ACUTE ISCHEMIC STROKE

Current Treatment Approaches for Acute Ischemic Stroke
2015 FOCUSED UPDATE TO 2013 GUIDELINES FOR THE EARLY MANAGEMENT OF ACUTE ISCHEMIC STROKE

Critical to Success Outcomes for Ischemic Stroke Patients

1. **rapid identification of a stroke**
2. **immediate EMS transport to closest appropriate stroke center**
3. **Standard of Care:**
   Alteplase (IV r-tPA) within 4.5 hrs of onset
   
   1.9 times as likely to have a more favorable outcome
Critical to Success Outcomes for Ischemic Stroke Patients Continued

Mechanical thrombectomy with patients with large vessel occlusion (after IV r-tPA) within 6 hrs of onset

- 70% improvement with patients.*
- Improved early neurological recovery
- Improved functional outcome at 3 months
- No significant safety concerns

Assess the patient for the administration for alteplase (IV r-tPA). If eligible, all acute ischemic stroke patients should receive Alteplase (IV r-tPA).

- **Criteria for Alteplase (IV r-tPA) within 3 Hours from Symptom Onset**
  - Diagnosis of ischemic stroke causing measurable neurological deficit
  - Onset of symptoms <3 hours before beginning treatment
  - Satisfies exclusion criteria*

- **Criteria for Alteplase (IV r-tPA) within 3 – 4.5 Hours from Symptom Onset**
  - Diagnosis of ischemic stroke causing measurable neurological deficit
  - Onset of symptoms within 3 – 4.5 hours before beginning treatment
  - Satisfies exclusion criteria*

Alteplase (IV r-tPA) within 4.5 hours of stroke onset remains the standard of care for most ischemic stroke patients.

*Do not administer alteplase to treat acute ischemic stroke in the following situations in which the risk of bleeding is greater than the potential benefit: current intracranial hemorrhage, subarachnoid hemorrhage, active internal bleeding, recent (within 3 months) intracranial or intraspinal surgery or serious head trauma, presence of intracranial conditions that may increase the risk of bleeding (e.g., some neoplasms, arteriovenous malformations, or aneurysms), bleeding diathesis, current severe uncontrolled hypertension. Refer to the alteplase package insert for more information.
Exclusion Criteria for Alteplase (IV r-tPA)  Up to 4.5 Hours From Symptom Onset

- Age > 80 years
- Severe stroke (NIHSS > 25)
- History of diabetes and prior stroke
- Taking an oral anticoagulant regardless of INR

For a complete list of exclusion criteria, please see the AHA/ASA 2015 AIS Guideline Update and 2013 Early Management of Ischemic Stroke.
After the patient is administered alteplase (IV r-tPA), and the cause is deemed to be occlusion of a large cerebral artery in the anterior circulation, considered endovascular therapy, best accomplished with a stent retriever.

Criteria for **Endovascular Therapy**

- Pre-stroke modified Rankin Score (mRs 0-1)
- Acute ischemic stroke receiving alteplase (IV r-tPA) within 4.5 hours of onset according to guidelines from professional medical societies
- Causative occlusion of the internal carotid artery or proximal Middle Cerebral Artery (M1)
- Age 18 years or older
- National Institutes of Health Stroke Scale (NIHSS) score of 6 or greater
- Alberta Stroke Program Early Computed Tomography Score (ASPECTS) of 6 or greater
- Treatment can be initiated (groin puncture) within 6 hours of symptom onset.
Recommendations for Endovascular Therapy

- After alteplase (IV r-tPA) initiation in carefully selected patients with large vessel occlusion, early mechanical thrombectomy within 6 hours of stroke onset using stent retrievers leads to faster and more complete reperfusion.

- Initial treatment with intra-arterial fibrinolysis is beneficial for carefully selected patients with major ischemic strokes of <6 hours duration caused by occlusions of the MCA.
Emergency nonenhanced CT imaging of the brain is recommended before any specific treatment for acute stroke.

Eligible patients should receive intravenous r-tPA even if endovascular treatments are being considered.

Noninvasive intracranial vascular imaging should be obtained as quickly as possible after IV r-tPA.

Patients should receive endovascular therapy with a stent retriever if they meet all the criteria.

To ensure benefit, reperfusion to TICI grade 2b/3 should be achieved as early as possible and within 6 hours of stroke onset.

BENEFITS AND RISKS
The original 2 NINDS trials first showed the safety and efficacy of alteplase (IV r-tPA) in 1995.

Patients who are treated with alteplase (IV r-tPA) have better overall outcome (43% versus 32%), are more able to perform activities of daily living (53% versus 32%) and are more likely to have good outcome with no or minimal deficit 1 year after stroke (39% versus 26% at 3 months).

Patients who are treated with alteplase (IV r-tPA) are discharged home earlier, are more often discharged home rather than to a nursing home and report a better quality of life.

RISKS OF ALTEPLASE (IV r-tPA) AT 0 – 3 HOURS

- Bleeding is the major risk (greatest risk bleeding into the brain, gums, urine, retroperineal, etc.).
- Death - Mortality in the 2 treatment groups was similar at 3 months.

