



Emergency Neurological Life Support Acute Ischemic Stroke Protocol Version 4.0

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Checklist

- Activate stroke code system (if available)
- Vital signs
- Supplemental oxygen to maintain saturation $\geq 94\%$
- Determine time of onset / last known well time (LKW)
- Determine NIHSS score
- CT, CTA
- Medication list*
- IV access - 18g peripheral IV
- Labs: Fingerstick glucose, CBC with platelets, PT/ INR, PTT, and beta-HCG for women of childbearing age
- EKG

*When asking about medications, be sure to ask specifically about anticoagulants and when medication was last taken/administered.

Communication

- Age
- Airway status
- Last known well time (LKW)
- NIHSS
- Coagulation parameters – PT, PTT, INR
- CT – Dense MCA sign, MCA dot sign, dense basilar sign, ASPECTS score, early ischemic changes
- CTA/MRA – Large vessel occlusion (ICA, M1, M2, Basilar, PCA)
- CTP – Volume of core and penumbra, matched or mismatched perfusion
- Thrombolytic administration – yes (Initiation, completion time); no (reason)
- Endovascular intervention (time to groin puncture, recanalization, TIC1 score)
- Target BP

Sample Sign-Off Narratives

Prehospital to ER:

“I am signing out a 62 yo male with known hypertension and atrial fibrillation who is not on anticoagulation”.

“He was found down on the floor at 7:10 am by his wife. He was last seen normal at 10 pm last night. He is aphasic with right-sided weakness, GCS of 11, HR of 130/minute and BP of

200/110 mmHg. IV Metoprolol 5 mg given and his follow up HR was 94/minute and BP was 182/90 mmHg”

ER to ICU:

“Upon arrival to the ER at 9:10 am his NIHSS was 21 - global aphasia, left gaze preference, right hemiplegia and neglect.”

“CT completed at 9:26 am showed a left dense MCA sign. CTA showed a left M1 occlusion. CTP showed a core of 38 ml, penumbra of 140 ml, mismatch volume 102 ml, mismatch ratio 3.7.”

“He was out of the IV tPA window. Endovascular team was notified at 9:38 am”.

“He was taken to the cath lab at 9:50 am. His HR was 106/minute and BP was 190/106 mmHg. Groin puncture was attained at 10:06 am. TIC13 revascularization was achieved. He had started moving his right arm and leg few minutes after the procedure”.

“His target post procedural BP should be <140/80 mmHg”. MRI brain is pending”.

Acute Ischemic Stroke

Acute ischemic stroke (AIS) is a neurological emergency that can be treated with time-sensitive interventions, including both intravenous thrombolysis and endovascular approaches for thrombus removal. Numerous studies have demonstrated that rapid, protocolized assessment and treatment is essential to improving neurological outcomes. These interventions are often completed simultaneously to achieve a safe and fast medical and/or surgical intervention. The protocol focuses on the early identification and initial management, within the first hour(s) following acute onset of a neurological deficit.

IV tPA Administration

Once a patient is deemed a candidate for IV thrombolytics

After placing two peripheral IV lines:

- Weigh the patient; do not estimate body weight. If patient cannot be weighed, then two people should estimate weight.
- Mix by swirling (do not shake) 0.9 mg/kg tPA, total dose not to exceed 90 mg.
- Give 10% of the total dose of tPA by bolus over 1 minute, then infuse the remaining dose over 1 hour.
- The remaining tPA in the IV tubing at the end of the infusion should be administered by running an additional 100 ml of saline at the same rate of the tPA infusion until the line is cleared.

Alternative dosing strategies utilizing lower doses has been evaluated in the literature; however, currently these dosing strategies are not endorsed by the AHA/ASA guidelines and should not be routinely implemented.

Footnote:

As tPA is dispensed in 50 and 100 mg bottles, it is suggested to withdraw and discard any excess tPA from the vial to avoid accidental infusion of excess tPA.

Endovascular Treatment

Consider mechanical thrombectomy

Mechanical thrombectomy should be considered if the patient has a large vessel occlusion (proximal (M1) MCA, intracranial ICA, basilar or vertebral artery) and is within a 24-hour time window of last known well time. If the patient is a candidate for IV thrombolytics, it should be administered expeditiously, regardless of endovascular procedure candidacy.

