systolic FV-diaastolic FV}/\text{mean FV}]\)) for all major intracranial arteries (middle, anterior posterior cerebral, and basilar arteries) and the Lindegaard ratio. Suggested cut-off values are presented in Table 4. It should also be kept in mind that the diagnostic accuracy has been validated against angiographic evidence of vasospasm, and that there is little evidence for DCI detection. A recent meta-analysis reviewed the evidence for TCD as a tool to predict vasospasm or DCI showed good accuracy, with a sensitivity of 98% and a specificity of 70%, which were likely overestimated as the study did not distinguish between both types of event.\(^\text{16}\) When reported, the sensitivity of TCD changes for DCI is usually lower, in the order of 50 to 60%.\(^\text{17}\) It is also important to remember that TCD are not feasible in up to 20% of patients, for a variety of reasons, mostly a lack of an adequate bone window for insonation. The diagnostic accuracy in other arteries than the MCA has not been thoroughly studied. Nevertheless, TCD is still recommended\(^\text{5,12}\), and we use it, mostly to monitor the time course of vasospasm.

**Continuous EEG monitoring**

The electroencephalography (EEG) signal is the closest available measure of brain function and is very sensitive to ischemia.\(^\text{18}\) Continuous EEG monitoring (CEEG) with the assistance of quantitative EEG can identify changes suggestive of impeding ischemia (see Table 4) before irreversible infarction occurs. Several small studies in SAH suggested it can be successfully applied to early DCI detection with good sensitivity and specificity, both in comatose and awake patients.\(^\text{19}\) These preliminary findings have been recently confirmed by a large prospective study in 103 patients with poor grade SAH, of which 52 developed DCI. The sensitivity and specificity of CEEG were 96% and 81%, respectively, outperforming TCD studies.\(^\text{20}\) Importantly, EEG changes suggestive of ischemia occurred a median of 2 days before the diagnosis of DCI. To which extent usual EEG confounders, such as sedation might limit the diagnostic accuracy of CEEG has not been studied, although EEG monitoring is successfully used for ischemia monitoring in sedated patients undergoing carotid surgery. Its use in SAH is suggested.\(^\text{12}\) Recently, intracortical EEG (ICE) with a depth electrode has been included in the bundle of multimodality monitoring and might provide additional clinically useful information (see below: invasive multimodality monitoring).\(^\text{21}\)

**Brain CT with angiography and perfusion imaging**
Brain computed tomography (CT) scan without iodine contrast is of little use for DCI management as it is mostly able to identify the presence of infarction once it has occurred. More useful are CT angiography and perfusion CT based on iodine contrast enhancement.\textsuperscript{22} CT angiography assesses the caliber of large intracranial arteries and can detect the presence of vasospasm. It compares favorably to conventional digital subtraction angiography. Perfusion CT imaging allows the non-invasive study of whole-brain cerebral perfusion by providing maps of cerebral blood flow (CBF), cerebral blood volume (CBV) and various time parameters, such as the mean transit time (MTT) or time to maximal perfusion (Tmax) of the contrast agent. A mismatch between prolonged MTT/prolonged Tmax/low CBF and normal CBV indicates the presence of penumbra, which in the setting of SAH suggests DCI without irreversible infarction. Early perfusion defects and edema, suggesting early brain injury, are associated with a higher risk of DCI.\textsuperscript{23,24} Perfusion imaging requires technical expertise and may be confounded by blood-brain-barrier dysfunction, the presence of focal or diffuse brain injury or the presence of systemic hemodynamic issues. Risks of CT imaging include allergic reactions, renal toxicity and exposure to radiation. It requires the patient to be transported to the CT suite and thus cannot be performed frequently. We typically perform CT with angiography and perfusion imaging on day 1 after admission to obtain baseline angiographic images and perfusion maps for later comparison.

