Protocol for Acute Ischemic Stroke Management

Acute stroke management is progressing very rapidly. Our team offers several options for acute stroke therapy, including clinical trials, and is available for immediate consultation 24 hours per day and 7 days per week.

1. When should the stroke team be called?

- Contact the Stroke Team at **(513) 844-7686** as soon a potential candidate for treatment is identified (preferably before the CT scan is completed).
- Potential treatment candidates are:
  - Patients of any age with a suspected ischemic stroke who were "Last Seen Normal" within 6 hours of symptom onset
  - Patients with a suspected TIA or minor ischemic stroke patient that were "Last Seen Normal" within 12 hours of symptom onset (to screen for the POINT Trial)

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

- Determine "Last Seen Normal" time. **WITHIN 10 MINUTES OF ED ARRIVAL**
  - Patients are eligible for IV rtPA up to *4.5 hours* from onset.
  - Select stroke patients are eligible for intra-arterial therapies up to *6 hours* from onset.
  - TIA and minor stroke patients may be eligible for the POINT Trial up to*12 hours* from onset.
- Perform brief neurological exam and activate Stroke Team (513-844-7686). **WITHIN 15 MINUTES OF ED ARRIVAL**
- Perform non-contrast CT scan rapidly to rule out intracranial hemorrhage. **WITHIN 25 MINUTES OF ED ARRIVAL**
- Draw bloods for lab tests (CBC, Renal, Coags, Pregnancy, fingerstick glucose).
  - NOTE: Fingerstick glucose should be obtained promptly to determine IV rtPA eligibility. tPA administration should not be delayed to wait for other lab results unless there is clinical suspicion for potential abnormalities.
- Establish two IV lines.

- Record blood pressure.
  - Gently treat (ie, labetolol 10 mg to start) if >185/110 if potential IV rtPA candidate.
- Perform EKG.
- Review eligibility criteria for IV rtPA (details below)
- Interpret CT scan to rule out ICH or significant ischemic changes. **WITHIN 45 MINUTES OF ARRIVAL**
- Store IV rtPA in Emergency Dept pyxus for ready accessibility.
- Start IV rt-PA bolus if eligible. **WITHIN 60 MINUTES OF ARRIVAL**

3. Treatment

- Mix IV rtPA - 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.
- Monitor the patient carefully, especially blood pressure.
  - Treat BP>180/105 (as below)
  - Repeat head CT stat if increased BP, headache, nausea, vomiting, or decline in neurological status
  - Call stroke team MD with any questions or concerns – 513-844-7686

4. Adjunctive / Additional Therapy

- Potential IV rtPA treatment candidates **should not** receive antiplatelet (aspirin, clopidogrel) or anticoagulant (heparin, warfarin, or other novel oral agents such as dabigatran) medications upon arrival to the Emergency Department if potential reperfusion treatment candidate.
- However, patients who have taken antiplatelet medications prior to arrival in the Emergency Department **are** still considered candidates and those taking anticoagulant medications **may** still be considered candidates for thrombolytic therapy.
- No concomitant antiplatelet or anticoagulant medications during the first 24 hours after symptom onset. At 24 +/- 6 hours, a non-contrast CT scan or MRI must be performed (to rule out any intracranial hemorrhage) before starting an antiplatelet or anticoagulant medication.
- Endovascular reperfusion therapies (as primary treatment of IV rtPA-ineligible patients or adjunctive therapy among IV rtPA patients with severe strokes) will be considered in select patients as per the stroke team's clinical judgment and rapidly evolving evidence. Considerations will be based on, but not limited to, the following criteria:
  - Age <85 years
  - Time from stroke onset <6 hours
  - IV rtPA ineligibility
  - Location and severity of acute thrombus (if known)
    - Including basilar artery or intracranial internal carotid thrombus (ICAT)

5. Criteria for IV rtPA Eligibility (2013 AHA/ASA Clinical Guideline, Tables 10 and 11)

Table 10. Inclusion and Exclusion Characteristics of Patients With Ischemic Stroke Who Could Be Treated With IV rtPA Within 3 Hours From Symptom Onset