Large vessel occlusion can be suspected by seeing a hyperdense sign (clot within the vessel) on non-contrast CT imaging but this sign is insensitive. The probability of a large vessel occlusion increases with NIHSS score. An NIHSS >6 should raise suspicion for a large vessel occlusion. CTA or MRA is diagnostic, as is conventional angiography.

- Contact the neurointerventional physician on call; if the treating hospital does not have this capability, consider transfer to a comprehensive stroke center
- Based on the results of DAWN and DEFUSE 3 Trials, mechanical thrombectomy should be considered based on CTP, DWI – MRI + MRI perfusion is recommended to aid in the selection of patients for mechanical thrombectomy who meet the eligibility criteria

Hospital Admit or Transfer

While waiting for ICU bed

After IV, endovascular intervention or no specific treatment consider the following initial admission orders:

- Neuro check every 15 min for 2 hours, then every 30 minutes for 6 hours, then hourly
- Oxygenation to keep O₂ sat > 94%
- Blood pressure (BP) check every 15 min for 2 hours, then every 30 minutes for 6 hours, then every hour for 16 hours
- After IV tPA thrombolysis maintain BP <180/105 mmHg (note: this is lower than pretreatment values); if no tPA given, keep BP < 220/120 mmHg
- Bedside swallow test is quickly performed by giving 30 ml water by mouth. Dysphagia screening should be performed before administering anything else orally. Certain stroke patients are at high risk of aspirating. If the patient coughs or chokes during the bedside swallow test, then they should remain NPO until additional formal testing can be performed
- Keep glucose 140-180 mg/dl, consider insulin drip if blood glucose is persistently > 200 mg /dl.
- IVF (normal saline) at 1.5 ml/kg/hour to keep euvolemia
- Monitor for A-fib for at least 72 hours after admission
- Monitor for and prevent fever. Fever is detrimental to already injured brain. Treat fever sources with antibiotics or therapies while preventing fever with antipyretics. Rectal or IV acetaminophen or IV ketorolac will help control fever. Therapeutic hypothermia has not been proven effective to improve clinical outcome after acute stroke.
- Avoid indwelling urinary catheter to avoid nosocomial infection
- For large cerebral infarctions, it may be prudent to keep the head of bed elevated 30 degrees to help reduce edema. Decompressive surgery (including prophylactically) is recommended in some patients with malignant edema who have/to prevent sudden deterioration due to herniation from this massive swelling.

If tPA was administered:

- Avoid inserting urinary catheter, nasogastric tubes (NGT), intra-arterial (IA) catheters. If absolutely needed avoid insertion of urinary catheter during tPA infusion and at least 4 hours afterward. NGT and IV catheters should be avoided for 24 hours. Do not give anticoagulant/antiplatelet therapy for 24 hours; repeat head CT or MRI at 24 hours before starting anticoagulant/antiplatelet medications

Watch for complications of tPA, including

- Angioedema – with potential for airway obstruction. Most will treat just as an allergic reaction with
 - H-1 blockers, e.g. diphenhydramine 50 mg IV
 - H-2 blockers, e.g. ranitidine 50 mg IV, and

- Steroids, e.g. methylprednisolone 125 mg IV
- Epinephrine 0.3 mg subcutaneously or via nebulizer
- Icatibant (bradykinin antagonist) 30 mg subcutaneous in abdominal wall, repeat in 6 hours, and maximum of 90 mg in 24 hours
- FFP (contains C1 esterase inhibitor) may be required as targeted therapy for hereditary angioedema and ACEI-related angioedema.
- Consider early/rapid intubation if there are early signs of airway compromise. It is typically not necessary if there is only isolated lip or tip of tongue swelling.
- Hemorrhage - stop tPA
- Sudden deterioration in mental status - see below
- Severe hypertension or hypotension - may be signs of ICH or systemic hemorrhage

