Protocol for IV Thrombolytic Treatment of Acute Ischemic Stroke

Adapted from the 2018-2019 AHA/ASA Guidelines for Acute Ischemic Stroke

1. Potential IV thrombolytic 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* thrombolytic *eligibility.*
  - *Do not delay thrombolytic 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 systolic or ≥110 diastolic if potential IV thrombolytic candidate (details below).*
- Review eligibility criteria for IV thrombolytic (details below)
- Interpret CT scan -- rule out bleed or subacute ischemia. **WITHIN 35 MIN OF ARRIVAL**
- Start IV thrombolytic bolus if eligible. **WITHIN 45 MIN OF ARRIVAL**

3. Treatment

- Mix IV thrombolytic (rt-PA)
  - **Tenecteplase (TNKase) - 0.25mg/kg (maximum 25mg)**. Administer as a bolus over 5 seconds, followed by a 10mL bolus of 0.9% sodium chloride (NS).
  - **OR, if tenecteplase is not available, use** alteplase (Activase) - 0.9 mg/kg dose (maximum 90 mg). Administer 10% as bolus over 1-2 minutes and the remainder as an infusion over 60 minutes.
  - Do **not** use the cardiac dose.
  - Do **not** exceed the maximum dose.
  - Use rt-PA = tenecteplase = TNKase. Do **not** use other thrombolytic agents. Use alteplase (Activase) only if tenecteplase is unavailable in the adult population. Note that the dose is different for each IV thrombolytic (see above).
  - 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 IV thrombolytic candidates **should not** receive antiplatelets (aspirin, clopidogrel) or anticoagulants (heparin, warfarin, or DOACs) upon arrival to Emergency Department
- However, patients who have taken antiplatelets prior to arrival in the Emergency Department **are** still considered IV thrombolytic 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 or anticoagulant medication.

5. Key criteria for IV thrombolytic eligibility (from 2018 AHA/ASA Guidelines)

- Within 4.5 hours
  - No upper age limit
  - SBP <185 or DBP <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/mm3, 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 (based on 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.**
  - 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 IV thrombolytic eligibility other than time from last known well

6. Post-IV thrombolytic stroke monitoring

- Admit patient to ICU and follow post-IV thrombolytic 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 SBP≥180 or DBP ≥105 (details below)
  - **Call stroke physician at 513-584-8282 if there is a decline in neuro status, 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 thrombolytic candidates**: BP should be brought to SBP <185 mmHg or DBP <110 mmHg if possible. This must be done without aggressive antihypertensive treatment for the patient to remain eligible for IV thrombolytic. If blood pressure remains ≥185 systolic or ≥110 diastolic with nonaggressive measures (rarely), then the patient is not eligible for IV thrombolytic.

BLOOD PRESSURE MANAGEMENT PRIOR TO IV THROMBOLYTIC 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 IV thrombolytic not planned**, then permissive HTN up to 220/120 may be reasonable.

- **POST TREATMENT:**
  - **During/after treatment with thrombolytic or other acute reperfusion intervention, BP must be aggressively maintained at SBP <180 or DBP <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 thrombolytic

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

Management of ICH after thrombolysis is the same with tenecteplase as it is with alteplase.

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_2 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