Disclosures

Free!

Clinical Policy: Use of Intravenous tPA for the Management of Acute Ischemic Stroke in the Emergency Department

This clinical policy is the result of a collaborative effort of the American College of Emergency Physicians and the American Academy of Neurology.

Ann of EM 2013

Patient Management Recommendations

**Level A recommendation.** In order to improve functional outcomes, IV tPA should be offered to acute ischemic stroke patients who meet National Institute of Neurological Disorders and Stroke (NINDS) inclusion/exclusion criteria and can be treated within 3 hours after symptom onset.

**Level B recommendation.** In order to improve functional outcomes, IV tPA should be considered in acute ischemic stroke patients who meet European Cooperative Acute Stroke Study (ECASS III) inclusion/exclusion criteria and can be treated between 3 to 6 hours after symptom onset.

*The effectiveness of tPA has been less well established in institutions without the systems in place to safely administer the medication.*

tPA is an Effective, Proven Therapy for Acute Stroke
MAST-I Lancet 1995
Tx Time < 6 hours
Streptokinase
No Benefit

ECASS I JAMA 1995
Intravenous Thrombolytic With Recombinant Tissue Plasminogen Activator for Acute Hemispheric Stroke
The European Cooperative Acute Stroke Study (ECASS)
Tx Time < 6 hours
Streptokinase
No Benefit

ECASS I JAMA 1995

Two Studies
Part 1 - 291 patients
Time < 3 hours
Outcome - 24 hours
No Benefit
ICH 6.4% vs. 0.6%
NNH = 16
NEJM 1995

Part 2 - 333 patients
Time < 3 hours
Outcome - 90 days
NNT = 8
**Thrombolytic Therapy with Streptokinase in Acute Ischemic Stroke**

**MAST-E NEJM 1996**
- Tx Time < 6 hours
  - Streptokinase
  - HARM - STOPPED EARLY

**Streptokinase for Acute Ischemic Stroke With Relationship to Time of Administration**
- ASK JAMA 1996
- Tx Time < 4 hours
  - Streptokinase
  - HARM - STOPPED EARLY

**ECASS II Lancet 1998**
- Randomized double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischemic stroke (ECASS II)
- Tx Time < 6 hours
  - Alteplase
  - No Benefit

**ATLANTIS B JAMA 1999**
- Tx Time < 6 hours
  - Alteplase
  - HARM - STOPPED EARLY

**DIAS-2 Lancet Neurol 2009**
- Tx Time 3 - 9 hours
  - Desmoteplase
  - No Benefit

**NEJM 2008**
- Treatment Time: 3 - 4.5 hours
  - Outcome: More favorable neuro outcome, no mortality difference
  - NNT = 15

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**3 Categories of Scientific Misconduct:**

1. Fabrication
   - Making up data

2. Falsification
   - Distorting data

3. Questionable Research Practices:
   - Cooking data
   - Authoring data
   - Concealing conflicts of interest
Modified Rankin Scale

0 - No Symptoms
1 - No significant disability
2 - Slight disability
3 - Moderate disability (can walk unassisted)
4 - Moderately Severe disability
5 - Severe disability
6 - Dead

Modified Rankin Scale

0 - No Symptoms
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5 - Severe disability
6 - Dead

Treatment Time: 0 - 6 hours

Outcome: No diff in primary outcome
Short Term Mortality Incr by 4%

Lancet 2012

No Benefit	Harm	Benefit

MAST-I	MAST-E	NINDS II
ECASS I	ASK	ECASS III
NINDS I	ATLANTIS B
ECASS II	ATLANTIS A
DIAS
IST-3

WITH A STROKE, TIME LOST IS BRAIN LOST.

Learn more at StrokeAssociation.org or 1-888-4-STROKE.
The benefits and harms of intravenous thrombolysis with recombinant tissue plasminogen activator within 6 hours of acute ischemic stroke: The third international stroke trial (IST-3), a randomized controlled trial.

Lancet 2012

Thrombolysis for acute ischemic stroke


NO DIFFERENCE ACROSS TIME WINDOWS

Cochrane Database 2009

AN INTERNATIONAL RANDOMIZED TRIPLE-PLACED THROMBOLYTIC STRATEGY FOR ACUTE ISCHEMIC INFARCTION

NEJM 1993

<table>
<thead>
<tr>
<th>Table 3. Incidence of Stroke and Bleeding Complications.</th>
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</thead>
<tbody>
<tr>
<td>Stroke Type</td>
</tr>
<tr>
<td>Within 1-hr window</td>
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<tr>
<td>Within 3-hr window</td>
</tr>
<tr>
<td>After 3-hr window</td>
</tr>
<tr>
<td>Thrombolysis</td>
</tr>
<tr>
<td>N = 720</td>
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<tr>
<td>Ischemic stroke</td>
</tr>
<tr>
<td>2.34</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
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<tr>
<td>0.45</td>
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</tbody>
</table>

NEJM 1993

NO EVIDENCE THAT ONE LYTIC AGENT BETTER THAN ANOTHER

Cochrane Database 2013

Thrombolysis (different doses, routes of administration and agents) for acute ischemic stroke

Cochrane Database 1995
Use of Tissue-Type Plasminogen Activator for Acute Ischemic Stroke
The Cleveland Area Experience

JAMA 2000

Determining Intravenous rt-PA Eligibility in the Emergency Department

Neuro Crit Care 2007

Review, Historical Context, and Clarifications of the NINDS rt-PA Stroke Trials Exclusion Criteria
Part 1: Rapidly Improving Stroke Symptoms

Stroke 2013
TPA for TIA: The case for “off-label” use of thrombolytics

Am J EM 2013

No Benefit Harm Benefit
MAST-I MAST-E
ECASS I ASK
NINDS I ATLANTIS B
ECASS II ATLANTIS A
DIAS
IST-3

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