\textit{Other non-invasive monitoring tools}

Near-infrared spectroscopy (NIRS) evaluates the ratio of oxygenated to total hemoglobin, represented by the tissue oxygen saturation (StO\textsubscript{2}), which reflects oxygenation of the cortical tissue and informs on microvascular perfusion.\textsuperscript{15} Commercial devices use frontally-applied probes, hence they only assess frontal cortical regions. Studies in patients with SAH have shown a significant, albeit only partial, association between low StO\textsubscript{2} values and DCI. Limitations include the limited spatial sampling, lack of normal values for the absolute StO\textsubscript{2} (hence only changes from baseline are meaningful), contamination by ambient light.

\textit{Multimodal Invasive monitoring}

Both the European Society of Intensive Care Medicine and the Neurocritical Care Society strongly recommend the use of invasive monitoring of intracranial pressure (ICP), partial brain tissue oxygen (Pb\textsubscript{t}O\textsubscript{2}), and interstitial fluid microdialysis in patients with acute brain
injury at risk of ischemia, including patients with SAH.\textsuperscript{12} Recommendation for CBF monitoring is weaker. Monitoring probes are inserted through a multiple lumen bolt placed in a single burr-hole through the skull. The probes are located in the right frontal lobe, unless the ruptured aneurysm is on the left MCA, in which case it is placed in the left frontal lobe. More specifically, we place the probes in the watershed territory between the MCA and anterior cerebral artery territory. Intracortical EEG (ICE) recordings can be performed with a depth electrode inserted through the same multiple lumen bolt used for the other monitoring probes. Compared to scalp EEG, ICE offers a better signal-to-noise ratio and is more sensitive both for electrographic seizures detection and ischemia detection.\textsuperscript{21,25} It also allows the identification of cortical spreading depressions, albeit with a lower sensitivity than ECOG.

**Implementation of DCI monitoring**

At our institution, monitoring is divided in three levels, depending on the patient’s neurological and risk status (\textbf{Table 2}). Low-risk, awake and oriented patients (mFS 0-2 and WFNS I) can be followed by iterative clinical examination, non-invasive hemodynamic monitoring and daily transcranial Doppler (TCD) studies. Intermediate-risk, drowsy or confused patients (mFS 3-4 and WFNS 1; or WFNS II-III) also receive continuous EEG monitoring. High-risk, stuporous or comatose patients (mFS 3-4 and WFNS IV-V) also receive invasive hemodynamic monitoring. An external ventricular drain is placed in case of hydrocephalus and in Hunt-Hess 5 patients. Multimodal invasive monitoring (MIM) is considered and usually placed in comatose patients, deeply sedated patients, or patients who remain lethargic despite resolution of hydrocephalus with the EVD.

**Diagnosis and management of DCI**

No randomized controlled trial of the management of DCI has been performed and available evidence comes solely from small uncontrolled case series. Systematic reviews and meta-analyses are also available.\textsuperscript{26-29} Interventions include both systemic\textsuperscript{27} and local\textsuperscript{26,28,29} endovascular treatments aiming at improving cerebral perfusion and oxygen delivery. Our algorithm is detailed in \textbf{Figures 1 and 2}. The occurrence of DCI is suspected if pre-defined clinical, EEG or MIM thresholds are met (see \textbf{Table 4}). Upon suspicion of DCI, patients first receive vasopressors to increase MAP and CPP (\textbf{Figure 1}). Norepinephrine is started and
progressively increased to raise MAP by 10 mmHg steps until resolution of DCI or a threshold of 130 mmHg is reached. Nimodipine might be discontinued if it prevents reaching MAP target values. In case the maximal MAP threshold is reached and DCI has not resolved, we perform CT imaging with angiography and perfusion imaging. If DCI is confirmed by perfusion imaging, further treatment is administered, depending on the presence and location of vasospasm and hypoperfusion. Second-tier interventions are detailed in Figure 2. Arterial narrowing is treated by intra-arterial infusion (IA) of vasodilators, including in multiple arteries if required. Recent observational studies indicate that early and repeated endovascular treatment might be associated with better outcome. Several drugs can be used, including calcium channel blockers (nimodipine, nicardipine or verapamil) and phosphodiesterase inhibitors (milrinone, or papaverine), but none has been investigated in a controlled trial. We use nimodipine. If IA nimodipine fails to provide sustained improvement, it can be repeated or third-tier interventions can be used. In case of focal proximal arterial narrowing, we favor combine balloon angioplasty and IA nimdipine. If not successful, we resort to the placement of a catheter in the internal carotid artery for continuous IA infusion of vasodilators (usually nimodipine). An alternate strategy, which has been recently described, is the use of retrievable stents. Continuous intra-arterial (CIA) nimodipine infusion can also be offered in case of focal distal arterial narrowing that is not accessible to balloon angioplasty, or in case of diffuse arterial narrowing. Diffuse vasospasm refractory to CIA nimodipine or DCI in the absence of vasospasm are treated with systemic interventions. The first step is to increase cardiac output with CIV dobutamine, after optimization of volemia. Emerging rescue interventions in case of persisting DCI include CIV milrinone, levosimendan, stellate ganglion block, general anesthesia, inhaled NO, IT nicardipine and are selected on an individual basis and after multidisciplinary discussion.