Inclusion criteria
Diagnosis of ischemic stroke causing measurable neurological deficit
Onset of symptoms <3 hours before beginning treatment
Aged ≥18 years
Exclusion criteria
Significant head trauma or prior stroke in previous 3 months
Symptoms suggest subarachnoid hemorrhage
Arterial puncture at noncompressible site in previous 7 days
History of previous intracranial hemorrhage
Intracranial neoplasm, arteriovenous malformation, or aneurysm
Recent intracranial or intraspinal surgery
Elevated blood pressure (systolic >185 mm Hg or diastolic >110 mm Hg)
Active internal bleeding
Acute bleeding diathesis, including but not limited to
Platelet count <100 000/mm^3
Heparin received within 48 hours, resulting in abnormally elevated aPTT greater than the upper limit of normal
Current use of anticoagulant with INR >1.7 or PT >15 seconds
Current use of direct thrombin inhibitors or direct factor Xa inhibitors with elevated sensitive laboratory tests (such as aPTT, INR, platelet count, and ECT; TT; or appropriate factor Xa activity assays)
Blood glucose concentration <50 mg/dL (2.7 mmol/L)
CT demonstrates multilobar infarction (hypodensity >1/3 cerebral hemisphere)
Relative exclusion criteria
Recent experience suggests that under some circumstances—with careful consideration and weighting of risk to benefit—patients may receive fibrinolytic therapy despite 1 or more relative contraindications. Consider risk to benefit of IV rtPA administration carefully if any of these relative contraindications are present:
Only minor or rapidly improving stroke symptoms (clearing spontaneously)
Pregnancy
Seizure at onset with postictal residual neurological impairments
Major surgery or serious trauma within previous 14 days
Recent gastrointestinal or urinary tract hemorrhage (within previous 21 days)
Recent acute myocardial infarction (within previous 3 months)

The checklist includes some FDA-approved indications and contraindications for administration of IV rtPA for acute ischemic stroke. Recent guideline revisions have modified the original FDA-approved indications. A physician with expertise in acute stroke care may modify this list.

Onset time is defined as either the witnessed onset of symptoms or the time last known normal if symptom onset was not witnessed.

In patients without recent use of oral anticoagulants or heparin, treatment with IV rtPA can be initiated before availability of coagulation test results but should be discontinued if INR is >1.7 or PT is abnormally elevated by local laboratory standards.

In patients without history of thrombocytopenia, treatment with IV rtPA can be initiated before availability of platelet count but should be discontinued if platelet count is <100 000/mm^3.

aPTT indicates activated partial thromboplastin time; CT, computed tomography; ECT, ecarin clotting time;FDA, Food and Drug Administration; INR, international normalized ratio; IV, intravenous; PT, partial thromboplastin time; rtPA, recombinant tissue plasminogen activator; and TT, thrombin time.

Table 11. Additional Inclusion and Exclusion Characteristics of Patients With Acute Ischemic Stroke Who Could Be Treated With IV rtPA Within 3 to 4.5 Hours From Symptom Onset

Inclusion criteria
Diagnosis of ischemic stroke causing measurable neurological deficit
Onset of symptoms within 3 to 4.5 hours before beginning treatment
Relative exclusion criteria
Aged >80 years
Severe stroke (NIHSS>25)
Taking an oral anticoagulant regardless of INR
History of both diabetes and prior ischemic stroke

INR indicates international normalized ratio; IV, intravenous; NIHSS, National Institutes of Health Stroke Scale; and rtPA, recombinant tissue plasminogen activator.

6. Blood Pressure Control

- **Pretreatment**: BP should be <185/110 mmHg without aggressive antihypertensive treatment to be eligible for IV rtPA. (If not IV rtPA planned, then permissive HTN up to 220/120 is recommended).

BLOOD PRESSURE MANAGEMENT PRIOR TO IV rtPA ADMINISTRATION

- Up to two of the following agents may be used for nonaggressive treatment:
  - (1) Labetalol 10 to 20 mg IV over 1 to 2 minutes, may repeat X 1; (up to max total dose of 40 mg)
  - (2) 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 blood pressure attained, reduce to 3 mg/h)
  - (3) Enalaprilat 0.625 to 1.25 mg IV; (up to max dose of 1.25 mg)
  - (4) Hydralazine 10 mg IV over 1 to 2 minutes, may repeat X1; (up to max dose of 20 mg)
  - (5) Nitropaste 1 to 2 inches; (up to max dose of 2 inches)

- If blood pressure remains >185/110 with nonaggressive measures, then the patient is not eligible for IV rtPA

- **During and after treatment with rtPA 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 AFTER ADMINISTERING IV rtPA

Systolic 180 to 230 mm Hg or diastolic 105 to 120 mm Hg

Labetalol 10 mg IV over 1 to 2 minutes, may repeat every 10 to 20 minutes, maximum dose of 300 mg;
or
Labetalol 10 mg IV followed by an infusion at 2 to 8 mg/min

