Update in Neurocritical Care

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Nothing to disclose
Objectives

• Blood pressure: Management after stroke
• Neuromonitoring: Continuous EEG
• Hypothermia: Shivering control
• Medical Complications: SAH
• NICU Infections: Ventriculitis and VAP

Highlights
Frequency of Stroke by Subtype

Ischemic
- Thrombotic: 53%
- Embolic: 31%

Hemorrhagic
- Intracerebral: 10%
- Subarachnoid: 6%
Predictors of mortality in ICH

• GCS on admission
• Hematoma size (ICH volume)
• Blood pressure (pulse pressure)
• Intraventricular blood
• Hematoma enlargement
• Age

Broderick et al. Stroke 24:987-993, 1993
### TABLE 2. Suggested Recommended Guidelines for Treating Elevated Blood Pressure in Spontaneous ICH

1. If SBP is >200 mm Hg or MAP is >150 mm Hg, then consider aggressive reduction of blood pressure with continuous intravenous infusion, with frequent blood pressure monitoring every 5 minutes.

2. If SBP is >180 mm Hg or MAP is >130 mm Hg and there is evidence of or suspicion of elevated ICP, then consider monitoring ICP and reducing blood pressure using intermittent or continuous intravenous medications to keep cerebral perfusion pressure >60 to 80 mm Hg.

3. If SBP is >180 mm Hg or MAP is >130 mm Hg and there is not evidence of or suspicion of elevated ICP, then consider a modest reduction of blood pressure (e.g., MAP of 110 mm Hg or target blood pressure of 160/90 mm Hg) using intermittent or continuous intravenous medications to control blood pressure, and clinically reexamine the patient every 15 minutes.

SBP indicates systolic blood pressure; MAP, mean arterial pressure.
BP in ICH – Expert Consensus

- SBP > 200 mmHg or MAP > 150 mmHg
  - Consider aggressive reduction in blood pressure
- SBP > 180 mmHg or MAP > 130 mmHg
  - With suspicion for elevated ICP, consider ICP monitoring and target CPP > 60-80 mmHg
  - Without concern for ICP, MAP < 110 (BP 160/90) with close monitoring
- Maintain MAP < 130 mmHg (or BP ~ 180/110 mmHg), in patients with a h/o hypertension
- MAP < 100 mmHg post-op (if surgical evacuation); Keep SBP > 90 mmHg

Arbitrary expert opinion based on balancing concerns of rehemorrhage and perihematoma ischemia
BP lowering: how to do it

• Labetalol
  – 5-10 mg IV bolus every 10-15 minutes
  – Infusion, begin at 5 mg/hr and titrate up

• Nitroprusside
  – Infusion, start at 2 μ g/kg/min and titrate
  – Theoretical issues of increase in ICP (not a big deal)

• Nicardipine
  – We don’t bolus
  – Start IV infusion at 2.5 mg/hr and titrate up by 0.5 mg/hr increments
  – We use central lines for prolonged usage

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**TABLE 3. Intravenous Medications That May Be Considered for Control of Elevated Blood Pressure in Patients With ICH**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Intravenous Bolus Dose</th>
<th>Continuous Infusion Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labetalol</td>
<td>5 to 20 mg every 15 min</td>
<td>2 mg/min (maximum 300 mg/d)</td>
</tr>
<tr>
<td>Nicardipine</td>
<td>NA</td>
<td>5 to 15 mg/h</td>
</tr>
<tr>
<td>Esmolol</td>
<td>250 μg/kg IVP loading dose</td>
<td>25 to 300 μg·kg⁻¹·min⁻¹</td>
</tr>
<tr>
<td>Enalapril</td>
<td>1.25 to 5 mg IVP every 6 h*</td>
<td>NA</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>5 to 20 mg IVP every 30 min</td>
<td>1.5 to 5 μg·kg⁻¹·min⁻¹</td>
</tr>
<tr>
<td>Nipride</td>
<td>NA</td>
<td>0.1 to 10 μg·kg⁻¹·min⁻¹</td>
</tr>
<tr>
<td>Nitroglycerin</td>
<td>NA</td>
<td>20 to 400 μg/min</td>
</tr>
</tbody>
</table>

*IPV indicates intravenous push; NA, not applicable.