**Conclusions**

The mechanisms of vasospasm and DCI after subarachnoid hemorrhage are still poorly understood. Due to the scarcity of good quality data from well-designed trials, currently available guidelines are based on expert opinions derived from small observational studies. Our local protocols are largely in line with these recommendations. We focus on risk stratification to perform appropriate monitoring in patients at risk, including MIM in those with alteration of consciousness. We take general prophylactic and homeostatic measures...
aiming at controlling systemic and local factors that can cause or aggravate brain injury. Impeding DCI is initially treated by increasing MAP and CPP with vasopressors. Second-tier therapeutic options for refractory DCI are chosen based on the presence, location and extent of vasospasm and spans various complementary therapies, from focal IA nimodipine infusion and balloon angioplasty to systemic interventions with dobutamine. Further rescue therapies, including continuous IA infusion through in situ carotid catheters and continuous IV milrinone can be used on an individual basis after multidisciplinary discussion. This approach is deemed to evolve as ongoing and future trials provide stronger evidence to support interventions.

**Key messages**

- Delayed cerebral ischemia (DCI) occurs in 30% of patients with subarachnoid hemorrhage and is the leading cause of mortality and disability in patients who survived the initial bleed. Cerebral vasospasm is often associated with DCI, but they are distinct phenomenon and should not be confused.

- The management of DCI begins by closely monitoring the patient for early signs of ischemia, using a standardized multimodal approach including non-invasive (clinical examination, continuous electroencephalography [EEG], transcranial Doppler) and invasive (brain tissue oxygenation, microdialysis and intracortical EEG) methods, according to patients’ individual clinical status.

- Once suspected on the basis of pre-defined thresholds for each monitoring modality, DCI should be confirmed by perfusion computed tomography imaging.

- Several systemic and local therapeutic options to reverse DCI are available, although none has been validated in a randomized controlled trial. These interventions should be proposed following a standardized algorithm, taking into account the severity and extent of DCI On perfusion imaging and the presence and extent of vasospasm.
Figure legends

**Figure 1. First-tier interventions for delayed cerebral ischemia (DCI).** Abbreviations: BP = blood pressure; CO = cardiac output; PA = pulmonary artery; MAP = mean arterial pressure; CT = computed tomography; MIM = multimodality invasive monitoring.

**Figure 2. Second and third-tier interventions for refractory delayed cerebral ischemia (DCI).** Abbreviations: CIA = continuous intraarterial infusion; CIV = continuous intravenous infusion; NO = nitric oxide; IT = intrathecal.
Table 1. Definitions and operational criteria for delayed cerebral ischemia (DCI) and cerebral vasospasm.