A sudden decline in neurological exam during or following tPA administration may be due to an intracranial hemorrhage. This is often accompanied by a marked rise in blood pressure; however, a marked rise or fall in blood pressure alone may signal an ICH. Do the following immediately:

- STOP tPA infusion
- Monitor airway closely
- Vital signs every 15 minutes (assessment for signs of increased ICP). Assess GCS/pupil response. Treat blood pressure and use noninvasive interventions to lower ICP (raise HOB, neck midline).
- Obtain STAT head CT scan
- Notify your neurosurgeon on call; if not available begin the process to transfer the patient to a facility with neurosurgical capability if the CT scan shows hemorrhage
- Stat labs: PT, PTT, Platelets, fibrinogen, type and cross 2-4 unit PRBCs
- Give the following:
 - 10 units of cryoprecipitate IV over 10-30 min. Give more until fibrinogen level <200 mg/dL
 - And
 - Tranexamic acid 1000 mg IV over 10 min or
 - Aminocaproic acid IV 4-5 g over 1 hour followed by 1 g until bleeding stops (usually within 3 hours)
 - Consider transfusion of 1 bag of single donor platelets or 6 to 8 bags of random donor platelets.

Consider patient transfer if:

- the treating hospital cannot provide the level of care for the patient (no ICU for example). Patient outcomes have been shown to improve if the patient is treated in a stroke center.
- there is suspicion of large vessel occlusion (CTA/MRA, hyperdense vessel sign on imaging; or clinical findings consistent with an MCA stroke) and the patient can arrive and be treated at the receiving hospital within 24 hours of symptom onset.

Low Risk TIA

ABCD² Score 0-3

Patients at low risk of stroke can be treated as outpatients. This can begin in the ED or clinic starting with medications and expediting ECG and imaging of the carotids in 1-2 days following the ABCD² score calculation. Do the following:

- Start on antithrombotic agent (ASA 81 mg/day, clopidogrel 75 mg/day, or ASA/extended release dipyridamole 200 mg twice daily)
- Initiate high intensity statin if not taking one already (moderate intensity statin in patients > 75 years old)
- Obtain a 12-lead ECG or review the rhythm strip if available. If these show atrial fibrillation, consider starting anticoagulation (oral anticoagulant or low molecular weight heparin) or ASA 81 mg if anticoagulation is contraindicated; calculate CHADS2 or CHADS2Vasc and HAS-BLED score to help guide long term therapy.
- Consider initiating longer-term outpatient cardiac monitoring (30 days) if the TIA is embolic and atrial fibrillation is not identified already or if there is no other cause for TIA
- Arrange carotid imaging: ultrasound, CTA or MRA
- Consider transthoracic echocardiography
- Initiate smoking cessation counseling
- Counsel about the importance of compliance with medication regimen

No tPA unless BP is reduced

If the patient is a potential thrombolysis candidate, interventions to control BP should be initiated immediately. Short-acting intravenous and/or titratable IV antihypertensive agents can be used for the treatment of hypertension in the acute setting.

Blood pressure (BP) exceeds 185/110 mmHg

- This is too high for IV tPA administration and *requires* gentle reduction prior to initiating tPA.
- Labetalol 10-20 mg IV every 10 minutes (consider doubling dose (i.e. 20 mg, 40 mg, 80 mg) to maximum total dose of 300 mg. Start maintenance infusion.*
- Nicardipine IV- start 5 mg/hour, titrate up by 2.5 mg/hour at 5- to 15-minute intervals, maximum dose 15 mg/hour; when desired blood pressure attained, lower the dose.
- Clevidipine IV- begin with 1-2 mg/hour IV infusion; double medication dose every 90 seconds until BP goal is neared, then increase in smaller increments until desired BP goal is reached. Maximum dose is 32 mg/hour.
- Other medications. **

If BP falls below 185/110 mmHg, proceed to IV tPA administration.

If BP proves refractory to the above, the risk for intracerebral hemorrhage is considered too high and the patient should not be treated with tPA. Continue to treat BP to keep less than 220/120 mmHg, however. ***

Footnotes:

*Be sure to initiate a continuous infusion of the antihypertensive agent as boluses will wear off and BP will likely return to its previous high levels.

