VCMC/SANTA PAULA HOSPITAL CLINICAL PRACTICE GUIDELINE
STROKE : ACUTE ISCHEMIC NON-HEMORRHAGIC IV t-PA
(alteplase, Activase®)

The contents of this clinical practice guideline are to be used as a guide. Healthcare professionals should use sound clinical judgment and individualize patient care. This CPG is not meant to be a replacement for training, experience, CME or studying the latest literature and drug information.

I. CLINICAL USE GUIDELINES*:

Strict adherence to this protocol is required. Only a small percentage of patients presenting with ischemic stroke will qualify for this therapy. The sooner the t-PA is administered within the 4.5 -hour window the better the results. There is a 10 fold increase in risk of intracranial hemorrhage and no benefit in long-term mortality with this therapy. The HELP (partial or complete recovery) to HARM ratio is 33:1, if therapy is delivered within 3 hours. The HELP to HARM ratio is decreased if therapy is delivered in the 3-4.5 hour but is still 6:1.

An attending physician may initiate therapy after review of patient selection criteria, exclusion criteria and after phone consultation with VCMC neurology attending. Notify the VCMC neurosurgeon on-call that t-PA infusion is to be started. If t-PA is administered at Santa Paula Hospital, the patient should be transferred *during the infusion via* paramedic ambulance with nurse presence to VCMC emergency department.

A. Patient Selection CRITERIA *(note: ALL CRITERIAL MUST BE MET):*

1. Patient age ≥ 18 years **and**
2. Well defined onset of stroke symptoms <4.5 hours prior to IV t-PA administration **and**
3. Diagnosis of acute ischemic stroke with measurable and significant neurological deficits based on the NIHS Scale (see Table 1) **and**
4. Patient or family members understand potential risks and benefits of treatment.

B. Patient EXCLUSION CRITERIA

t-PA is contraindicated if any of the following are present:

1. Onset of stroke symptoms >4.5 hours from initiation of t-PA therapy, or UNCERTAIN TIME.
2. If therapy initiation being considered between 3-4.5 hours >80 years old patients taking oral anticoagulation regardless of the INR, NIHS score >25 and those with a combination of prior stroke and diabetes should be excluded.
3. Minor, isolated or rapidly improving stroke symptoms.
4. Seizure at onset of stroke if neurological impairments thought to be a postictal phenomenon.
5. Non-contrast head CT scan NOT done or if CT scan shows evidence of ICH.
6. Stroke symptoms suggestive of subarachnoid hemorrhage despite negative CT scan.
7. CT scan shows multilobar hypodensity consistent with an acute stroke involving >33% of the cerebral hemisphere or evidence of hemorrhage.
8. Caution should be exercised in treating a patient with major deficits (NIHS score >22 predict greater risk of intracranial hemorrhage)
9. Active bleeding, trauma or fracture.
10. History of stroke, serious head trauma, intracranial surgery or myocardial infarction within last 3 months.
11. History of previous intracranial hemorrhage at any time.
12. History of GI or urinary tract hemorrhage in previous 21 days.

13. History of myocardial infarction within 3 months.
14. History of major surgery or serious trauma within last 14 days.
15. Arterial puncture at non-compressible site or lumbar puncture within 7 days.
16. Intracranial pathology (i.e. neoplasm, AV-malformation, aneurysm, etc.)
17. Uncontrolled abnormal serum glucose: <50 mg/dL or >400 mg/dL. If neurological deficit persists after correction of blood glucose, may proceed with thrombolysis.
18. Platelet count <100,000/mm^3.
19. Persistent blood pressure elevation: SBP>185 or DBP >110 mmHg.
20. Recent anticoagulant therapy with elevated prothrombin INR $\geq$ 1.5 seconds or elevated aPTT according to upper limit of normal per laboratory.

C. DOSAGE and ADMINISTRATION:

1. Alteplase Dose = 0.9 mg/kg body weight, maximum 90 mg.
2. Dosing: Administer 10% of the total calculated dose as an IV bolus over 1 minute, followed by infusion of the remaining 90% of the dose over 60 minutes.
3. Admit patient to ICU.
4. Perform neurological assessment every 15 minutes during infusion; every 30 minutes thereafter for the next 6 hours, then hourly until 24 hours after treatment.
5. If patient develops severe headache, acute hypertension, nausea or vomiting, stop infusion and obtain emergency non contrast head CT scan.
6. Measure BP every 15 minutes for the first 2 hours, then every 30 minutes for the next 6 hours, then hourly until 24 hours after therapy.
7. Increase the frequency of BP measurement if SBP $\geq$180 mmHg or if DBP $\geq$105 mmHg; treat BP to keep BP below 185/110 mm hg
8. No placement of NG tubes, bladder catheters or intra-arterial lines.
9. Obtain follow-up non-contrast head CT scan at 24 hours before starting anticoagulants or anti-platelet drugs.

