AHA/ASA Scientific Statement

Recommendations for the Management of Cerebral and Cerebellar Infarction with Swelling

A Statement for Healthcare Professionals from the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists
Writing Committee

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On behalf of the American Heart Association Stroke Council

Endorsed by American Academy of Neurology, American Association of Neurological Surgeons and Congress of Neurological Surgeons, and the Neurocritical Care Society
Stroke Council Professional Education Committee

This slide presentation was developed by a member of the Stroke Council Professional Education Committee.

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## Applying classification of recommendations and levels of evidence

### Size of Treatment Effect

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>Benefit &gt;&gt; Risk</td>
<td>Procedure/Treatment SHOULD be performed/administered</td>
</tr>
<tr>
<td>Class IIA</td>
<td>Benefit &gt;&gt; Risk</td>
<td>Additional studies with focused objectives needed; IT IS REASONABLE to perform procedure/administer treatment</td>
</tr>
<tr>
<td>Class IIB</td>
<td>Benefit ≥ Risk</td>
<td>Additional studies with broad objectives needed; additional registry data would be helpful; Procedure/Treatment MAY BE CONSIDERED</td>
</tr>
<tr>
<td>Class III</td>
<td>Risk ≥ Benefit</td>
<td>Procedure/Treatment should NOT be performed/administered SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL</td>
</tr>
</tbody>
</table>

### Level A

- Multiple populations evaluated
- Data derived from multiple randomized clinical trials or meta-analyses
- Recommendation that procedure or treatment is useful/effective
- Sufficient evidence from multiple randomized trials or meta-analyses

### Level B

- Limited populations evaluated
- Data derived from a single randomized trial or nonrandomized studies
- Recommendation that procedure or treatment is useful/effective
- Evidence from single randomized trial or nonrandomized studies

### Level C

- Very limited populations evaluated
- Only consensus opinion of experts, case studies, or standard of care
- Recommendation that procedure or treatment is useful/effective
- Only expert opinion, case studies, or standard of care

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**Suggested phrases for writing recommendations**

- should
- is recommended
- is indicated
- is useful/effective/beneficial
- is reasonable
- can be useful/effective/beneficial
- is probably recommended or indicated
- may/might be considered
- may/might be reasonable
- usefulness/effectiveness is unknown/unclear/uncertain or not well established
- is not recommended
- is not indicated
- should not
- is not useful/effective/beneficial
- may be harmful

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Epidemiology

- Varying definitions have made true incidence difficult to estimate the true number of cases of severe brain edema caused by massive infarction.
- Several terms have surfaced throughout the years:
  - “Malignant middle cerebral artery (MCA) infarction” or “large hemispheric infarction” were based on some combination of neurological signs and symptoms, MCA occlusion, involvement of some or all of the MCA-perfusion brain territory on either CT or MRI diffusion-weighted imaging, radiographic evidence of brain edema, post-admission neurological deterioration, or use of decompressive craniectomy.
Epidemiology: Recommendations

• Standardized terms and definitions for severe hemispheric and cerebellar edema due to infarction should be established to facilitate multicenter and population-based studies of incidence, prevalence, risk factors, and outcomes. (Class I, Level of Evidence C)

• Additional data should be collected to determine the use of decompressive craniectomy in current clinical practice, including whether there is variation by physician, hospital, health system, or patient characteristics and preferences. (Class I, Level of Evidence C)
Definition and Clinical Presentation

• This target population is defined as follows:
  – Patients who are at high risk for, or who ultimately suffer, neurological deterioration attributable to cerebral swelling after ischemia.

• Hemispheric stroke:
  – Typically have occlusions of the internal carotid artery (ICA), middle cerebral artery (MCA), or both.
  – Infarction from MCA branch occlusions usually does not result in swelling with clinically significant mass effect.
  – Additional vascular territories, incomplete circle of Willis, and marginal leptomeningeal collateral supply are additional risk factors for the development of cerebral edema after ischemia.
Hemispheric stroke

- **Clinical features include** hemiplegia, global or expressive aphasia, severe dysarthria, neglect gaze preference, and visual field defect.
- Pupillary abnormalities are due to significant brainstem shift, usually not present on initial presentation, and develop within the first 3-5 days.
- Early Horner’s syndrome may point to an acute carotid artery occlusion or dissection.
- Initial NIHSS is often >20 with dominant hemispheric infarction and >15 in non-dominant hemispheric infarction (although this clinical predictor is not well validated in prospective studies).
- The initial score is a reflection of stroke severity and infarct volume, not a marker of tissue swelling.
- The most specific sign of significant cerebral swelling after stroke is a decline in the level of consciousness attributable to brain edema shifting the thalamus onto the brainstem, where major components of the ascending arousal system are situated.
- Neurological deterioration usually occurs in most patients within 72-96 hours.
Cerebellar Stroke