**Nitroglycerin paste (for patients with no IV access), labetalol, and nicardipine are recommended by the American Stroke Association. See ENLS: [Pharmacotherapy](#).

***Permissive hypertension is allowed for TIA, as it is for non-tPA treated patients, up to 220/120 mmHg. This may be gradually lowered over the next 24-48 hours.

High Risk TIA

TIA risk moderate or high, or unable to arrange timely outpatient work-up and follow-up

Admit for observation:

- Patients with an ABCD² scores > 3
- Permissive hypertension (not to exceed 220/120 mmHg), and BP should be gradually lowered over 24-48 hours.
- Keeping head of bed flat for 24 hours has been recommended in the past but is not evidence-based.
- Telemetry
- In a high risk TIA (ABCD² score ≥ 4) the CHANCE trial demonstrated that dual antiplatelet therapy using a combination of clopidogrel (initial dose of 300 mg followed by 75 mg/day) and aspirin 81 mg/day for 21 days followed by clopidogrel 75 mg/day for 90 days was superior to aspirin alone in reducing the risk of stroke.
- Similarly, the POINT trial from United States showed that combined use of clopidogrel at a loading dose of 600 mg once followed by 75 mg/day for 90 days plus aspirin 50-325 mg/day for first 21 days was superior to aspirin 50-325 mg/day for 90 day. Initiate high intensity statin if not taking one already (moderate intensity statin in patients > 75 years old).
- Initiate high intensity statins (ex: atorvastatin 80 mg daily or rosuvastatin 20 mg daily)
- Obtain a 12-lead ECG or review the rhythm strip if available. If these show atrial fibrillation, consider starting anticoagulation (oral anticoagulant or low molecular weight heparin) or ASA 81 mg if anticoagulation is contraindicated; calculate CHADS₂ or CHADS₂Vasc and HAS-BLED score to help guide long term therapy.
- Consider initiating longer-term outpatient cardiac monitoring (30 days) if the TIA is embolic and atrial fibrillation is not identified already or if there is no other cause for TIA.
- Arrange carotid imaging: ultrasound, CTA or MRA
- Consider transthoracic echocardiography
- Initiate smoking cessation counseling

Onset Less Than 3 hours

One of the chief criteria used to select patients for acute stroke interventions is the patient's time of stroke onset defined as LKW time or alternatively the time of symptom onset (if witnessed). Acute stroke treatment therapies such as thrombolysis are time sensitive, and delays can lead to a lower likelihood of a good outcome and an increased risk of intracranial hemorrhage. If you cannot establish the time with certainty, most providers will not treat with IV tPA.

Time from stroke symptom onset is less than 3 hours

Time of onset is when the patient was last seen normal.

- If patient or observer can verify when the first symptoms began, use that time.
- If a patient awakens with a stroke, the time of onset is when they last went to bed.

Patients with a shorter time to tPA administration have a higher likelihood of good outcome. Therefore, expediting care may greatly impact your patient.

Check eligibility for on-label (US and elsewhere) use of IV tPA:

- Diagnosis of ischemic stroke causing measurable neurological deficit. Tip: ask the patient if the deficit is disabling to them - can they carry out all of their normal and enjoyable activities as they could before this event?
- Onset less than 3 hours before initiating tPA
- Patient is at least 18 years of age (see section on Pediatric Stroke)

Alteplase is the only FDA-approved tPA for use in acute ischemic stroke in the U.S. However, the 2018 AHA/ASA Acute Ischemic Stroke Guidelines now give tenecteplase 0.4 mg/kg single IV bolus a class 2b recommendation as an alternate medication.

Absolute Exclusion Criteria if positive:

Most clinicians practice using a hybrid of AHA/ASA and FDA guidelines. Be aware that FDA lifting of restrictions is based on there being no study that has specifically validated a particular parameter. Previous guidelines were extensions based on the exclusion criteria under which the medication was originally trialed.

