Guidelines for the Administration of t-PA in Acute Ischemic Stroke

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The following recommended guidelines for the use of IV tPA have been established in response to the recently published favorable results of the NIH clinical trial, using IV tPA in acute ischemic stroke. This trial demonstrated an approximate 30% improvement in overall functional outcome at 3 months, but also a significant increase in symptomatic intracerebral hemorrhage within 36 hours of symptom onset in tPA treated patients. This document is also intended to broadly define two subgroups of acute stroke patients--those felt to be more likely to benefit from treatment (good risk to benefit ratio), and those in whom therapy with tPA is not recommended (poor risk to benefit ratio, see #3 below). There will be patients who do not clearly fit either category and in whom further individual judgment decisions by the consulting neurologist regarding the value of therapy will be necessary. There may be a subset of patients, particularly those not meeting the desired 3 hour therapeutic window for tPA, in whom intra-arterial thrombolysis may be considered.

1. Eligibility for tPA use in patients presenting to the ER with acute stroke symptoms is to be determined by the senior neurology resident in the ER in conjunction with the consulting neurologist.

2. The senior neurology resident on call to the ER and the consulting neurologist are immediately notified of patients with acute stroke symptoms as soon as the ER is aware they are enroute, to expedite decision making regarding thrombolytic therapy. The following should be obtained as soon as possible following patient admission to the ER:

   Baseline lab (CBC, electrolytes, APTT, PT, AST, glucose)

   EKG and CXR

   CT head without contrast

   Body weight

3. Pre-treatment management guidelines

	Consider tPA	No tPA
Clinical	• ≤3 hours(1) from focal anterior or posterior circulation ischemic symptom onset(2)	• > 3 hours from focal anterior or posterior circulation ischemic symptom onset(2)
	• Fixed significant or progressive deficit	• Rapidly resolving or minor deficit
	• Alert or somnolent patient	• Obtunded or comatose patient
	• No seizure(s) in association with stroke	• Seizure(s) at onset of stroke
	• No history of intracranial hemorrhage or bleeding diathesis	• History of intracranial hemorrhage or bleeding diathesis
	• No history of ischemic stroke or serious head injury within 3 months	• Ischemic stroke or serious head injury within 3 months(3)
	• BP elevations rapidly responsive to use of labetalol and similar agents and maintained at ≤185 mm Hg systolic, ≤110 mm Hg diastolic pre-treatment	• BP elevations persistently >185 mm Hg systolic, >110 mm Hg diastolic despite antihypertensive therapy. Patients requiring aggressive therapy to maintain above levels (e.g. sodium nitroprusside) excluded
	• Absence of GI, urinary tract hemorrhage within 21 days	• GI or UT hemorrhage within 21 days
	• No major surgery within 14 days	• Major surgery within 14 days
	• No recent myocardial infarction	• Recent myocardial infarction
	• No recent arterial puncture at a non-compressible site	• Recent arterial puncture at a non-compressible site(4)
	• No recent lumbar puncture	• Recent lumbar puncture(4)
	• Female patient who is not pregnant	• Pregnant female patient
	• Normal APTT, INR </=1.5; not on warfarin or heparin	• On heparin with elevated APTT; or, not on anticoagulation and INR >1.5; or, on warfarin with any INR(5)
	• Platelet count ≥ 100,000/mm^3	• Platelet count <100,000/mm^3
	• Glucose 50-400 mg/dl	• Glucose <50 or >400 mg/dl
CT	• No evidence for significant early infarction(6), hemispheric swelling, or hemorrhage	• Evidence for significant early infarction (6) with focal mass effect, hemispheric swelling, or hemorrhage
	• Absence of intracranial tumor	• Intracranial tumor

(1) There is no evidence that IV tPA given 3-6 hours after onset of symptoms is efficacious, and it is typically not used after 3 hours following symptom onset. Intra-arterial thrombolysis may still be considered in selected patients who have had symptoms for longer than 3 hours.

(2) For patients who wake up with stroke symptoms, the time they went to sleep defines the time of symptom onset.

