Ischemic Stroke Update 2016

J. Stephen Huff, MD

Professor of Emergency Medicine and Neurology
University of Virginia

Virginia College of Emergency Physicians
Hot Springs, Virginia  2016
Stroke update 2016

Diagnostic issues
Treatment update
AHA Statement 2016
Intra-arterial treatments
Diagnostic issues

Stroke mimics – false positives

Stroke chameleons – false negatives
Cutoff Point A:
↑ Sensitivity
↓ False Negative Rate
↓ Specificity
↑ False Positive Rate

Cutoff Point B:
↓ Sensitivity
↑ False Negative Rate
↑ Specificity
↓ False Positive Rate
Stroke mimics

Non-stroke conditions symptoms similar to stroke
10-25% presentations
Stroke mimics

Non-stroke conditions that may present with symptoms similar to stroke

10-25% presentations

- intracranial hemorrhage
- seizures / postictal paralysis
- hypoglycemia
- migraine
- old stroke / reactivation
- mass lesions
- spinal cord lesions
- functional
Stroke mimics

When is it a mimic?

Up to 30% of patients treated with IV tPA were mimics in some series
Stroke chameleons

Stroke takes on appearance of something else
altered mental status
TIA
vertigo
movement disorders
pain syndromes
Diagnostic issues

What is the best biomarker?

- history and physical examination
- imaging
  - CT
  - CT-A
  - MRI / MRA

Weigh against time-sensitive treatment
Diagnostic issues

Accurate diagnosis vs. meeting metrics

What is acceptable miss rate? complication rate?
Stroke Treatment

NINDS trial – inclusions
age $\geq$ 18
measurable deficit
time onset < 3 hours
Stroke Treatment

NINDS trial – Phase 2 safety trial

Exclusions

- intracranial hemorrhage
- large infarction
- uncontrolled hypertension
- seizure
- coagulopathy
- recent major surgery, trauma, GI bleed
- mild stroke symptoms
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AHA/ASA new statement 2016
- expansion of use IV tPA
- include older patient in treatment
- include severe strokes
- include mild disabling strokes

Time
- include 3 to 4.5 hour from onset
AHA/ASA Scientific Statement

Scientific Rationale for the Inclusion and Exclusion Criteria for Intravenous Alteplase in Acute Ischemic Stroke
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 group known to chairman
Approved by AHA committees

January 16, 2016
Levels of Evidence     Levels A, B, C

Size of Treatment Effect     Class I, IIa, IIb, III
Time From Symptom Onset: Recommendations

1. The time from last seen normal to treatment with intravenous alteplase should be <3 hours for eligible patients with the use of standard eligibility criteria (*Class I; Level of Evidence A*).

2. Intravenous alteplase treatment in the 3- to 4.5-hour time window is also recommended for those patients <80 years of age without a history of both diabetes mellitus and prior stroke, NIHSS score <25, not taking any OACs, and without imaging evidence of ischemic injury involving more than one third of the MCA territory (*Class I; Level of Evidence B*).
Stroke Severity: Recommendations

1. For severe stroke symptoms, intravenous alteplase is indicated within 3 hours from symptom onset of ischemic stroke. Despite increased risk of hemorrhagic transformation, there is still proven clinical benefit for patients with severe stroke symptoms (Class I; Level of Evidence A)
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For patients with mild but disabling stroke symptoms, intravenous alteplase is indicated within 3 hours from symptom onset of ischemic stroke. There should be no exclusion for patients with mild but nonetheless disabling stroke symptoms in the opinion of the treating physician from treatment with intravenous alteplase because there is proven clinical benefit for those patients (Class I; Level of Evidence A).
Within 3 hours from symptom onset, treatment of patients with milder ischemic stroke symptoms that are judged as nondisabling may be considered. Treatment risks should be weighed against possible benefits; however, more study is needed to further define the risk-to-benefit ratio (*Class IIb; Level of Evidence C*).
Intravenous alteplase treatment is reasonable for patients who present with moderate to severe ischemic stroke and demonstrate early improvement but remain moderately impaired and potentially disabled in the judgment of the examiner (Class IIa; Level of Evidence A).