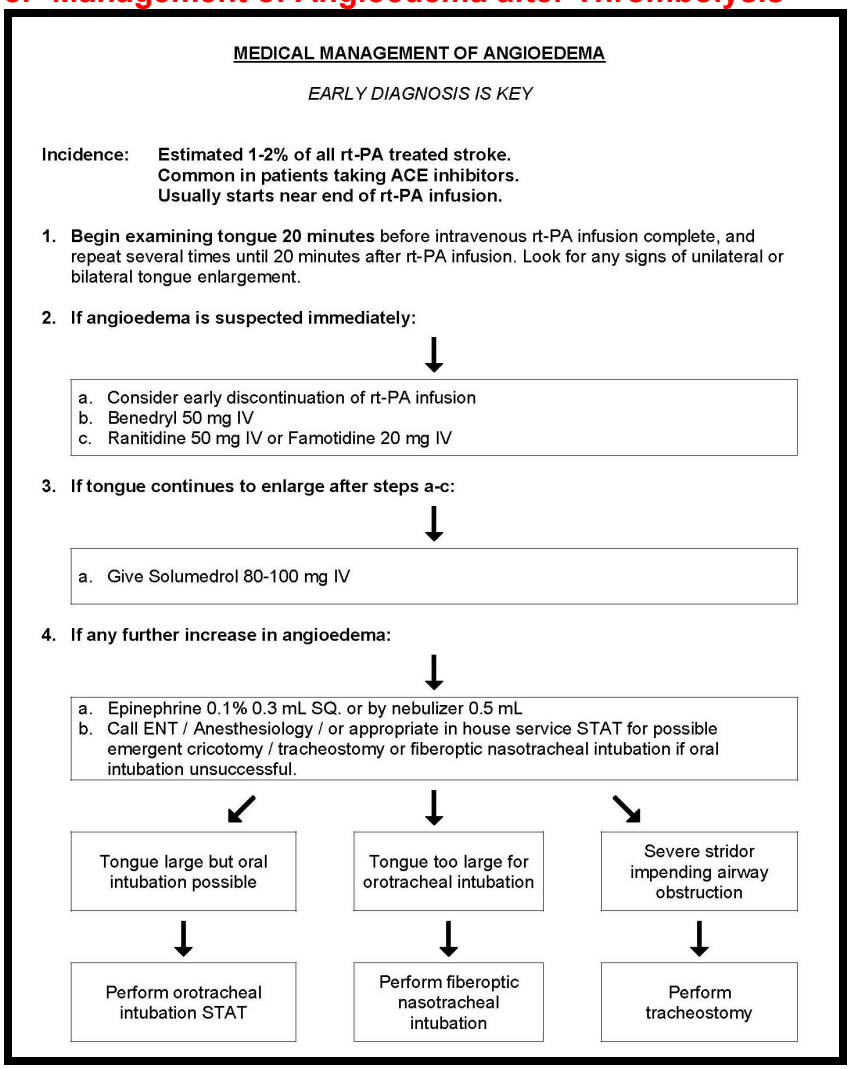
Systolic _230 mm Hg or diastolic 121 to 140 mm Hg

Labetalol 10 mg IV over 1 to 2 minutes, may repeat every 10 to 20 minutes, maximum dose of 300 mg;
or
Labetalol 10 mg IV followed by an infusion at 2 to 8 mg/min;
or
Nicardipine infusion, 5 mg/h, titrate up to desired effect by increasing 2.5 mg/h every 5 minutes to maximum of 15 mg/h
If blood pressure not controlled, consider sodium nitroprusside

7. Management of intracranial hemorrhage after thrombolysis

- If an intracranial hemorrhage is suspected, the stroke team treating MD (513-844-7686) should be contacted IMMEDIATELY.
- Suspect intracranial hemorrhage if there is any acute neurological deterioration (new headache, acute hypertension, seizure, or nausea and vomiting).
- If hemorrhage is suspected, then do the following:
  - Discontinue rt-PA infusion until ICH is ruled out.
  - Immediately perform CT scan
  - Draw blood for INR, PT, aPTT, platelet count, fibrinogen and type and screen
  - Prepare for administration of 6 to 8 units of cryoprecipitate.
  - Prepare for administration of 6 to 8 units of platelets.
- If intracranial hemorrhage present:
  - Consider administering 6-8 units cryoprecipitate followed by 6-8 units platelets
  - Consider emergent neurosurgical consultation
  - Notify patient's family or next-of-kin.

8. Management of Angioedema after Thrombolysis



9. Post IV rtPA Stroke Monitoring

- Admit patient to ICU and follow post-tPA order set, including:
  - Frequent monitoring of BP and neuro status
    - Q15 min X 2 hours, q30 min X 6 hours, then q1 hour X 16 hours
  - Call stroke MD if BP>180/105, decline in neuro status, or new headache, nausea, or vomiting
  - NPO until swallowing assessed
  - DVT prophylaxis with intermittent stocking compression devices (SCDs)
- 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
  - Posterior circulation syndrome that may require more aggressive endovascular measures in upcoming hours.