



**Protocol for IV Alteplase Treatment of Acute Ischemic Stroke**  
*Adapted from 2018 AHA/ASA Guidelines for Acute Ischemic Stroke*

**1. Potential IV alteplase candidates**

- ◆ Patients of any age with suspected ischemic stroke **within 4.5 hours** of last known well.
- ◆ Selected patients **beyond 4.5 hours** from last known well, with unwitnessed time of onset.
- ◆ See more details regarding eligibility criteria below (#5).

**2. Sequence of events by ED (FASTER TREATMENT = BETTER CLINICAL OUTCOMES)**

- ◆ Determine “Last Known Well” time. **WITHIN 5 MIN OF ED ARRIVAL**
- ◆ Activate Stroke Team (513-584-8282) **WITHIN 10 MIN OF ED ARRIVAL**
- ◆ Perform non-contrast CT scan and CTA (head/neck). **WITHIN 20 MIN OF ED ARRIVAL**
- ◆ Draw bloods for lab tests (CBC, renal, coags, pregnancy, fingerstick glucose).
  - ◆ *Obtain fingerstick glucose promptly to determine IV alteplase eligibility.*
  - ◆ *Do not delay alteplase for other lab results unless clinical suspicion of abnormality.*
- ◆ Establish two IV lines.
- ◆ Record blood pressure.
  - ◆ *Gently treat (usually labetalol 10 mg to start, assuming no clinical contraindications) if >185/110 if potential IV alteplase candidate (details below).*
- ◆ Review eligibility criteria for IV alteplase (details below)
- ◆ Interpret CT scan -- rule out bleed or subacute ischemia. **WITHIN 35 MIN OF ARRIVAL**
- ◆ Start IV alteplase bolus if eligible. **WITHIN 45 MIN OF ARRIVAL**

**3. Treatment**

- ◆ Mix IV alteplase - 0.9 mg/kg dose (maximum 90 mg). Administer 10% as bolus over 1-2 minutes and remainder as infusion over 60 minutes.
  - Do not use the cardiac dose.
  - Do not exceed the 90 mg maximum dose.
  - Use rtPA=Activase=Alteplase. Do not use other thrombolytic agents.
  - Do not give aspirin, clopidogrel, heparin, warfarin or other oral anticoagulants for the first 24 hours after IV rt-PA.

**4. Adjunctive / Additional therapies**

- ◆ Potential alteplase candidates **should not** receive antiplatelets (aspirin, clopidogrel) or anticoagulants (heparin, warfarin, or DOACs) upon arrival to Emergency Dept.
- ◆ However, patients who have taken antiplatelets prior to arrival in the Emergency Department **are** still considered alteplase candidates and those taking anticoagulant medications **may** still be candidates as well.
- ◆ At 24 +/- 6 hours, a non-contrast CT scan or MRI should be performed (to rule out any intracranial hemorrhage) before starting an antiplatelet/anticoagulant medication.

## 5. **Key criteria for IV alteplase eligibility (from 2018 AHA/ASA Guidelines)**

- Within 4.5 hours
  - No upper age limit
  - BP <185/110 (see pretreatment recommendations below)
  - Exclusions
    - CT brain imaging exhibits extensive regions of clear hypoattenuation
    - Ischemic stroke within 3 months
    - Severe head trauma within 3 months
    - Intracranial/intraspinal surgery within 3 months
    - History of intracranial hemorrhage
    - Suspected subarachnoid hemorrhage
    - GI malignancy or recent GI bleed
    - Platelets <100 000/mm<sup>3</sup>, INR >1.7, aPTT >40 s, or PT >15 s
    - LMWH within 24 hours
    - DOAC within 48 hours
    - High suspicion of infectious endocarditis
    - Suspected aortic dissection
    - Suspected intra-axial intracranial neoplasm
- Beyond 4.5 hours from last known well (newly emerging therapy based on recently published WAKE UP trial: <https://www.nejm.org/doi/full/10.1056/NEJMoa1804355>)
  - Unwitnessed event (recognized symptoms upon awakening or unable to report timing of onset due to, for example, confusion or aphasia)
  - MRI suggestive of more recent onset of event
    - Based on MRI-DWI positivity and FLAIR negativity
  - **Note that acute MRI may be challenging to obtain in some practice environments and this may limit eligibility by this criteria at this time.**
  - Age up to 80 years and functionally independent
  - No large vessel occlusion (LVO); LVO patients are prioritized for EVT
  - Not severe stroke (NIHSS <=25)
  - Meets other standard alteplase eligibility other than time from last known well

## 6. **Post IV alteplase stroke monitoring**

- ◆ Admit patient to ICU and follow post-alteplase order set, including:
  - Monitor BP and neuro status
    - Q15 min X 2 hours, q30 min X 6 hours, then q1 hour X 16 hours
  - Treat BP>180/105 (details below)
  - Call stroke physician at 513-584-8282 if BP>180/105, decline in neuro status, or new headache, nausea, or vomiting
    - Hold infusion and repeat head CT stat
  - NPO until swallowing assessed
  - DVT prophylaxis with intermittent stocking compression devices (SCDs) but no anticoagulants
- ◆ Consider transfer to a Neuroscience Intensive Care Unit for patients needing specialized monitoring and management including:
  - Severe (NIHSS ≥10) stroke with risk of malignant MCA syndrome requiring anticipation and consideration of decompressive hemicraniectomy by neurosurgery

- Cerebellar stroke with risk of malignant edema requiring anticipation and consideration of posterior decompression by neurosurgery,
- Fluctuating neurological symptoms requiring specialized blood pressure management
- Large vessel occlusion that may require endovascular measures in upcoming hours, given the higher risk of neurological deterioration.

