Management of Ischemic Stroke in the Intensive Care Unit

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Outline

Why ICU care matters for ischemic stroke patients

Patient Cases
To illustrate:
Complications following ischemic stroke
Subsequent treatments

Introduction
Phases of Stroke Diagnosis and Treatment
1. Making the Diagnosis
   • Variable complexity of presentation
2. Deciding about Immediate Treatment
   • tPA, endovascular therapy
3. Subsequent Care
   • Prevention of further damage and deterioration
   • Treating potential complications
   • ICU Care
Stroke Treatment
- How many patients receive acute treatment?

- 370,351 acute ischemic stroke primary discharge diagnosis
  - 0.4% received tPA
  - 0.5% received endovascular therapy

- Continued efforts to increase acute treatment rates
  - Subsequent care is important


Neurocritical Care

ICU Care Matters

- Management by a neurocritical care team
  - Decreased hospital length of stay
  - Decreased ICU length of stay
  - Increased proportion of home discharges


Case #1

62 year old male woke up with
- Mild right arm weakness
- Minor facial droop
- Partial arm sensory loss
Last known normal 7 hours prior
NIHSS 3

Past Medical History: Diabetes, Hypertension, Hyperlipidemia
Social History: Smoking
Case #1

- Not a candidate for tPA or endovascular therapy
- CT head shows no hemorrhage
- Blood pressure is 210/110

What should be done for the patient’s blood pressure?

Hypertension

- Treatment threshold BP > 220/120
- Lower threshold for complications (e.g. CHF)
- BP must be <185/110 to qualify for tPA
- Maintain BP <180/105 for 24 hours after tPA

Many patients will be hypertensive after stroke
- SBP >139 in 77% and >184 in 15% upon arrival to ED

Why allow such a high blood pressure?


- To perfuse the penumbra, the area of brain that is at risk
- Impaired autoregulation, thus, dependent on systemic BP

www.radiologyassistant.nl
Blood Pressure After tPA

• 11,080 patients treated with tPA from 2002 to 2006

![Graph showing Blood Pressure After tPA](image)


Blood Pressure Management

For admission BP in acute ischemic stroke:
• Some studies have found U-shaped relationships
• Others report linear relationships

Elevated BP while in the hospital
• More consistent linear relationship with poor outcome


Blood Pressure Management

BP following ischemic stroke:
• A dynamic process
• Needs to be monitored frequently
• Potential trends and fluctuations that require intervention

Hypotension following ischemic stroke is rare
• Study of 11,080 patients: only 0.6% with SBP <100
• Often indicates another cause
  • Cardiac dysfunction, vascular dissection, shock
  • Brain is very vulnerable to low BP following stroke

Case #1 Revisited

62 year old male woke up with
- Mild right arm weakness
- Minor facial droop
- Partial arm sensory loss

Last known normal 7 hours ago
NIHSS 3
Blood pressure 180/90

2 hours later

Worsening weakness of right face, arm, leg, aphasia
NIHSS increased: 3 to 11
Blood pressure decreased: 180/90 to 130/70

Should the patient’s blood pressure be increased?

Pressor Therapy

Therapy to increase blood pressure in ischemic stroke
A potential therapy in the ICU
Evidence from small studies
- Suggest safety and effectiveness in select patients

Which patients?
Pressor Therapy

1) Patients with sustained SBP < 130 to 150 mm Hg OR those with evidence of a symptomatic BP decrease (20 mm Hg) following ischemic stroke
2) Severe ipsilateral large extracranial or intracerebral vessel stenosis or occlusion
3) Presenting within 12 hours or perhaps 24 hours of symptom onset
4) Without obvious exclusion criteria to pressor therapy, (e.g. EF < 25%, recent CHF, MI, past medical history of arrhythmias)


Case 2

57 yo Female found down
Aphasia, right sided hemiplegia, L gaze preference
NIHSS 22
LKN: 8 hour prior