BENEFITS OF ALTEPLASE (IV r-tPA) AT 3 – 4.5 HOURS

- Treatment with alteplase (IV r-tPA) is not FDA-approved during this time window. However, several large studies have demonstrated its safety and potential efficacy in a selected patient population.

- The ECASS III trial excluded people >80 years old, those with very severe strokes (baseline NIHSS>25), those taking oral anticoagulants and those who had the combination of a previous stroke and diabetes mellitus.

- Patients in this study who received alteplase (IV r-tPA) had less disability at 90 days than their placebo treated counterparts (52.4% had zero or minimal disability compared to 45.2% in the placebo arm).
Bleeding is the major risk. Change in neurologic status due to bleeding in the brain occurred in 2.8% of patients treated with alteplase (IV r-tPA) and 0.2% of patients given placebo (ECASS III study, 3 – 4.5 hours).

Death - Studies show no differences in mortality with or without IV r-tPA.
Rapid intravenous therapy with *alteplase (IV r-tPA)* in appropriate patients remains the Gold Standard and should be administered in all eligible patients prior to *endovascular therapy*.

Patients in most of these studies also received alteplase (IV r-tPA).

- Eligible patients should receive endovascular therapy after receiving alteplase (IV r-tPA) for a large vessel occlusion (carotid artery or M1 segment of the MCA).
- Endovascular therapy may be administered if patient is out of the *window for alteplase* (IV r-tPA) in select patients.

Endovascular therapy may be more effective, and therefore preferable, for treating larger clots in patients with severe neurological deficits and radiographic evidence of occlusion of a major artery in the brain.

In 4 recent trials, the average of patients reaching a modified Rankin Scale of 0-2 in 90 days*

- 28% for the control group
- 47% for endovascular treatment

70% improvement

### SUMMARY OF CLINICAL TRIALS

<table>
<thead>
<tr>
<th></th>
<th>MR CLEAN</th>
<th>SWIFT PRIME</th>
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<tbody>
<tr>
<td><strong>NUMBER OF PATIENTS (C/A</strong>)**</td>
<td>233/267</td>
<td>98/98</td>
</tr>
<tr>
<td><strong>ASPECTS (MEDIAN)</strong></td>
<td>9/9</td>
<td>9/9</td>
</tr>
<tr>
<td><strong>NIHSS (MEAN)</strong></td>
<td>17/18</td>
<td>17/17</td>
</tr>
<tr>
<td><strong>ENROLLMENT BY CTA/MRA/DSA</strong></td>
<td>ICA 0.4/1.1, ICA+M1 25.5/28.2, M1 66.1/62.0, M2 7.77/9.9, A1/A2 6.0/6.9</td>
<td>ICA 18.3/16.0, M1 67/77, M2 14/6</td>
</tr>
<tr>
<td><strong>ALTEPLASE (IV r-PA) (ONSET TO TREATMENT) (MEDIAN)</strong></td>
<td>85/87 mins</td>
<td>110.5/117 mins</td>
</tr>
<tr>
<td><strong>ENDOVASCULAR THERAPY</strong></td>
<td>81.5% SR** (21% intra-arterial therapy)</td>
<td>88.8% SR</td>
</tr>
<tr>
<td><strong>TIME TO GROIN PUNCTURE (MEDIAN) MINS</strong></td>
<td>260</td>
<td>224</td>
</tr>
<tr>
<td><strong>RECANALIZATION TO TICI 2B/3</strong></td>
<td>59%</td>
<td>88%</td>
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*C/A = CONTROL/ACTIVE TREATMENT **SR = STENT RETRIEVER
<table>
<thead>
<tr>
<th>TRIALS</th>
<th>EXTEND IA</th>
<th>ESCAPE</th>
<th>REVASCAT</th>
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<tr>
<td><em><em>NUMBER OF PATIENTS (C/A</em>)</em>*</td>
<td>35/35</td>
<td>165/150</td>
<td>102/103</td>
</tr>
<tr>
<td><strong>ASPECTS (MEDIAN)</strong></td>
<td>not given</td>
<td>9/9</td>
<td>7/8</td>
</tr>
<tr>
<td><strong>NIHSS (MEAN)</strong></td>
<td>17/13</td>
<td>16/17</td>
<td>17/17</td>
</tr>
<tr>
<td><strong>ENROLLMENT BY CTA/MRA/DSA</strong></td>
<td>ICA 31/31, M1 57/51, M2 11/17</td>
<td>ICA+M1 27.5/28.5, M1/all M2 66.1/71.4, M2 3.7/2.0</td>
<td>ICA 0/1, ICA+M1 26/27, M1 65/64, M2 10/8</td>
</tr>
<tr>
<td><strong>ALTEPLASE (IV r-PA) (ONSET TO TREATMENT) (MEDIAN)</strong></td>
<td>127/145 mins</td>
<td>110/125 mins</td>
<td>118/105 mins</td>
</tr>
<tr>
<td><strong>ENDOVASCULAR THERAPY</strong></td>
<td>77% SR**</td>
<td>72.5% SR</td>
<td>95% SR</td>
</tr>
<tr>
<td><strong>TIME TO GROIN PUNCTURE (MEDIAN) MINS</strong></td>
<td>210</td>
<td>not given</td>
<td>269</td>
</tr>
<tr>
<td><strong>RECANALIZATION TO TICI 2B/3</strong></td>
<td>86%</td>
<td>72%</td>
<td>66%</td>
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</table>