<table>
<thead>
<tr>
<th>Definition</th>
<th>Delayed cerebral ischemia (DCI)</th>
<th>Cerebral vasospasm</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition</strong></td>
<td>Occurrence of focal neurological deficits (such as hemiparesis, aphasia, apraxia, hemianopia, or neglect), or a decrease of at least 2 points on the GCS (either on the total score or on one of its individual components). This should last for at least 1 hour, is not apparent immediately after aneurysm occlusion, and cannot be attributed to other causes by means of clinical assessment, CT or MR scanning of the brain, and appropriate laboratory studies.”</td>
<td>Presence of arterial narrowing demonstrated by a radiological test (either CT angiography, MR angiography, or digital subtraction angiography),</td>
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<tr>
<td><strong>Delayed ischemic neurological deterioration (DIND)</strong></td>
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<tr>
<td><strong>Delayed infarction</strong></td>
<td>Presence of cerebral infarction on CT or MR scan of the brain within 6 weeks after SAH, or on the latest CT or MR scan made before death within 6 weeks, or proven at autopsy, not present on the CT or MR scan between 24 and 48 hours after early aneurysm occlusion, and not attributable to other causes such as surgical clipping or endovascular treatment.</td>
<td></td>
</tr>
<tr>
<td>Notes</td>
<td>Hypodensities on CT imaging resulting from ventricular catheter or intraparenchymal hematoma should not be regarded as cerebral infarctions from DCI.</td>
<td>Not to be applied to clinical manifestations of DCI. Not to be used as a surrogate outcome measure. Not to be defined by transcranial Doppler</td>
</tr>
</tbody>
</table>

Abbreviations: GCS = Glasgow Coma Scale; CT = computed tomography; MR = magnetic resonance.
Table 2. Stratification of risk of delayed cerebral ischemia (DCI), based on clinical and radiological factors, and of intensity and invasiveness of monitoring.

<table>
<thead>
<tr>
<th>Low risk</th>
<th>Intermediate risk</th>
<th>High risk</th>
<th>Very high risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCS 15 (WFNS I) and mFS 1-2</td>
<td>GCS 15 (WFNS I) and mFS 3-4 OR GCS 13-14 (WFNS II-III)</td>
<td>GCS 9-12 (WFNS IV$^\text{5}$) and not intubated</td>
<td>GCS &lt;9 (WFNS V$^\text{5}$) OR Intubated</td>
</tr>
<tr>
<td>Neurological examination Non-invasive hemodynamic monitoring Transcranial Doppler</td>
<td>Neurological examination Non-invasive hemodynamic monitoring Transcranial Doppler CEEG</td>
<td>Neurological examination Invasive hemodynamic monitoring Transcranial Doppler CEEG</td>
<td>Neurological examination Invasive hemodynamic monitoring Transcranial Doppler CEEG EVD MIM</td>
</tr>
</tbody>
</table>

Abbreviations: GCS = Glasgow Coma Scale; WFNS = World Federation of Neurosurgical Societies; mFS = modified Fisher Scale; CEEG = continuous EEG monitoring; EVD = external ventricular drain; MIM = multimodality invasive monitoring.
Table 3. Prophylactic measures in patients with aneurysmal subarachnoid hemorrhage (SAH).

| Pharmacological prevention of vasospasm | Oral/enteral nimodipine 60 mg q4h for up to 21 days
This is the only Class 1 Level of Evidence A intervention. |
<table>
<thead>
<tr>
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<th></th>
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<tbody>
<tr>
<td>Intracranial pressure (ICP)</td>
<td>Maintain ICP below 15 mmHg (20 cmH$_2$O) using external CSF drainage, hypertonic saline or mannitol, barbiturates, or hypothermia.</td>
</tr>
<tr>
<td>Systemic factors of secondary brain injury</td>
<td>-</td>
</tr>
<tr>
<td><strong>Body temperature</strong></td>
<td>Avoid hyperthermia (&lt;38°C)</td>
</tr>
<tr>
<td><strong>Blood volume and pressure</strong></td>
<td>If aneurysm is not secured, maintain SBP &lt;160 mmHg (non-invasive monitoring) or MAP &lt;105 mmHg (invasive monitoring) When aneurysm secured, maintain euvoolemia, avoiding hypovolemia and maintain MAP &gt; 80 mmHg; if ICP monitoring available, maintain CPP &gt; 60 mmHg.</td>
</tr>
<tr>
<td><strong>Hemoglobin</strong></td>
<td>Maintain Hb &gt; 7 g/dl</td>
</tr>
<tr>
<td><strong>PaO$_2$</strong></td>
<td>Maintain normal PaO$_2$ (80-120 mmHg) and SaO$_2$ (94-96%)</td>
</tr>
<tr>
<td><strong>PaCO$_2$</strong></td>
<td>Maintain normal PaCO$_2$ (35-40 mmHg)</td>
</tr>
<tr>
<td><strong>Glycemia</strong></td>
<td>Maintain normal glycemia (80-180 mg/dl), avoiding hypoglycemia</td>
</tr>
<tr>
<td><strong>Sodium</strong></td>
<td>Maintain normal natremia (135-145 mEq/l), using hypertonic saline and fludrocortisone acetate</td>
</tr>
<tr>
<td><strong>Anti-seizure prophylaxis</strong></td>
<td>Prophylactic anti-seizure medication with levetiracetam 1000mg single IV load followed 500 mg q12h.</td>
</tr>
</tbody>
</table>
The use of prophylactic ASM is only suggested in the AHA/ASA guidelines (Class IIb; Level of Evidence B) but we feel the risk is very small, even if the benefit is still uncertain.