## 7. Blood pressure management considerations

### ◆ PRETREATMENT

- ◆ **For IV alteplase candidates:** BP should be brought to <185/110 mmHg if possible. This must be done without aggressive antihypertensive treatment for the patient to remain eligible for IV alteplase. If blood pressure remains >185/110 with nonaggressive measures (rarely), then the patient is not eligible for IV alteplase.

#### **BLOOD PRESSURE MANAGEMENT PRIOR TO IV ALTEPLASE ADMINISTRATION**

- *Up to two of the following agents may be used for nonaggressive treatment:*
  - *Labetalol 10 to 20 mg IV over 1-2 minutes, may repeat X 1\_(max dose 40 mg)*
  - *Nicardipine infusion, 5 mg/h, titrate up by 2.5 mg/h at 5-15-minute intervals (up to max dose 15 mg/h; when desired BP attained, reduce to 3 mg/h)*
  - *Enalaprilat 0.625 to 1.25 mg IV\_(up to max dose of 1.25 mg)*
  - *Hydralazine 10 mg IV over 1-2 minutes, may repeat X1\_(max dose 20 mg)*
  - *Nitropaste 1 to 2 inches\_(up to max dose of 2 inches)*
- ◆ **If not IV alteplase not planned,** then permissive HTN up to 220/120 may be reasonable.

### ◆ POST TREATMENT:

- ◆ **During/after treatment with alteplase or other acute reperfusion intervention, BP must be aggressively maintained at <180/105**
  - ◆ Monitor BP every 15 minutes for first 2 hours, then every 30 minutes for next 6 hours, then every hour for the next 16 hours.
  - ◆ Monitor blood pressure every 15 minutes during the antihypertensive therapy. Observe for hypotension.

#### **BLOOD PRESSURE MANAGEMENT DURING/AFTER ADMINISTERING IV alteplase**

*If systolic BP >180–230 mm Hg or diastolic BP >105–120 mm Hg:*

- *Labetalol 10 mg IV followed by continuous IV infusion 2–8 mg/min; or*
- *Nicardipine 5 mg/h IV, titrate up to desired effect by 2.5 mg/h every 5–15 minutes, maximum 15 mg/h*

*If BP not controlled or diastolic BP >140 mm Hg:*

- *Consider IV sodium nitroprusside*

## 8. Management of intracranial hemorrhage after thrombolysis

- ◆ If an intracranial hemorrhage is suspected, the treating stroke physician (513-584-8282) should be contacted IMMEDIATELY.
- ◆ Suspect intracranial hemorrhage if there is any acute neurological deterioration (new headache, acute hypertension, seizure, or nausea and vomiting) or acute increase in BP.
- ◆ If hemorrhage is suspected, then do the following:

**Table 8. Management of Symptomatic Intracranial Bleeding Occurring Within 24 Hours After Administration of IV Alteplase for Treatment of AIS**

Class IIb, LOE C-EO
Stop alteplase infusion
CBC, PT (INR), aPTT, fibrinogen level, and type and cross-match
Emergent nonenhanced head CT
Cryoprecipitate (includes factor VIII): 10 U infused over 10–30 min (onset in 1 h, peaks in 12 h); administer additional dose for fibrinogen level of <200 mg/dL
Tranexamic acid 1000 mg IV infused over 10 min OR ε-aminocaproic acid 4–5 g over 1 h, followed by 1 g IV until bleeding is controlled (peak onset in 3 h)
Hematology and neurosurgery consultations
Supportive therapy, including BP management, ICP, CPP, MAP, temperature, and glucose control

## 9. Management of angioedema after thrombolysis

**Table 9. Management of Orolingual Angioedema Associated With IV Alteplase Administration for AIS**

Class IIb, LOE C-EO
Maintain airway
Endotracheal intubation may not be necessary if edema is limited to anterior tongue and lips.
Edema involving larynx, palate, floor of mouth, or oropharynx with rapid progression (within 30 min) poses higher risk of requiring intubation.
Awake fiberoptic intubation is optimal. Nasal-tracheal intubation may be required but poses risk of epistaxis post-IV alteplase. Cricothyroidotomy is rarely needed and also problematic after IV alteplase.
Discontinue IV alteplase infusion and hold ACEIs
Administer IV methylprednisolone 125 mg
Administer IV diphenhydramine 50 mg
Administer ranitidine 50 mg IV or famotidine 20 mg IV
If there is further increase in angioedema, administer epinephrine (0.1%) 0.3 mL subcutaneously or by nebulizer 0.5 mL
Icatibant, a selective bradykinin B <sub>2</sub> receptor antagonist, 3 mL (30 mg) subcutaneously in abdominal area; additional injection of 30 mg may be administered at intervals of 6 h not to exceed total of 3 injections in 24 h; and plasma-derived C1 esterase inhibitor (20 IU/kg) has been successfully used in hereditary angioedema and ACEI-related angioedema
Supportive care