24 hour follow-up CT
Malignant Ischemic Stroke

Malignant MCA syndrome

Some with large strokes will deteriorate in initial 24-48 hours
Massive edema and severe midline shift

Malignant strokes constitute up to 10% of strokes
Mortality is as high as 80%
Early identification is essential

Risk factors for malignant cerebral edema:

1) Early CT hypodensity greater than 50% of the MCA territory
   OR
   Diffusion lesion volume greater than 82mL within 6 hours of stroke onset

2) Involvement of adjacent vascular territories (such as ACA or PCA)


Malignant Edema Treatment

Decompressive hemicraniectomy
To allow space for the swelling to occur
Reduce fluid shifts, pressure in the intracranial compartment

Is it beneficial?
Pooled analysis of 3 RCTs, 93 patients, 18-60 years old
NIHSS ≥15, CT with hypodensity ≥ 50% MCA
Maximum time of 48 hours from stroke onset

Decompressive Hemicraniectomy

Outcomes at 1 year following stroke

Mortality: 28% with surgery, 78% without
mRS 0-4: 75% with surgery, 24% without
mRS 0-3: 43% with surgery, 22% without

0 - No symptoms.
1 - No significant disability: Able to carry out all usual activities, despite some symptoms.
2 - Slight disability: Able to look after own affairs without assistance, but unable to carry out all previous activities.
3 - Moderate disability: Requires some help, but able to walk unassisted.
4 - Moderately severe disability: Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
5 - Severe disability: Requires constant nursing care and attention, bedridden, incontinent.
6 - Dead.

What about older patients?

122 patients with malignant MCA
≥ 61 years, (median 71, range 61-82)

Outcome at 6 months following stroke:

Mortality: 33% with surgery, 70% without
mRS 0-4: 38% with surgery, 28% without
mRS 0-2: No patients
mRS 3: 7% with surgery, 3% without
mRS 4: 32% with surgery, 15% without
mRS 5: 28% with surgery, 13% without


Hyperosmolar Therapy

- A treatment in the ICU for malignant edema

Mannitol
Typically administered as boluses Q 4 to 6 hours
Long history, considered by some to be “gold standard”

Hypertonic saline
Boluses or continuous infusion

Both reduce ICP through various mechanisms:
Volume redistribution, plasma expansion, rheologic modifications, anti-inflammatory effects

Adverse Effects

Mannitol:
Renal failure, electrolyte disturbances, initial plasma volume expansion, hypotension, ICP rebound

Hypertonic saline (HS):
Renal failure (less common), electrolyte disturbances, central pontine myelinolysis, infusion phlebitis

HS often described as having "more favorable side effect profile."


Mannitol vs. HS: Which is more effective?
Limited evidence:
• In ischemic stroke:
  16 of 16 episodes of increased ICP responded to HS
  10 of 14 responded to mannitol
• Mean ICP reduction 11 mm Hg with HS, 5 mm Hg with Mannitol
• Meta-analysis of 5 trials for elevated ICP (3 included stroke):
  ICP successfully reduced 78% of the time with mannitol, 93% with HS

Should HS be the new gold standard?


Case 3

• 51 year old male, sudden onset of vertigo, vomiting
• Unable to stand or walk independently
• BP 160/85
• Glucose 170
• NIHSS 1 (ataxia)
• Onset of symptoms 2 hours prior, treated with IV tPA
Case 3

- Posterior circulation stroke
  Can result in severe complications due to:
  - Obstructive hydrocephalus from compression of the 4th ventricle
  - Direct compression of the brainstem

With signs of brainstem compression, mortality about 80% without surgery
Surgery reduces mortality
  20% for those treated surgically in comatose state


24 hour repeat CT

Case 3

48 hour repeat CT
Monro-Kellie Doctrine

The brain is enclosed in the skull
Thus, the volume is constant

Average adult male, approximately 1500 ml
1250 ml Brain
150 ml Cerebrospinal Fluid
100 ml Blood