*Because of the risk of precipitous blood pressure lowering, the enalapril first test dose should be 0.625 mg.

Stroke 2007; 38; 2001-2023
Blood pressure trials: ATACH

- ATACH: Antihypertensive Treatment in Acute Cerebral Hemorrhage
- NIH sponsored pilot study in 60 patients
- “Dose-escalation” study of feasibility of achieving 3 successive BP goals for 24 hours after acute ICH
- Safety evaluation by decline in GCS of 2 points or NIHSS of 4 points
- Results: Early BP reduction within 3 hours was well-tolerated; no significant difference in outcomes in the treatment groups.
Blood pressure trials: INTERACT

- INTERACT: Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage
- 404 patients treated within 6 hours of onset
- Intensive group: SBP goal 140 mmHg (n = 203) vs. Standard group; SBP 180 mmHg (n = 201)
- Outcomes: hematoma volume at 24 hours; 90 day safety and clinical outcomes
- Results: RR 36% lower hematoma growth in intensive group; ARR 8% (CI 1.0-17%, p = 0.05)

Ischemic stroke: Pathophysiology

- Time dependent
- Focal ischemia is different from global ischemia
- Energy failure -> $\text{Ca}^{++}$ entry and cell death
- Glutamate toxicity
- Apoptosis
- ECASS-III (Randomized, Controlled)
- NINDS
- PROACT
- IMS-I, IMS-II (Prospective, Non-randomized)
- MERCI, Multi MERCI, Penumbra

- 0 hours
- 3
- 4.5
- 6
- 8
- 12
HTN after Acute Stroke

- Acute HTN is common after acute ischemic stroke
- Current guidelines suggest treatment for SBP > 220 mmHg or DBP > 120 mmHg or if evidence of end-organ damage
- With thrombolytic therapy, goal BP < 180/105 mmHg
- Risk of acute deterioration with aggressive reduction of BP

- Blood pressure reduction within 24 hours is associated with poor outcome
  - OR 1.89 per 10% decrease (p = 0.047) of poor outcome at 3 months

Neurology 2003; 61:1047-51
Blood pressure goals

• Optimal blood pressure after acute stroke is controversial
  – t-PA limit 185/110 mmHg
  – Lower BP by 15% if exceeds 220/120
  – Choice of BP agent is controversial; labetolol, nicardipine don’t raise ICP
Controversy over BP

- Lower blood pressure can worsen ischemia in the penumbra, leading to larger infarcts
- Higher blood pressure can lead to increase cerebral edema and increase risk of hemorrhagic changes
Ischemic Stroke Penumbra
Induced Hypertension

- Remains experimental
- Consider in specific cases
  - Hypotension unresponsive to fluid resuscitation
  - Fluctuating neurological symptoms with hemodynamic changes
  - Increase BP by 10-20% using pressors and observe for symptom resolution
  - Potential to incorporate perfusion imaging
Induced Hypertension

For
May increase pial-pial blood flow
Increase perfusion to the ischemic penumbra
Is probably safe

Against
Requires ICU care and central line access
May cause coronary or gut ischemia
Could cause cerebral vasoconstriction
Induced Hypertension

• Rordorf, et al, 1997
  • Retrospective safety study in acute stroke patents
    • 30 controls vs. 30 treated with neosynephrine
    • 10/30 treated patients had BP threshold
    • No increased cardiac morbidity
Evidence for Induced Hypertension