(3) Selected patients with minor cerebral infarction within the last 3 months may be considered for IV tPA depending on clinical circumstances.

(4) The risk of hemorrhagic complication in the setting of a recent lumbar puncture or arterial puncture at a non-compressible site is uncertain. Treatment in these situations should be considered cautiously for selected patients after review of the findings of the LP or arterial puncture, the clinical circumstances, and review with the consulting neurologist.

(5) The safety of use of tPA in patients on warfarin, at any INR, has not been documented. Treatment in patients on warfarin should be considered cautiously for selected patients after review with the consulting neurologist.

(6) The safety and efficacy of tPA in patients with CT scan showing early infarct changes (EICs) is still controversial and its use in these patients should be decided by the consulting neurologist. However, in general, IV tPA is not contraindicated in patients with EICs. In most patients with early findings suggesting a significant cerebral infarction (i.e., >1/3 of MCA distribution), tPA is typically not used because of hemorrhage risk, and low likelihood of efficacy.

4. A formal consent form is not necessary, however documentation of patient consent (direct or next of kin) when possible will be recorded in the hospital notes.

5. **Treatment Guidelines**

A. If patient eligibility is confirmed and available consent obtained, tPA is to be administered by the Neurology Service in the recommended dose of 0.9 mg/kg of body weight (maximum, 90 mg), 10% given as a bolus, followed by the remaining 90% as a constant infusion over 60 minutes. The tPA may be obtained by calling the Central Pharmacy 5-5732. (Central Pharmacy will ask for the following information: 1) patient name/clinical number and allergies; 2) where in the ER or hospital that the patient is located; 3) patient weight; 4) total dose to be delivered (the pharmacy will then split this dose between the bolus and infusion as noted above).

B. All patients given tPA will be admitted to the 8MB Unit Neurology Critical Care Service.

6. **Post-Treatment Management Guidelines**

A. IV Heparin and antiplatelet agents should not be used for the first 24 hours following tPA administration.

B. Blood pressure management after tPA administration:

Monitor blood pressure for the first 24 hours after starting tPA treatment

every 15 minutes for 2 hours after starting the infusion,
then
every 30 minutes for 6 hours
then
every hour from the eighth hour until 24 hours after tPA started

If for two readings 5 to 10 minutes apart,
the systolic blood pressure is between 180-230 mm Hg
or
the diastolic pressure is in the range 105-120 mm Hg

Give labetalol 10 mg intravenously over 1 to 2 minutes. The dose may be repeated and/or doubled every 10-20 minutes up to 150 mg. Monitor blood pressure every 15 minutes during treatment. Observe for hypotension.

If the systolic blood pressure is greater than 230 mm Hg
or
the diastolic pressure is in the range 121-140:

Give labetalol 10 mg intravenously over 1 to 2 minutes. The dose may be repeated and/or doubled every 10 minutes up to 150 mg. If satisfactory response is not obtained, use nitroprusside. Monitor blood pressure every 10 minutes during treatment. Observe for hypotension.

If the diastolic blood pressure is greater than 140 mm Hg:

Infuse sodium nitroprusside (0.5 to 10 mcg/kg/minute). Monitor blood pressure every 15 minutes during treatment. Observe for hypotension.