Something (i.e. blood or CSF) must be pushed out if pressure rises

Monro-Kellie Doctrine
Treatments for Posterior Circulation Stroke:
EVD: External Ventricular Drain
Decompulsive Surgery

Making the diagnosis is key
Close monitoring in the ICU setting
Early MRI
Involve a neurosurgeon early
Temporizing measures if indicated
Hyperosmolar therapy
ICU care following EVD placement and/or decompressive craniotomy

Case 4
72 year old female, left face/arm/leg weakness, right gaze preference, left sided neglect
LKN 24 hours prior
NIHSS 16
BP 160/90
Glucose 350
Hyperglycemia

Thought to increase metabolic demand in the brain
Results in lactic acid, various free radical
Neuronal cell lysis, damage to blood brain barrier

Negative outcomes noted in hyperglycemic stroke patients
  • Increased cerebral edema
  • More hemorrhagic conversion
  • More disability and death

Lindsberg et al. Stroke. 2004 Feb;35(2):363-4

Hyperglycemia

Controlling blood glucose levels
NICE-SUGAR study:
  • 6,104 medical/surgical ICU patients
  • Randomized to intensive control (glucose 81-108) vs. conventional
    (glucose < 180)
  • Higher mortality in intensive control (27.5 vs. 24.9%)
  • More severe hypoglycemia (4.0%) in intensive control (6.8 vs 0.5%)


SHINE Trial

Stroke Hyperglycemia Insulin Network Effort (SHINE) Trial
Acute ischemic stroke, RCT of 1400 patients
Enrolled within 12 hours of symptom onset
Randomized to
  • Insulin gtt to maintain glucose 80-130 for up to 72 hours
  • Standard care, i.e. sliding scale insulin to keep glucose <180
Outcome: Functional outcome at 3 months (mRS)
Recent guidelines: Glucose 140 to 180
More potential stroke patients on insulin infusions?
Case 5
79 year old male, aphasia and right sided weakness
LKN 2 hours prior
No tPA for INR 2.3
BP 160/90
Glucose 120
12 hours after admission:
Temperature 101.5

Temperature Management
Elevated temperature after neurologic injury
  • Increased brain metabolic demand
  • Elevated levels of excitatory amino acids
  • Increased ischemic depolarizations
  • Blood-brain barrier breakdown
  • Impaired function of enzymes

Meta-analysis with 14,431 patients with stroke and other brain injury
  Increased temperature associated with worse outcomes
  7 measures including clinical, functional, economic outcome


Types of temperature management:
  Acetaminophen
  Pharmacologic sedation
  Surface cooling
  Endovascular cooling catheters

Normothermia vs. Hypothermia
How is temperature measured? Core temperatures?
The assumption that fever is harmful
Temperature Management

Small studies have evaluated feasibility of TTM in stroke
Potential side effects: arrhythmias, hypotension, pneumonia
Systematic review: No clear benefit or harm

Shivering can be a major issue
  Increases metabolic demand, potentially increases ICP

Hypothermia can reduce ICP
  Potentially dangerous rebound increase with more rewarming


Hertog et al. Cochrane Database Syst Rev. 2009 Jan 21

Large number of unanswered questions:
  When to start hypothermia?
  What target temperature? For what duration?
  How fast to rewarm?

What type of temperature management? (Surface, invasive)
Which stroke patients? (e.g. only large strokes with edema?)
With other therapies? (e.g. tPA, angiography, hemicranectomy)
By itself or with other neuroprotectants?

Case 6

64 year old female
Sudden onset R arm and leg weakness/numbness
IV tPA treatment at 1.5 hours
Diagnosis of new onset atrial fibrillation
Symptoms improved following tPA
Admitted to ICU

Family member asks: “I take warfarin for A-Fib to help prevent strokes. She just had a stroke. Why isn't she getting blood thinners?”
Anticoagulation

Early administration of anticoagulants following stroke?
• Increased risk of bleeding
  Evidence from clinical trials
  Includes both UFH and LMWH
• Does not lessen risk of early neurological worsening
• Does not lower risk of early recurrent stroke
  Including cardioembolic strokes (A-Fib)


Anticoagulation

The AHA Guidelines state:
“Data are insufficient to indicate whether anticoagulants might be effective among some potentially high-risk groups, such as those people with intracardiac or intra-arterial thrombi.”