| Abbreviations: MAP = mean arterial pressure; ICP = intracranial pressure; CPP = cerebral perfusion pressure; Hb = hemoglobin. |
Table 4. Monitoring modalities for Delayed cerebral ischemia (DCI).

<table>
<thead>
<tr>
<th>Modality</th>
<th>Abnormal findings suggestive of delayed cerebral ischemia (DCI)</th>
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</thead>
<tbody>
<tr>
<td><strong>Non-invasive modalities</strong></td>
<td></td>
</tr>
<tr>
<td>Bedside neurological examination</td>
<td>New focal deficit</td>
</tr>
<tr>
<td></td>
<td>Decrease in level of consciousness (Decrease by at least 2 points on the GCS)</td>
</tr>
<tr>
<td>Transcranial Doppler ultrasonography</td>
<td>MCA mean flow velocity &gt;200cm/s</td>
</tr>
<tr>
<td></td>
<td>MCA mean flow velocity &gt;120cm/s and Lindegaard ratio &gt;3</td>
</tr>
<tr>
<td>CEEG with QEEG</td>
<td>New focal slowing or attenuation of fast activity</td>
</tr>
<tr>
<td></td>
<td>Decreasing relative alpha variability</td>
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<tr>
<td></td>
<td>Decreasing ADR</td>
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<tr>
<td></td>
<td>Emerging or increasing epileptiform discharges</td>
</tr>
<tr>
<td>Brain CT angiography and perfusion CT imaging</td>
<td>Reduction in intracranial artery caliber</td>
</tr>
<tr>
<td></td>
<td>Mismatch between reduced CBF/prolonged MTT and normal CBF</td>
</tr>
<tr>
<td></td>
<td>Reduced CBF/prolonged MTT and reduced CBV.</td>
</tr>
<tr>
<td><strong>Invasive modalities</strong></td>
<td></td>
</tr>
<tr>
<td>Partial brain tissue oxygen pressure</td>
<td>&lt; 20 mmHg</td>
</tr>
<tr>
<td>Cerebral interstitial fluid microdialysis</td>
<td>Glucose &lt; 0.4 μmol/l</td>
</tr>
<tr>
<td></td>
<td>Lactate &gt; 4.0 μmol/l</td>
</tr>
<tr>
<td></td>
<td>Lactate:Pyruvate ratio (LPR) &gt;40</td>
</tr>
<tr>
<td></td>
<td>Glutamate &gt; 10 μmol/l</td>
</tr>
</tbody>
</table>
| ICE with QEEG | New slowing or attenuation of fast activity  
|              | Decreasing relative alpha variability  
|              | Decreasing ADR  
|              | Emerging or increasing epileptiform discharges |

Abbreviations: CT = computed tomography; GCS = Glasgow Coma Scale; MCA = middle cerebral artery; CBF = cerebral blood flow; MTT = mean transit time; CBV = cerebral blood volume; CEEG = continuous EEG monitoring; QEEG = quantitative EEG; ADR = alpha:delta ratio; ICE = intracortical EEG.
References