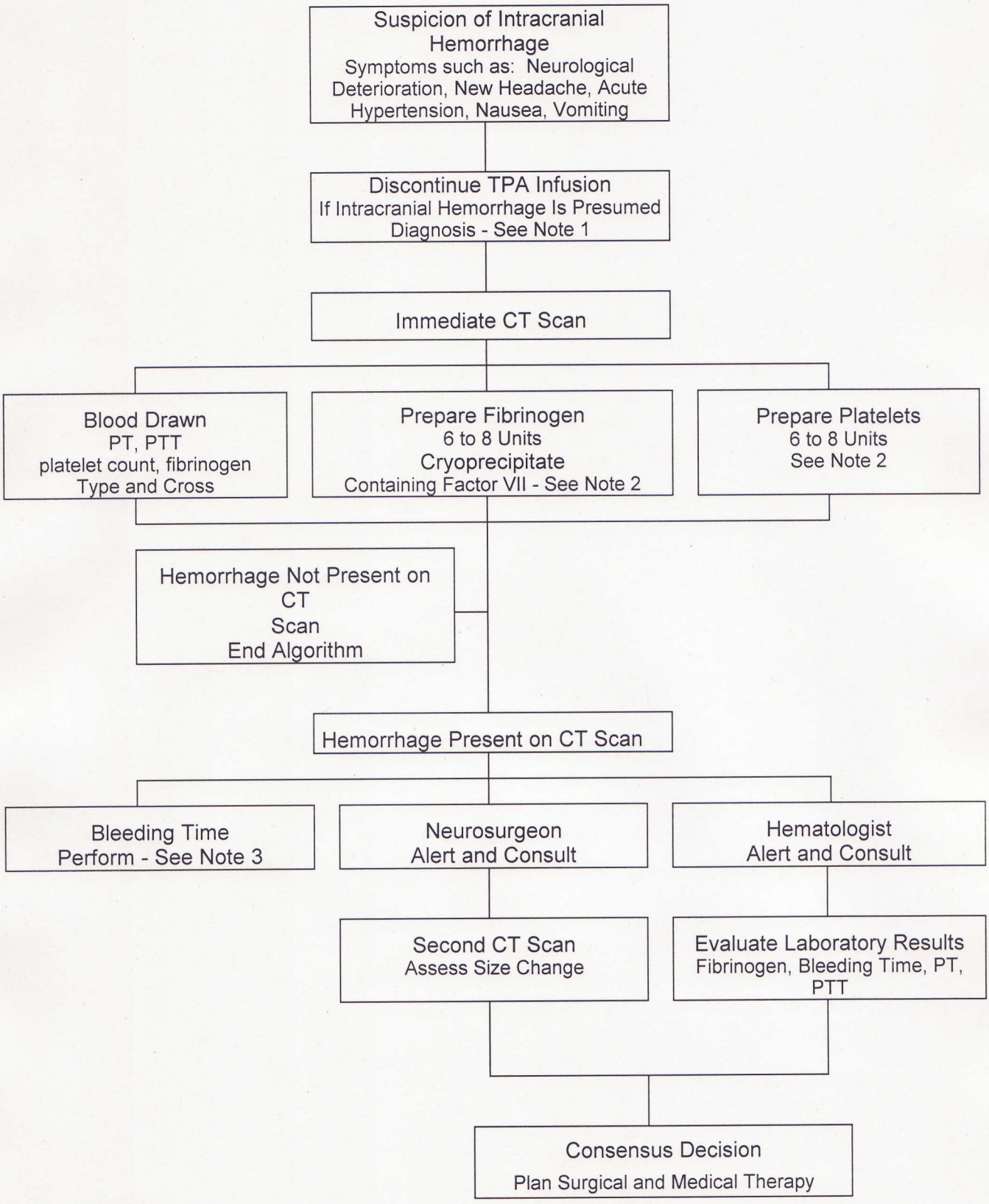
C. **Nursing Observation**

Neurologic observations are obtained at the same time that vital signs are checked:

every 15 minutes for 2 hours after starting the infusion
then
every 30 minutes for 6 hours
then
every hour from the eighth hour until 24 hours after tPA was started.

Particular attention is paid to possible markers of bleeding-changes in neurologic function, nausea or vomiting, or elevations in blood pressure. Patients are also observed for signs of external bleeding, particularly from puncture sites.

D. Algorithm for suspected intracranial hemorrhage



NINDS Trial Notes:

Note 1 The tPA infusion lasted only one hour and often was not ongoing when events signaling a possible symptomatic intracranial hemorrhage occurred. Stopping the infusion was not mandatory if other causes of neurological deterioration were apparent. However, CT scan was required in all cases.

Note 2 Preparations for giving platelets and fibrinogen were initiated at the first suspicion of hemorrhage so that they would be ready if needed, but not wasted if they were not part of the treatment plan.

Note 3 In practice, there was usually not time available to perform this test.