*C/A = CONTROL/ACTIVE TREATMENT  **SR = STENT RETRIEVER
Major risk is intracranial hemorrhage due to: vessel perforation (ripping the blood vessel) or stent retriever device perforating a vessel while attempting to remove the blood clot from the artery.

- Systemic bleeding
- Bleeding at the site of catheter introduction
- Infection due to catheter introduction
- Death
RESOURCES FOR YOU AND YOUR PATIENTS

Professional Resources:
- 2015 Focused Update to the 2013 AIS Guidelines
- 2015 Focused Update to the 2013 AIS Guidelines quick sheet
- and Healthcare professional guide

Patient Resources:
- In-Hospital Patient Education Deck
- Patient Brochures
- and more!

Coming Soon:
- Healthcare Professional In-Hospital Webinar
- EMS/Pre-Hospital Resources
- and more!

StrokeAssociation.org/Resources
INFORMATION FOR PATIENTS AND FAMILIES
The following information can help support conversations with patients and their families about acute ischemic stroke treatment.

- Current treatment recommendations for eligible patients with acute ischemic stroke have proved highly beneficial with acceptable risk.
- Early IV r-tPA followed by mechanical stent thrombectomy is the new standard of care for patients who qualify.
- Alternate interventions are also beneficial for patients who do not qualify.
- Rapid intervention is critical to successful treatment.
- Interventions without general anesthesia are associated with a better outcome.
- Systems of care are being organized to facilitate the delivery of this care.

For additional information, please refer to the AHA/ASA 2015 AIS Guideline Update and 2013 Early Management of Ischemic Stroke.
CASE STUDY 1 & 2

Courtesy of:
Mitchell S.V. Elkind, MD, Columbia University
and Shadi Yaghi, MD. Brown University
CASE 1

- 20 YO man with no past medical history presented to an outside hospitalist with sudden left sided weakness and imbalance followed by decreased level of consciousness. CT were performed showing no hemorrhage and no acute changes, hyper-dense basilar artery and CTA done showed a mid basilar occlusion. He received intravenous tPA and was transferred to a comprehensive stroke center where he underwent mechanical thrombectomy. His exam improved and he was discharged to home after 2 days. On 3 months follow up, he was back to normal and was back to college.
A 20 year old man with no past medical history presented to a primary stroke center with sudden left sided weakness and imbalance followed by decreased level of consciousness. Head CT showed no hemorrhage, no acute ischemic changes, and a hyper-dense basilar artery (Figure 1, arrow). CT angiography showed a mid-basilar occlusion (Figure 2, arrow).
He received intravenous tPA and was transferred to a comprehensive stroke center where angiography confirmed mid-basilar occlusion (Figure 3, arrow). He underwent mechanical thrombectomy (Figure 4) with recanalization of the basilar artery.

His neurological exam improved and he was discharged to home after 2 days. At 3 month follow up, he was back to normal and was back to college.
CASE 2
CASE 2

- 62 YO woman with a history of hypertension and hyperlipidemia presented with sudden onset left sided weakness. She presented to an outside hospital ED where her exam showed an NIHSS = 22 (right sided plegia, left gaze preference, right HH, right facial droop, global aphasia, and dysarthria). CT brain showed no acute changes. CTA showed a left middle cerebral artery occlusion. She was given intravenous tPA at 2 hours from symptoms onset and transferred to a comprehensive stroke center where she underwent mechanical thrombectomy. The next day, she had very mild expressive aphasia and her NIHSS was 2 (1 for aphasia and 1 for a facial droop). 3 months later she was back to normal and back to normal (full recovery with NIHSS of 0).
A 62 year old woman with a history of hypertension and hyperlipidemia presented to a primary stroke center with sudden onset of weakness of the right side. On examination, she had a global aphasia, left gaze preference, right homonymous hemianopsia (field cut), right facial droop, dysarthria, and right hemiplegia (NIH Stroke Scale = 22). Head CT showed only equivocal hypodensity in the left middle cerebral artery territory (Figure 1). CT angiography showed a left middle cerebral artery occlusion (Figure 2, arrow). She was given intravenous tPA at 2 hours from symptom onset and transferred to a comprehensive stroke center, where digital subtraction angiography confirmed left middle cerebral artery occlusion (Figures 3 and 4, arrows). She underwent mechanical thrombectomy with recanalization of the MCA (Figure 5). The next day, she had only a very mild expressive aphasia and right facial droop (NIHSS = 2). Three months later she was back to normal.