- Koenig, et al. (2006)
  - 100 patients randomized to either induced HTN or standard therapy
  - Used perfusion MRI to select patients with ischemic penumbra (mismatch DWI/PWI)
  - Non-significant decrease in NINDS scores at discharge in treated group, but with longer LOS, ICU time
  - No difference in adverse events
Autoregulation

\[ CBF = \frac{CPP}{CVR} = \frac{MAP - ICP}{CVR} = K \]

Arteriolar Vasomotor Tone
Vasodilatory Response

- Cerebral blood volume
- Pial vessel caliber
- CBF

Graph showing the change in % of cerebral blood volume, pial vessel caliber, and CBF with respect to CPP (mm Hg⁻¹).
Pressure Autoregulation/CO$_2$ Reactivity

![Graph showing pressure autoregulation and CO$_2$ reactivity](image)

Anesthesiology 43: 447, 1975
Continuous EEG monitoring

The technique: prolonged (hrs, days or wks) of continuously recorded digital EEG in critically ill patients

Potential applications
• Ictal activity
• Ischemia or hypoxia
• Prognostication
• Endpoint for treatment
• Multimodality brain monitoring
• Controversial EEG patterns
• Artifacts
Is a routine EEG enough?

<table>
<thead>
<tr>
<th></th>
<th>Clin events</th>
<th>EEG szs</th>
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</thead>
<tbody>
<tr>
<td>N=105</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Routine EEG</td>
<td>21%</td>
<td>11%</td>
</tr>
<tr>
<td>(&gt;30 mins)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cDVEEG</td>
<td>40%</td>
<td>27%</td>
</tr>
<tr>
<td>(mean 2.9d)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>0.01</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Time to record the first seizure

- Pandian ArchNeurol 2004
- Claassen Neurol 2004
Prophylactic AED in Acute Brain Injury

- Avoid indiscriminate prophylactic AED
- It worsens our patients’ complications and outcome
- Monitor with EEG as much as possible
- Detect pre-ictal or ictal events
- Risk stratify EEG results: justifies AED risk/benefit ratio
- If no EEG monitoring performed:
  - Identify patients with high risk potential for SZ
  - Short-term use of AED
MILD THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC OUTCOME AFTER CARDIAC ARREST

THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP*

INDUCED HYPOTHERMIA AFTER OUT-OF-HOSPITAL CARDIAC ARREST

TREATMENT OF COMATOSE SURVIVORS OF OUT-OF-HOSPITAL CARDIAC ARREST WITH INDUCED HYPOTHERMIA

Hypothermia – clinical trials

- European study – NEJM 2002; 346:549-56
  - V fib arrest; still comatose after resuscitation
  - 24 hours of external cooling (special mattress) – 33°C
  - 6 month outcome (NNT= number needed to treat= 6)
    - Hypothermia 55%
    - Normothermia 39% (RR 1.4 [1.08-1.81])

- Australian study – NEJM 2002; 346:557-63
  - V fib arrest; still comatose after resuscitation
  - 12 hours of surface cooling; often started prehospital
  - Outcome at hospital discharge (NNT= 4)
    - Hypothermia 49%
    - Normothermia 26% (P = 0.046)
Shivering management

- Acetaminophen 650 mg q4H NG/ PR route
- Buspirone 30 mg PO q8H NG route
- Mg++ infusion
  - 20gm/1L -0.5-1 gm/hr
    - Hypotension
    - Serum level q 8 hr
    - Serum level 3-4 mg/dl
- Skin Counterwarming
  - Set at 43 degrees C (BAIR Hugger)

- Dexmedetomidine
  - 0.3 –1.5 μg/kg/hr
    - Bradycardia
- Meperidine 25-100 mg IV
  - Creatinine clearance
  - Seizures
  - MAOI use
- Fentanyl 50-200 μg/hr
  - Hypotension
  - Ileus
- Propofol 25-100 μg/kg/min
  - Hypotension
- Neuromuscular blockade