- The symptoms of stroke should not be suggestive of subarachnoid hemorrhage. (2015 FDA label, changed to subarachnoid hemorrhage)
- No major head trauma in previous 3 months
- No prior stroke within previous 3 months (removed in 2015 FDA label)
- No intracranial or intraspinal surgery in the previous 3 months
- No arterial puncture at a non-compressible site or lumbar puncture in the previous 7 days
- No history of previous intracranial hemorrhage (contraindication removed in 2015 FDA label, warning added for recent ICH)

- No history of intracranial neoplasm, aneurysm, or arteriovenous malformation. Note that it is probably prudent to give IV tPA to a patient with an ischemic stroke and a small asymptomatic, unsecured intracranial aneurysm.
- Blood pressure not elevated (systolic < 185 mmHg and diastolic < 110 mmHg) (in 2015 FDA label, specific BP values removed from contraindication, warning for BP > 185/110 mmHg remains)
- No evidence of active bleeding or acute trauma (fracture) on examination.
- Not taking an oral anticoagulant or, if anticoagulant being taken, INR < 1.7 or PT > 15 seconds.
- No current use of direct thrombin inhibitors or direct factor Xa inhibitors or elevated sensitive laboratory tests (such as aPTT, INR, platelet count, and ECT (ecarin clotting time); TT (thrombin time); or appropriate factor Xa assays *
- If receiving heparin in previous 48 hours, aPTT must be in normal range.
- Platelet count <100 000 mm³.
- Blood glucose concentration < 50 mg/dl (2.7 mmol/l) **(FDA 2015 label, removed entirely). In spite of the FDA removal of limitation, a blood glucose test (serum or capillary) is the only test result one should have back before administering tPA.
- CT does not show a multilobar infarction (hypodensity >1/3 cerebral hemisphere) (removed from FDA 2015 label)

Relative Exclusion Criteria if positive:

Use caution in recommending tPA if one or more are positive:

- The neurological signs are rapidly improving ***(removed from 2015 FDA label)
- The neurological signs are minor and isolated ****(removed from 2015 FDA label)
- Pregnancy
- Seizure with postictal residual neurological impairments
- Major surgery or major trauma in the previous 14 days
- Gastrointestinal or urinary tract hemorrhage in previous 21 days
- Myocardial infarction in the previous 3 months

Some additional considerations:

- Caution should be exercised in treating a patient with major deficits.
- Caution using tPA in patients treated with low molecular weight (LMW) heparin in the past 24 hours. Note that prophylactic dose of LMW heparin is NOT a contraindication, only the full treatment dose.
- The patient or family members understand the potential risks and benefits from treatment. No written consent is required but the conversation should be documented in the clinical notes. Do not delay therapy if surrogate is not available.

* Novel new direct thrombin inhibitors or direct factor Xa inhibitors pose a new conundrum in determining tPA eligibility. Without available blood tests and based on drug half-lives, most

practitioners are using a cut-off of 48 hours (or 5 half-lives) since last use of any of these medications before recommending tPA.

** The original tPA guidelines for acute ischemic stroke included an exclusion for patients with serum or capillary glucose level > 400 gm/dl. While this parameter has been removed for many years, a level this high should prompt the consideration of an alternate diagnosis. Similarly, a low blood glucose level may be symptomatic and should be corrected and the patient's neurologic status be reassessed.

*** Some stroke patients will have stuttering symptoms or they may have mild improvement, e.g. from a NIHSS of 12 to 8 points, but then hold at 8 with no further improvement. The recommendation is to still treat these patients.

**** In the past, many physicians used an NIHSS of 4 or 5 points as a lower end cut-off for recommending tPA. It must be noted that patients may have significant residual stroke symptoms with low NIHSS scores (e.g. isolate hemianopsia, or aphasia, or brain stem injury). tPA administration should strongly be considered in these patients. Asking the patient about how disabling their symptoms are will help with the tPA recommendation.

Onset Between 3 and 4.5 Hours

Time from stroke onset is between 3 and 4.5 hours

Time of onset is when the patient was last seen normal.

- If the patient or an observer can corroborate when the first symptoms began, use that time.
- If a patient awakens with a stroke, the time of onset is when they last went to bed.

