2018 Early Management of Acute Ischemic Stroke Guidelines Update

Brandi Bowman, PhC, Pharm.D.
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Pharmacist Objectives

• Describe the recommendations for emergency medical services and hospital systems that ensure timely management of acute strokes

• Identify patients eligible for IV alteplase therapy and design an appropriate dosing strategy for a given patient

• Describe the role of antiplatelet and anticoagulation therapy to prevent early recurrence of stroke, and select an appropriate antiplatelet for a given patient

• Prevent complications in stroke patients by selecting appropriate blood pressure and blood glucose goals in the acute and initial post-stroke period
Technician Objectives

- Identify stroke symptoms and determine the appropriate action for someone in the community who you suspect may be having a stroke
- Explain why timely administration of IV alteplase is important for eligible patients
- Describe contraindications to IV alteplase therapy for acute stroke patients
- Discuss the pharmacologic options for providing supportive care to acute stroke patients with hypertension

Stroke Background

- >795,000 Americans have a stroke each year
  - ~140,000 Americans die from a stroke annually
  - 1/20 deaths is due to stroke
  - Stroke is a leading cause of long-term disability
- ~87% of strokes are ischemic strokes
- HTN, high cholesterol, smoking, obesity and diabetes are leading causes of stroke

https://www.cdc.gov/stroke/facts.htm
Primary Topics Covered

- Systems of care
- Acute reperfusion therapy
- In-hospital supportive care
- In-hospital initiation of secondary prevention
Your 74 year old grandmother suddenly started slurring her speech and developed weakness in her left arm. You live less than 10-minutes from an emergency room, so drive you her there immediately and call ahead.

Was this an optimal response?
93% of people recognize sudden one-sided numbness as a stroke symptom.

Only 38% know all major symptoms, and to call 911 if someone is having a stroke.

https://www.cdc.gov/stroke/facts.htm

Time is Brain...

Hospital Stroke Teams

- The primary door-to-needle goal should be 60-minutes for ≥ 50% of patients treated with IV alteplase
- It may be reasonable to establish a secondary door-to-needle time of 45 minutes
- It is recommended to designate an acute stroke team to provide clinical assessment of stroke patients
  - Physicians, nurses, and laboratory/radiology personnel
- Protocols should be developed to ensure adherence to guidelines and current standards of care
- Participation is a stroke data repository is recommended

Initial Evaluation

It is recommended to use a stroke severity scale, preferably the NIHSS

<table>
<thead>
<tr>
<th>Category</th>
<th>Score/Description</th>
</tr>
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<tbody>
<tr>
<td>1a. Level of Consciousness (Alert, drowsy, etc.)</td>
<td>0 = Alert 1 = Drowsy 2 = Stuporous 3 = Coma</td>
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<tr>
<td>1b. LOC Questions (Numb. age)</td>
<td>0 = Answers both correctly 1 = Answers one correctly 2 = Incoherent</td>
</tr>
<tr>
<td>1c. LOC Comments (Open/close eyes, make faster go)</td>
<td>0 = Open both correctly 1 = Open one correctly 2 = Incoherent</td>
</tr>
<tr>
<td>2. Body Gaze (Eye open - patient follows examiner’s finger or gaze)</td>
<td>0 = Normal 1 = Partial gaze palsy 2 = Forced deviation</td>
</tr>
<tr>
<td>3. Visual Fields (Indicate visual stimulus/treat to the visual field quadrant)</td>
<td>0 = No visual loss 1 = Partial hemianopsia 2 = Complete hemianopsia 3 = Bilateral hemianopsia (Blind)</td>
</tr>
<tr>
<td>4. Facial Paralysis (Shine teeth, raise eyebrows and squeeze eye shut)</td>
<td>0 = Normal 1 = Minor 2 = Paralytic 3 = Complete</td>
</tr>
<tr>
<td>5a. Motor Arm - Left</td>
<td>0 = No palsy 1 = Bilateral 2 = Unilateral 3 = Complete</td>
</tr>
<tr>
<td>5b. Motor Arm - Right</td>
<td>0 = No palsy 1 = Bilateral 2 = Unilateral 3 = Complete</td>
</tr>
<tr>
<td>6a. Motor Leg - Left</td>
<td>0 = No dist 1 = Dist 2 = Can’t resist gravity 3 = No affect against gravity</td>
</tr>
<tr>
<td>6b. Motor Leg - Right</td>
<td>0 = No movement 1 = Unilateral 2 = Bilateral</td>
</tr>
</tbody>
</table>