II. TREATMENT ALGORITHM for ARTERIAL HPERTERNSION

A. BP management prior to thrombolysis

Systolic BP > 185 mmHg or diastolic BP > 110 mmHg

Labetalol 10-20 mg IV over 1-2 minutes, may repeat X 1

OR
Nitro paste 1 to 2 inches

OR

Nicardipine infusion 5 mg per hour, titrate up by 2.5 mg/hour @ 5 to 15 minute intervals to a maximum dose 15 mg/hour. If goal reached, then decrease dose by 3 mg/hour.

B. BP management during or after thrombolysis

Measure the BP every 15 minutes during treatment and the next 2 hours, then every 30 minutes for the next 6 hours, then hourly for 16 hours with continuous cardiac monitoring.

If SBP 180-230 mmHg or DBP 105-120 mmHg;

Labetalol 10 mg IV over 1-2 minutes, may repeat every 10-20 minutes to maximum dose of 150 mg every 24 hours;

OR

Labetalol 10 mg IV followed by infusion @ 2-8 mg/min. Start at 0.5 mg/min. Maximum dose is 4mg/min.

If SBP >230 mmHg or DBP 121-140 mmHg

Labetalol 10 mg IV over 1-2 minutes, may repeat every 10-20 minutes to maximum dose 300 mg.

OR

Labetalol 10 mg IV followed by infusion @ 2-8 mg/minute. Start at 0.5 mg/min. Maximum dose is 4mg/min.

OR

Nicardipine infusion 5 mg per hour, titrate up to the desired effect by increasing 2.5 mg/hour every 5 minutes to a maximum dose of 15 mg/hour.

If BP not controlled consider sodium nitroprusside.

III. MANAGEMENT OF INTRACEREBRAL HEMORRHAGE

1. If neurologic status worsens, consider bleeding until excluded by non-contrast head CT.
2. Immediately discontinue thrombolytic drug.
3. Obtain emergent non contrast head CT scan.
4. Obtain type and cross match, PT/INR, activated PTT, platelet count and fibrinogen level.
5. If intracerebral hemorrhage confirmed by CT:
    a. Administer 10 units **cryoprecipitate** to increase fibrinogen (half life 2-4 days) and Factor 8.
    b. Give 1 unit single donor platelet pack (6-8 units of platelets).
    This should increase platelet count by 50-70,000.
    c. If UFH given, administer **protamine** 1 mg for every 100 U UHF received in the preceding 4 hours.

    STAT order 6 units of cryoprecipitate, 4 units FFP, and 1 unit platelet pheresis to bedside and prepare to infuse if CT Head shows Intracerebral hemorrhage.

6. Obtain emergent neurosurgical consultation. Surgery, if indicated, may proceed 30-60 minutes after above therapy has been given.

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* Based upon the National Institute of Neurological Disorders (NIND) t-PA in acute ischemic stroke study. (NINDS. *NEJM* 1995; 333:1581).

AHA/ASA Guideline for Early Management of Adults with Ischemic Stroke (Stroke 2007; 38:1655-1711)

Jauch, E. C. , et al. 2013. Guidelines for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*; 44.

Maarten G. Lansberg, Erich Bluhmki and Vincent N. Thijs (2009), A Meta-analysis Efficacy and Safety of Tissue Plasminogen Activator 3 to 4.5 hours after Acute Ischemic Stroke
Stroke. 2009; 40:2438-2441;

Morgenstern LB, Hemphill JC III, Anderson C, et al; American Heart Association Stroke Council and Council on Cardiovascular Nursing. Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2010;41(9):2108-2129.

VCMC PHYSICIAN CHECKLIST: IV t-PA (alteplase, Activase®) for ACUTE STROKE

A. INCLUSION CRITERIA *(note: all criteria must be met):*

[ ] Patient age ≥ 18 years

[ ] Well defined onset of stroke symptoms < 4.5 hours prior to IV t-PA administration

[ ] Diagnosis of acute ischemic stroke with measurable and significant neurological deficits on the NIHS Scale

[ ] Patient or family members understand potential risks and benefits of treatment

B. EXCLUSION CRITERIA *(tPA is contraindicated if any of the following are present):*

[ ] Onset of stroke symptoms > 4.5 hours from initiation of IV t-PA therapy, or UNCERTAIN TIME.