Because time from onset of symptoms to treatment has such a powerful impact on outcome, delaying treatment with intravenous alteplase to monitor for further improvement is not recommended (Class III; Level of Evidence C).
>80 years of age. Older age is an adverse prognostic factor in stroke but does not modify the treatment effect of thrombolysis. Although older patients have poorer outcomes, higher mortality, and higher rates of sICH than those <80 years of age, compared with control subjects, intravenous alteplase provides a better chance of being independent at 3 months across all age groups (Class I; Level of Evidence A).
The efficacy and risk of intravenous alteplase administration in the pediatric population (neonates, children, and adolescents <18 years of age) are not well established (Class IIb; Level of Evidence B).
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Anticoagulant Use: Recommendations

1. Intravenous alteplase may be reasonable in patients who have a history of warfarin use and an INR ≤1.7 (Class IIb; Level of Evidence B).
2. Intravenous alteplase in patients who have a history of warfarin use and an INR >1.7 is not recommended (Class III; Level of Evidence B).
3. Intravenous alteplase in patients who have received a dose of LMWH within the previous 24 hours is not recommended. This applies to both prophylactic doses and treatment doses (Class III; Level of Evidence B).
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The use of intravenous alteplase in patients taking direct thrombin inhibitors or direct factor Xa inhibitors has not been firmly established but may be harmful (Class III; Level of Evidence C). The use of intravenous alteplase in patients taking direct thrombin inhibitors or direct factor Xa inhibitors is not recommended unless laboratory tests such as aPTT, INR, platelet count, ecarin clotting time, thrombin time, or appropriate direct factor Xa activity assays are normal or the patient has not received a dose of these agents for >48 hours (assuming normal renal metabolizing function).
Given the extremely low risk of unsuspected abnormal platelet counts or coagulation studies in a population, it is reasonable that urgent intravenous alteplase treatment not be delayed while waiting for hematologic or coagulation testing if there is no reason to suspect an abnormal test (Class IIa; Level of Evidence B).
Extended 3- to 4.5-Hour Window: Recommendations

1. Intravenous alteplase is recommended for carefully selected patients who meet ECASS III criteria and are treated in the 3½ to 4.5-hour window (Class I; Level of Evidence B).
2. For patients >80 years of age presenting in the 3- to 4.5-hour window, intravenous alteplase treatment is safe and can be as effective as in younger patients (Class IIa; Level of Evidence B).
3. For patients taking warfarin and with an INR <1.7 who present in the 3- to 4.5-hour window, intravenous alteplase treatment appears safe and may be beneficial (Class IIb; Level of Evidence B).
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Opinion

4. The benefit of intravenous alteplase administration for acute stroke patients with a baseline NIHSS score >25 and presenting in the 3- to 4.5-hour window is uncertain (Class IIb; Level of Evidence C).

5. In acute ischemic stroke patients with prior stroke and diabetes mellitus presenting in the 3- to 4.5-hour window, intravenous alteplase may be as effective as treatment in the 0- to 3-hour window and may be a reasonable option (Class IIb; Level of Evidence B).
Uncontrolled Hypertension, Severe Hypertension, Repeated Blood Pressure, or Requiring Aggressive Treatment: Recommendations

1. Intravenous alteplase is recommended in patients whose blood pressure can be lowered safely (to <185/110 mm Hg) with antihypertensive agents, with the physician assessing the stability of the blood pressure before starting intravenous alteplase (Class I; Level of Evidence B).

2. If medications are given to lower blood pressure, the clinician should be sure that the blood pressure is stabilized at the lower level before beginning treatment with intravenous alteplase and maintained below 180/105 mm Hg for at least the first 24 hours after intravenous alteplase treatment (Class I; Level of Evidence B).
Rapidly Improving: Recommendations

1. Intravenous alteplase treatment is reasonable for patients who present with moderate to severe ischemic stroke and demonstrate early improvement but remain moderately impaired and potentially disabled in the judgment of the examiner (*Class IIa; Level of Evidence A*).

2. Because time from onset of symptoms to treatment has such a powerful impact on outcome, delaying treatment with intravenous alteplase to monitor for further improvement is not recommended (*Class III; Level of Evidence C*).
Seizure at Stroke Onset Syndrome: Recommendation

1. Intravenous alteplase is reasonable in patients with a seizure at the time of onset of acute stroke if evidence suggests that residual impairments are secondary to stroke and not a postictal phenomenon (Class IIa; Level of Evidence C).
Psychogenic/Conversion/Malingering SM: Recommendation

1. The risk of symptomatic intracranial hemorrhage in the SM population is quite low; thus, starting intravenous alteplase is probably recommended in preference over delaying treatment to pursue additional diagnostic studies (Class IIa; Level of Evidence B).
tPA + IR

clear stroke syndrome/large vessel
IV lytic therapy limited benefit
Are other options available?
intra-arterial devices after IV t-PA
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Intra-arterial therapy / new trials
Better patient selection
internal carotid
proximal MCA occlusion
groin puncture within 6 hours
Newer devices
faster reperfusion
less vascular trauma
Intra-arterial therapies
Stent retrieval devices
New trials
  MR CLEAN
  ESCAPE
  EXTEND-IA
  SWIFT-PRIME
  REVASCAT
Future research

Biomarkers
 Patients with mild stroke
 Multimodal cerebral imaging
 Patients taking anticoagulants
 Patients with preexisting deficits
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University of Virginia

huff@virginia.edu