• Can be difficult to diagnose, especially when the chief complaints are dizziness, vertigo, or vomiting.
• Attention should be paid to speech, gait, coordination, and eye movements to make the diagnosis.
• Truncal ataxia is a common miss when assessing the patient.
• Consequences of swelling after cerebellar infarction may result in pontine compression, acute hydrocephalus secondary to obstruction of the 4th ventricle, and often both.
• Clinical symptoms of tissue swelling are decreased level of consciousness and arousal. Pontine compression can lead to opthalmoparesis, breathing irregularities, and cardiac dysrhythmias.
Hemorrhagic Transformation (HT) of Strokes

- HT is a common complication of severe strokes and includes manifestation of damage to the blood brain barrier, loss of microvascular integrity, and disruption of the neurovascular unit.
- May be a consequence of recanalization and reperfusion of an infarcted area.
- Clinically HT may be associated with little change in neurological findings, worsening of existing deficits, or sudden rapid decline as a result of new mass effect.
  - This is commonly seen in large severe stroke at high risk of swelling.
  - Increased risk of HT may be due to the primary injury or a higher incidence of rtPA therapy.
  - Advanced age and hyperglycemia have been associated with HT, which increases mortality, especially in cerebellar stroke.
Hemorrhagic Transformation

CT scan showing a right hemispheric stroke with hemorrhagic transformation
Definition and Clinical Presentation: Recommendations

- Identification of patients with or at high risk for infarction and swelling should be made using clinical data, including vessel occlusion status. (Class I, Level of Evidence B)
Neuroimaging

- Cerebral infarction is characterized by progressive cerebral edema and mass effect, with ipsilateral sulcal effacement, compression of the ipsilateral ventricular system, and then a shift of the midline structures.
- The foramen of Monro and 3rd ventricle are blocked, leading to entrapment and dilatation of the contralateral lateral ventricle and obstructive hydrocephalus (might cause increased ICP).
- Brainstem displacement may lead to widening of the ipsilateral ambient cistern.
- Cerebellar infarction with swelling and effacement of the 4th ventricle is a key radiological marker followed by basal cistern compression, followed by brainstem deformity, hydrocephalus, and downward tonsillar herniation, and upward transtentorial herniation is also seen.
Neuroimaging: Recommendations

• A noncontrast CT scan of the brain is a useful first-line diagnostic test and modality of choice to monitor patients with hemispheric cerebral or cerebellar infarcts with swelling. Serial CT findings in the first 2 days are useful to identify patients at high risk for developing symptomatic swelling. (Class I, Level of Evidence C)

• Frank hypodensity on head CT within the first 6 hours, involvement of ≥ one third of the MCA territory, and early midline shift are CT findings that are useful in predicting cerebral edema. (Class I, Level of Evidence B)

• The measurement of MRI DWI volume within 6 hours is useful, and volumes >80 mL predict rapid fulminant course. (Class I, Level of Evidence B)
Large Hemispheric Stroke

MRI with diffusion showing a large left hemispheric stroke
Basics of Support

• Management of ischemic stroke:
  – Guidelines for the Early Management of Adults with Acute Ischemic Stroke, Jauch Ed et al.
    http://stroke.ahajournals.org/content/44/3/870.full.pdf+html

• Triage Recommendations:
  – Transfer to an intensive care or stroke unit is recommended for patients with a large territorial stroke to plan close monitoring and comprehensive treatment. (Class I, Level of Evidence C)

  – Triage to a higher level center is reasonable if comprehensive care and timely neurosurgical intervention is not available locally. (Class Ila, Level of Evidence C)
Airway and Mechanical Ventilation: Recommendations

- Maintaining normocarbia is reasonable. (Class IIa, Level of Evidence C)
- Intubation may be considered for patients with decreased levels of consciousness resulting in poor oxygenation or impaired control of secretions. (Class IIb, Level of Evidence C)
- Prophylactic hyperventilation is not recommended. (Class III, Level of Evidence C)
Hemodynamic Support and Blood Pressure Management: Recommendations

- Aggressive treatment of worsening cardiac arrhythmias with appropriate medications and continued cardiac monitoring is recommended. (Class I, Level of Evidence C)
- There are insufficient data to recommend a specific systolic or mean arterial blood pressure target. Blood pressure--lowering drugs may be considered for treatment of extreme hypertension. Specific blood pressure targets are not established. (Class IIb, Level of Evidence C)
- Use of adequate fluid administration with isotonic fluids might be considered (Class IIb, Level of Evidence C)
- Hypotonic or hypo-osmolar fluids are not recommended. (Class III, Level of Evidence C)
- Use of prophylactic osmotic diuretics before apparent swelling is not recommended. (Class III, Level of Evidence C)
Glucose Management: Recommendations

- Hyperglycemia should be avoided, and glucose levels from 140–180 mg/dL are recommended. (Class I, Level of Evidence C)
- “Tight” glycemic control (glucose <110 mg/dL) is not indicated, but an insulin infusion may be used to avoid significant hyperglycemia. (Class IIb, Level of Evidence C)
- Hypoglycemia should be avoided at all times. (Class III, Level of Evidence C)
Temperature Management: Recommendations