Pharmacist Participation in Stroke Care Associated with Improved Door-to-Needle Times

Rech et al. 2017
- ED or inpatient stroke codes
- Pharmacist presence associated with a median DTN of 48 vs. 73 minutes (p<0.01)
- DTN ≤60 minutes in 71% vs. 29% of patients (p<0.01)

Gosser et al. 2016
- ED strokes
- Median DTN shorter when pharmacist present: 69.5 vs. 89.5 minutes (p<0.01)
- More strokes meeting DTN ≤60 minutes: 29.9% vs. 15.8% of patients (p<0.01)

Initial Evaluation

- All patients with suspected stroke should receive brain imaging on arrival
  - Non-contrast CT in most cases
  - Within 20 minutes of arrival in 50% of tPA or thrombectomy candidates
- Only blood glucose assessment should precede the initiation of IV alteplase
  - Hematologic and coagulation studies may be required in some patients only if there is suspicion for an abnormality
- Baseline EKG and troponin levels are recommended, but should not delay the administration of IV alteplase
Which of the following patients has an absolute exclusion to tPA therapy?

A. An 86 year old male that present 3.5 hours from symptom onset
B. A 52 year old female that had right-sided facial droop and difficulty speaking when she woke up this morning (45 minutes ago)
C. A 69 year old male with 1 prior stroke 3 years ago, whose symptoms are improving on presentation
D. A 48 year old female who takes warfarin for atrial fibrillation, with an INR of 1.6 on presentation

IV Alteplase (tPA) for Acute Stroke

- In a 2014 meta-analysis, more patients that received tPA had a good outcome
  - 33% vs. 23% within 3 hours
  - 35% vs. 30% from 3 to 4.5 hours
- In a registry of 58,000 patients, each 15-minute reduction in time to tPA associated with:
  - 4% increase in odds of walking at discharge
  - 4% decrease in odds of death prior to discharge
- Intracerebral hemorrhage in 5%-7% of patients in clinical trials

Emerson et al. Lancet 2014;384(9958):1929
Saver et al. JAMA 2013;309(23):2480
http://usmle.biochemistryfomedics.com/immediate-treatment-of-acute-mi/
tPA Recommendations

• tPA is recommended for selected patients who may be treated within 3-hours of stroke-symptom onset
• tPA is also recommended for selected patients who may be treated within 4.5-hours of stroke-symptom onset
• tPA dosing:
  • 0.9 mg/kg, max dose of 90 mg
  • 10% given as a bolus over 1 minute
  • Remaining given over 60 minutes

Contraindications:
• Time of onset > 3 or 4.5 hours
• Acute intracranial hemorrhage
• Ischemic stroke, head trauma, intracranial/spinal surgery within 3 months
• History of intracranial hemorrhage
• Subarachnoid hemorrhage
• BP >185/110
• GI/genitourinary bleed within 21 days
• Coagulopathy (INR > 1.7, platelets <100,000)
• Treatment-dose LMWH w/in 24 hours or DOAC use within 48 hours
• Glucose <50mg/dL
• Non-compressible arterial puncture within 7 days

Stroke 2018;49(3):e46-e110
tPA candidates

Relative contraindications
• Minor deficits – nondisabling
• Seizure at onset
• MI within last 3 months
  • Consider initial tPA for concurrent MI
• Pregnancy
• Stroke Mimics

No longer listed
• Age < 18
• Glucose > 400
• Improving symptoms

Stroke 2018;49(3):e46-e110

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tPA candidates: 3- to 4.5- hour interval