Starting anticoagulants within 24 hours of IV-tPA is not recommended

Patient at high risk for further worsening due to arterial thrombus?
  Anticoagulation potentially started in ICU
  Often high level decision with much discussion

Anticoagulation

To answer the family member’s question:
  The patient will be placed on anticoagulation, but not now
  Currently, the risk of bleeding is more than the potential benefit
  Treatment should be started after the risk of hemorrhage into the stroke tissue has reduced
Case 7

78 year old female with R MCA stroke 3 days ago
More difficult to arouse since having a seizure 2 hours ago
Seizure treated with Lorazepam
Thought to be sleepy secondary to this

With reassessment, slight twitching of facial noted
Mental status improves with further seizure treatment
Patient is monitored in ICU for more seizures with cEEG

The intern asks, “Did we forget to start AEDs?”

Seizures After Ischemic Stroke

Incidence varies, usually reported in <20% of ischemic strokes
More common with hemorrhagic transformation
Recurrence seizures? Late onset? Incidence varies significantly

No demonstrated benefit of prophylactic anticonvulsants
Recommendations based on established guidelines for treating seizures in any neurologic illness

Advanced monitoring for seizures (cEEG) in the ICU setting

Case 8

48 year old male

- Onset of R sided weakness and aphasia 24 hours ago
- Transferred from OSH for ICU care
- Concern for edema
- Neurosurgery consulted for hemicraniectomy

Medical student asks: "I have seen other ICU patients with brain swelling have these complicated monitors placed. Will this patient have that done?"
**Advanced Monitoring**

Multimodal Monitoring in the ICU
- Intracranial pressure (ICP)
- Brain temperature
- Brain tissue oxygenation
- Jugular venous oxygen saturation
- EEG

Biochemical milieu of the brain
- e.g. Microdialysis, testing brain microenvironment molecules

Currently, more commonly performed for:
- Traumatic brain injury
- Subarachnoid hemorrhage

Does this monitoring provide more information than the neurologic examination?
- Where to place monitors
- Focal injury vs diffuse
- Invasive vs non-invasive monitors
- Similar parameters to other disease states? e.g. TBI
  - Potential differences in ICP and venous oxygen saturation

Likely more monitoring in the future
Goal of optimizing recovery and reducing secondary injury
Blood pressure after stroke involves complicated physiology
- Current Guidelines for first 24 hours:
  - BP <220/120 without tPA, <180/105 after tPA
- Select patients might benefit from pressors
- Low BP is rare—think about other causes

Malignant edema can occur after stroke
- Potential treatments include hemicraniectomy, hypertonic fluid
  - Hemicrani- life saving vs. function saving?
  - Hypertonic saline vs. mannitol

Summary

Posterior circulation stroke can be difficult to diagnose
- Can result in obstructive hydrocephalus, herniation, death
- EVD and surgical treatment can be life saving

Hyperglycemia is thought to be harmful to the brain following stroke
- Is aggressive treatment helpful? Hypoglycemia?
- Current guidelines: Maintain glucose 140-180
- Look for results of SHINE trial

Temperature management following stroke is important
- Fever is thought to be bad
- Limited evidence for hypothermia vs. normothermia
- Hypothermia in stroke patients has unique challenges

Anticoagulation early after stroke is not a common treatment
- Select patients might benefit
- More commonly patients are started on anticoagulation later

Summary
Seizures can occur after stroke
- cEEG monitoring can take place in the ICU
- Treat actual seizures based on established general guidelines
- Prophylactic anticonvulsants are not recommended

Advanced multimodal monitoring has substantial potential
- Many unanswered questions about best methods
- Likely more use in the future

THANK YOU!