Adapted from Columbia University
Medical complications after SAH

- Life-threatening complications occur in up to 40% of SAH patients
- Contributes to 23% of overall mortality

<table>
<thead>
<tr>
<th>Medical Complication</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Cardiac arrhythmia</td>
<td>30%</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>23%</td>
</tr>
<tr>
<td>Hepatic dysfunction</td>
<td>20%</td>
</tr>
<tr>
<td>Renal failure</td>
<td>7%</td>
</tr>
</tbody>
</table>

Association with poor outcomes

- Fever, hyperglycemia and anemia requiring transfusion were most associated with poor neurological outcomes (mRS > 2)
- Cardiac complications are common, but mostly benign.
- Troponin leak and cardiac dysfunction have been associated with worse outcome
Cardiac complications

• Sympathetic stimulation induces catecholamine release in the myocardium
• Leads to impaired systolic and diastolic function, repolarization abnormalities, and myocardial damage
• Definite causal relationship with worse vasospasm and neurological outcome remains unclear

Fever Management

• Growing evidence that fever is associated with poor neurological outcomes
• 25% from non-infectious etiologies
• Small studies of safety of aggressive fever control
• Significant practice variability
Glucose control

- Hyperglycemia is associated with worse outcomes
- Aggressive treatment of hypoglycemia after SAH generally beneficial in subgroup analyses
- Limited safety data on insulin infusion
  - Microdialysis studies showing cerebral hypoglycemia
  - Target serum glucose <140 mg/dl
Optimal Hgb/Hct?

• Anemia requiring transfusion associated with worse outcome

• Hemodilution advocated for vasospasm
  – Target Hct 30% to optimize O2 delivery and blood viscosity
  – New measures of PbtO2 and microdialysis suggest cerebral hypoxia at these levels
Hyponatremia

- Occurs 1/3 of patients
- Associated with hypovolemia in cerebral salt wasting
- SIADH less common
- Complex interplay of neurohormonal effects
  - hyperreninemic hypoaldosterone syndrome
EVD Infections

• Data favor some antibiotic prophylaxis
  – Antibiotics at insertion reasonable
  – No data to support continuing antibiotic prophylaxis
  – Not counting emergence of resistant organisms
• Routine changing of EVDs not helpful
• Minocycline/rifampin coated EVDs reduce infection risk of catheters in place > 1 week
• Meticulous insertion technique and early discontinuation may be best
Ventilator associated pneumonia

- Common in patients with severe traumatic brain injury, and likely other severe neurological injury
- Associated with the development of non-neurological organ dysfunction, increased ventilator days, increased ICU length of stay but NOT hospital mortality
- Prevented by prophylactic antibiotics (EOP) and povidone-iodine oral wash but reductions in patient morbidity has not been demonstrated
- Larger trials are needed
Guidelines for the Management of Aneurysmal Subarachnoid Hemorrhage. A Statement for Healthcare Professionals From a Special Writing Group of the Stroke Council, American Heart Association
Stroke published online Jan 22, 2009;
DOI: 10.1161/STROKEAHA.108.191395
Guidelines for the Management of Spontaneous Intracerebral Hemorrhage in Adults: 2007 Update: A Guideline From the American Heart Association/American Stroke Association Stroke Council, High Blood Pressure Research Council, and the Quality of Care and Outcomes in Research Interdisciplinary Working Group: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists.

Joseph Broderick, Sander Connolly, Edward Feldmann, Daniel Hanley, Carlos Kase, Derk Krieger, Marc Mayberg, Lewis Morgenstern, Christopher S. Ogilvy, Paul Vespa and Mario Zuccarello

*Stroke* 2007;38;2001-2023; originally published online May 3, 2007;
DOI: 10.1161/STROKEAHA.107.183689

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Guidelines for the Early Management of Adults With Ischemic Stroke: A Guideline From the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists


*Stroke* 2007;38;1655-1711; originally published online Apr 12, 2007;
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