• It may be reasonable to give tPA to those with:
  • Age >80
  • On warfarin with INR ≤ 1.7
  • History of stroke and diabetes

• The benefit of tPA is uncertain in patients with very severe stroke symptoms (NIHSS score >25)

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Options to treat hypertension in patients who are candidates for tPA

<table>
<thead>
<tr>
<th>BP &gt; 185/110 mmHg, but otherwise tPA candidates</th>
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<tbody>
<tr>
<td>Labetalol 10-20mg IV, may repeat x1</td>
</tr>
<tr>
<td>Nicardipine 5mg/hour, titrate every 5-15 mins to max of 15mg/hour</td>
</tr>
<tr>
<td><strong>Maintain BP &lt;180/105 mmHg during and after tPA therapy</strong></td>
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<tr>
<td>Monitor BP every 15 minutes for 2 hours, then every 30 min for 6 hours, then hourly</td>
</tr>
<tr>
<td><strong>If SBP &gt;180-230 mmHg or DBP &gt;105-120 mmHg</strong></td>
</tr>
<tr>
<td>Labetalol 10mg IV followed by continuous infusion</td>
</tr>
<tr>
<td>Nicardipine continuous infusion</td>
</tr>
<tr>
<td><strong>If BP not controlled</strong></td>
</tr>
<tr>
<td>Consider IV sodium nitroprusside</td>
</tr>
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*Other agents may be considered based on comorbidities, etc.*
Mechanical Thrombectomy

- Patients should receive mechanical thrombectomy if they meet the following criteria:
  - Pre-stroke mRS of 0-1
  - ≥ 18 years of age
  - NIHSS score ≥ 6
  - Can be initiated within 6 hours of symptom onset (may be reasonable in up to 24 hours in select patients)
  - Dependent on location of the causative occlusion

- Patients eligible for IV alteplase should receive IV alteplase even if EVTs are being considered
Antiplatelet Therapy

• Administration of aspirin is recommended within 24 to 48 hours of onset
  • Delay until 24 hours in patients treated with tPA
  • 160-300mg
• Treatment for 21 days with dual antiplatelet therapy can be beneficial for early secondary stroke prevention for a period of up to 90 days of symptom onset
  • Aspirin and clopidogrel
  • Begun within 24 hours

CHANCE Trial

Clopidogrel in High Risk Patients with Acute Nondisabling Cerebrovascular Events

• Clopidogrel + aspirin for 21 days, then clopidogrel to 90 days
• Less recurrent stroke at 90 days with dual antiplatelet therapy
  • HR: 0.68, p<0.001
  • Durable treatment effect at 1-year
Anticoagulants

• Urgent anticoagulation with the goal of preventing early recurrence, preventing worsening of neuro symptoms or improving outcomes is not recommended for patients with acute stroke

General Support
A 57-year old female presents to the ED for an acute stroke with a blood pressure of 196/102 mmHg, but is otherwise a candidate for tPA. What is the best course of action?

A. Do not give tPA
B. Start a nifedipine continuous infusion. You can start the tPA once her BP is $\leq 140/90$ mmHg
C. Start a nifedipine continuous infusion. You can start the tPA once her BP is $\leq 180/105$ mmHg
D. Start a nifedipine continuous infusion. You can stat the tPA once her BP is $\leq 185/110$ mmHg

A 57-year old female with uncontrolled hypertension presents to the ED for acute ischemic stroke with a blood pressure of 196/102 mmHg. She is outside the window for tPA use, but her neurologic symptoms seem to still be unstable. What is the best course of action?