• Temperature management is part of basic support, and a normal temperature is reasonable. (Class IIa, Level of Evidence C)
• The effectiveness of the use of therapeutic hypothermia before brain swelling is not known. (Class IIb, Level of Evidence C)
Intracranial Pressure Management: Recommendations

- Ventriculostomy is recommended in obstructive hydrocephalus after a cerebellar infarct but should be followed or accompanied by decompressive craniectomy. (Class I, Level of Evidence C)

- Routine ICP monitoring is not indicated in hemispheric ischemic stroke. (Class III, Level of Evidence C)
Cerebellar Stroke

MRI of Large Right Cerebellar Stroke at High Risk for Swelling
Miscellaneous Medical Measures: Recommendations

• Deep venous thrombosis prophylaxis using subcutaneous or low-molecular-weight heparin should be used. (Class I, Level of Evidence C)
• Intravenous heparin or combination antiplatelet agents are not recommended in patients with swollen strokes. (Class III, Level of Evidence C)
• Seizure prophylaxis in patients without seizures at presentation is not indicated. (Class III, Level of Evidence C)
Recognition of Deterioration: Recommendations

- Clinicians should frequently monitor level of arousal and ipsilateral pupillary dilation in patients with supratentorial ischemic stroke at high risk for deterioration. Gradual development of midposition pupils and worsening motor response may also indicate deterioration. (Class I, Level of Evidence C).

- Clinicians should frequently monitor for level of arousal or new brainstem signs in patients with cerebellar stroke at high risk for deterioration. (Class I, Level of Evidence C)
Medical Options: Recommendations

• Osmotic therapy for patients with clinical deterioration from cerebral swelling associated with cerebral infarction is reasonable. (Class IIa, Level of Evidence C)

• There are insufficient data on the effect of hypothermia, barbiturates, or corticosteroids in the setting of ischemic cerebral or cerebellar swelling and therefore are not recommended. (Class III, Level of Evidence C)
Neurosurgical Options: Recommendations

- In patients <60 years of age with unilateral MCA infarctions that deteriorate neurologically within 48 hours despite maximal medical therapy, decompressive craniectomy with dural expansion is effective. The effect of later decompression is not known but should be strongly considered.  
  (Class I, Level of Evidence B)
- Suboccipital craniectomy with dural expansion should be performed in patients with cerebellar infarctions who deteriorate neurologically despite maximal medical therapy.  
  (Class I, Level of Evidence B)
- Although the optimal trigger for decompressive craniectomy is unknown, it is reasonable to use a decrease in level of consciousness and its attribution to brain swelling as selection criteria.  
  (Class IIa, Level of Evidence A)
- The efficacy of decompressive craniectomy in patients older than 60 years of age and the optimal timing of surgery are uncertain.  
  (Class IIb, Level of Evidence C)
Biomarkers: Recommendations

• The usefulness of serum biomarkers as predictors of ischemic brain swelling is not well established. *(Class IIb, Level of Evidence C)*

• The usefulness of electrophysiological studies as predictors of deterioration after a hemispheric stroke is not well established. *(Class IIb, Level of Evidence C)*
Outcome and Family Discussion: Recommendations

- Clinicians may discuss with family members that a third of the patients with massive hemispheric infarctions, even after decompressive craniectomy, are severely disabled and fully dependent on care. (Class IIb, Level of Evidence C)

- Clinicians may discuss with family members that the outcome after cerebellar infarct can be good after suboccipital craniectomy. (Class IIb, Level of Evidence C)
Summary

- Strokes that swell demand immediate and close attention. Medical and surgical options are discussed in this statement.
- The principles for emergent care involve avoidance of permanent brainstem injury from tissue shift.
- Decompressive craniectomy reduces mortality from avoiding the progression to brain death.
  - It also reduces the probability of permanent coma that can lead to de-escalation of care and death.
  - In surviving patients, morbidity can be substantial in one third of patients, but the remaining two thirds of patients have potential for recovery after rehabilitation.
- Further research targeted at preventing cerebral edema is urgently needed.
Future Directions

• Gaps exist in knowledge of recognition, management, and prognostication of patients with swollen stroke.
  – Urgent research is needed.

• Brain swelling is the cause of significant neurological morbidity and mortality in acute brain injury.
  – Fundamental, basic research in this area is needed and has been lacking.

• Mechanistic pathways of edema formation after ischemia still needs clarification.
  – Future work is needed to identify the following: biological mediators, the role of intracellular and vascular sources of swelling, and time course of relative contributions.

• Clinical areas of uncertainty include the following:
  – Incidence of significant swelling after ischemia and assessment of ongoing swelling. Improved understanding of the relationship between edema and outcomes. The role of vessel occlusion, collateral circulation and perfusion status in edema formation is not known – especially in patients who receive IV or endovascular reperfusion therapy. There are gaps in neuroimaging capability to quantify brain swelling after ischemia.

• Clarification of medical management of these patients is needed.

• In order to advance novel therapeutic and management strategies, the development and validation of patient-centered outcomes that incorporate the severity of illness are urgently needed.