[ ] If therapy initiation being considered between 3-4.5 hours, patients >80 years old, patients taking oral anticoagulation regardless of the INR, NIHS score >25 and those with a combination of prior stroke and diabetes should be excluded.

[ ] Minor, isolated or rapidly improving stroke symptoms.

[ ] Seizure at onset of stroke if neurological symptoms thought to be a postictal phenomenon.

[ ] CT scan shows evidence of ICH.

[ ] Stroke symptoms suggestive of subarachnoid hemorrhage despite negative CT scan.

[ ] CT scan shows multilobar hypodensity consistent with an acute stroke involving >33% of the cerebral hemisphere or evidence of hemorrhage.

[ ] Acute bleeding or trauma or fracture.

[ ] History of stroke, serious head trauma, intracranial surgery or MI within last 3 months. [ ]
History of intracranial hemorrhage at any time.

[ ] History of GI or urinary tract hemorrhage within 21 days. [ ]
History of myocardial infarction within 3 months.

[ ] History of major surgery or serious trauma with in last 14 days.

[ ] Arterial puncture at non-compressible site or lumbar puncture within 7 days. [ ]
Intracranial pathology (i.e. neoplasm, AV-malformation, aneurysm).

[ ] Uncontrolled abnormal serum glucose: <50 mg/dL or >400 mg/dL.
(If neurological deficit persists after correction of blood glucose, may proceed with thrombolysis)

[ ] Persistent blood pressure elevation: SBP>185 or DBP >110 mmHg.

[ ] Platelet count <100,000/mm^3.

[ ] Recent anticoagulant therapy with elevated INR ≥ 1.7 seconds or elevated aPTT.

C. PATIENT WEIGHT: _____ Kg.

D. DOSAGE and ADMINISTRATION:

- **Dosage: 0.9 mg/kg body weight. Dose = _____ mg (maximum dose is 90 mg)**

* Based upon the National Institute of Neurological Disorders (NIND) t-PA in acute ischemic stroke study. (NINDS. *NEJM* 1995; 333:1581). AHA/ASA Guideline for Early Management of Adults with Ischemic Stroke (Stroke 2007; 38:1655-1711). Expansion of the Time Window for Treatment of Stroke With t-PA. Stroke 2009. Department of Medicine 01/2013

Table 1

The National Institutes of Health Stroke Scale

Item	Response
Level of consciousness	0=Alert 1=Lethargic 2=Responds to vigorous or noxious stimuli 3=Unresponsive
Level of consciousness questions • What is the month? • What is your age?	0=Answers both correctly 1=Answers one correctly 2=Answers neither correctly
Level of consciousness commands • Open and close your eyes • Have patient grip/release good hand	0=Performs both tasks correctly 1= Performs one task correctly 2= Performs neither task correctly
Best Gaze	0=Normal 1=Partial gaze palsy 2=Complete gaze palsy
Visual Fields	0=No visual field deficits 1=Partial hemianopsia 2=Complete hemianopsia 3=Bilateral hemianopsia
Facial Palsy	0=No palsies 1=Minor facial paralysis 2=Partial facial paralysis 3=Complete facial paralysis
Motor arm a. Left b. Right	0=No drift 1=Drift before 10 seconds 2=Falls before 10 seconds 3=No effort against gravity 4=No movement
Motor leg a. Left b. Right	0=Lifts leg to 30° position for 5 seconds 1=Drift down before 5 seconds 2=Falls before 5 seconds 3=No effort against gravity 4=No movement
Ataxia	0=Absent 1=One limb 2=Two limbs
Sensory	0=Normal 1=Mild loss 2=Severe loss
Language	0=Normal 1=Mild aphasia 2=Severe aphasia 3=Mute or global aphasia
Dysarthria	0=None 1=Mild dysarthria 2=Severe dysarthria
Extinction/inattention (Testing for neglect)	0=Normal 1=Mild deficits 2=Severe deficits
Total score based on adding up all the individual scores	

NIHSS Severity Scale: Mild: 1-5 Moderately Severe 6-14 Severe 15-24 Very Severe > 25

Adapted from the NIHSS form available at *http://www.ninds.nih.gov/doctors/NIH_Stroke_Scale.pdf.*