A. Start a nifedipine continuous infusion titrated to $\leq 140/90$ mmHg to prevent neurologic worsening
B. Start a nifedipine continuous infusion titrated to $\leq 180/105$ mmHg to prevent neurologic worsening
C. Start a nifedipine continuous infusion and titrate to a goal reduction of 15% in SBP to prevent neurologic worsening
D. There is no need to address her blood pressure at this time
Blood Pressure

• Early treatment of hypertension is indicated when required by comorbid conditions.
  • Acute coronary event, acute heart failure, aortic dissection, post-thrombolysis ICH, preeclampsia/eclampsia
  • Lower by 15% initially

• If BP <220/120 mmHg and tPA not given, lowering BP does not help prevent death or dependency

• If BP >220/120 mmHg and tPA not given, lowering BP by 15% in the 1st 24 hours is reasonable

• Reasonable to start/restart antihypertensives in patients with BP > 140/90 mmHg who are neurologically stable

Blood Glucose

• It is reasonable to treat hyperglycemia to achieve a blood glucose in the range of 140-180 mg/dL
  • Persistent in-hospital hyperglycemia during 1st 24 hours is associated with worse outcomes
  • Hypoglycemia (<60 mg/dL) should be treated
Deep Vein Thrombosis (DVT) Prophylaxis

- Intermittent pneumatic compression is recommended in immobile stroke patients (in addition to aspirin)
- The benefit of pharmacologic DVT prophylaxis with subcutaneous heparin or LMWH is not established
  - If given, drug choice is uncertain

Seizures

- Recurrent seizures after stroke should be treated similarly as when they occur otherwise. Anti-seizure drugs should be based on patient characteristics
- Prophylactic use of anti-seizure drugs is not recommended
In-Hospital Initiation of Secondary Prevention

Evaluation

Brain imaging
• Routine use of MRI is not cost-effective, and not recommended for initial diagnosis or to plan subsequent treatment

Vascular imaging
• Candidates for CEA or stenting should have noninvasive imaging of the cervical vessels within 24 hours of admission

Cardiac Evaluation
• Cardiac monitoring is recommended to screen for atrial fibrillation/other serious arrhythmias that require intervention for at least initial 24 hours
• The benefit of prolonged monitoring is uncertain

Stroke 2018;49(3):e46-e110
Screening for Secondary Prevention

- Glucose:
  - It is reasonable to screen all patients for diabetes mellitus
  - COR IIA, LOE C-EO

- Cholesterol
  - Routine measurement of lipids in all patients not taking a high-intensity statin is not recommended (COR: no benefit; LOE: B-R)
  - Measurement of lipids may be reasonable in patients on an optimized statin regimen may be useful in identifying patients who would be candidates for a PCSK9 inhibitors (COR: IIb; LOE: B-R)

Other Testing

- Routine screening for hyperhomocysteinemia is not indicated
- There is unknown utility of screening for thrombophilic states
  - Anticoagulation may be considered in patients with abnormal findings on coagulation testing after an ischemic stroke depending on the clinical circumstances
- Routine testing for antiphospholipid antibodies is not recommended
It is reasonable to switch a patient who developed an ischemic stroke on 162mg of aspirin daily to warfarin to prevent further strokes

A. True  
B. False

Antithrombotic Treatment

- Antiplatelet agents recommended over oral anticoagulation for non-cardioembolic stroke
- In patients with noncardioembolic stroke while on aspirin, the benefit of increasing the dose or switching to an alternative antiplatelet is not well established
- In patients with noncardioembolic stroke while on antiplatelet therapy, switching to warfarin is not beneficial for secondary prevention
- For most patients with stroke in the setting of atrial fibrillation, it is reasonable to initiate oral anticoagulation within 4-14 days after symptom onset
Antithrombotic Treatment

- For patients with ischemic stroke, atrial fibrillation and coronary artery disease
  - Utility of adding antiplatelet to anticoagulation is uncertain
  - May be warranted in unstable angina or coronary artery stenting
- In patients with hemorrhagic transformation, initiation/continuation of antiplatelet or anticoagulant therapy dependent on the clinical scenario
- In patients with stroke and extracranial carotid or vertebral arterial dissection, antiplatelet or anticoagulant therapy for 3 to 6 months may be reasonable

Statins

- It is reasonable to initiate/continue statin therapy during the acute period
- High-intensity statin therapy should be initiated/continued as 1st line therapy in patients with clinical ASCVD< 75 years of age
- In patients ≥75 years of age, it is reasonable to weigh risks vs. benefits
Questions?