The time of onset is critical for using tPA as the risk of intracerebral bleeding increases with increased time from stroke onset. If you cannot establish the time with certainty, most physicians will not treat with tPA.

In the US, tPA is not yet FDA approved for 3- 4.5-hour time window, although it is approved in Europe and Canada. Nonetheless, the 3- 4.5-hour window is endorsed by the American Heart and American Stroke Association. The inclusion criteria are similar to those of < 3 hours, but are modified as follows:

- Meet all criteria of < 3 hours since stroke onset
- Age < 80 years
- No anticoagulant use, regardless of INR
- NIHSS \leq 25
- No combined history of prior stroke and diabetes

Patient improves following tPA

Measurable improvement within 1 hour? LVO Present or Suspected

Often this is defined as a lowering of the NIHSS score, and there is no clear consensus as to how much. If the patient is suspected or confirmed to have a LVO, begin working on getting the patient to an endovascular center for evaluation right away.

Yes - Patient is an IV tPA Candidate

Is Blood Pressure (BP) less than 185/110 mmHg?

After reviewing the inclusion/exclusion criteria for IV tPA use, the patient is eligible to receive the drug. Current blood pressure is the last inclusion criteria.

Blood pressure (BP) measurements are vital and must be obtained frequently, especially in the early management of AIS. If the patient is a potential thrombolysis candidate, interventions to control BP should be initiated immediately. Target BP goals for patients eligible for IV tPA is < 185/110 mmHg, and once IV tPA is initiated, BP must be maintained below 180/105 mmHg for 24 hours after administration of IV tPA to limit the risk of intracranial hemorrhage. A strategy for careful BP lowering should be employed while ensuring large fluctuations in BP once at goal are limited.

Steps can be taken to lower blood pressure so as to make the patient eligible for tPA. See the ENLS: [Pharmacotherapy](#) protocol for dosing. Note that while the FDA has lifted absolute target BP numbers, the AHA/ASA guidelines still recommend getting and keeping BP down below 185/110 to start tPA and even lower below 180/105 while tPA is infusing

No - Patient is not an IV tPA or IA Treatment Candidate

Neither IV tPA or endovascular intervention is appropriate

Common exclusions for IV tPA are time (duration > 4.5 hours) or specific contraindications to tPA.

Endovascular intervention exclusions include lack of large vessel occlusion on CTA or MRA, large area of infarction already present on the brain imaging study (ASPECTS score < 6). CTA/CTP or MRI/MRA may show large infarct core and small penumbra indicating that endovascular intervention will not be successful and may in fact be dangerous.

Symptom Onset > 4.5 hours

Outside IV tPA window

Beyond 4.5 hours, IV tPA is associated with increased risks and unproven efficacy. Endovascular therapies are often helpful in this time window (and earlier as well) if there is a LVO.

The ABCD² Score

What is the predicted risk for stroke?

The ABCD² score is an ordinal scale that provides risk prediction of stroke following the TIA. It is scored as follows:

| ABCD ² Element | Points |
|--|--------|
| Age > 60 years | 1 |
| Blood pressure ≥ 140/90 mmHg on initial evaluation | 1 |
| Clinical features | |
| Speech disturbance without weakness | 1 |
| Unilateral weakness | 2 |
| Duration of symptoms | |
| 10 - 59 minutes | 1 |
| 60 minutes or greater | 2 |
| Diabetes mellitus in patient's history | 1 |
| Total score | 0 - 7 |

The following is the estimated risk (%) of a stroke occurring within various time ranges:

| Total risk | ABCD ² Score | 2 day | 7 day | 90 day |
|------------|-------------------------|-------|-------|--------|
| Low | 0-3 | 1.0 | 1.2 | 3.1 |
| Moderate | 4-5 | 4.1 | 5.9 | 9.8 |
| High | 6-7 | 8.1 | 12 | 18 |

Ref: Cucchiara B et al, Ann Emerg Med 2008, 52:S27-39

Based on this risk stratification, some physicians choose to admit high-risk patients and discharge those with low risk, and controversy exists about moderate-risk patients.

TIA

Symptoms have completely resolved

Diagnosis of TIA (transient ischemic attack) is based on new onset of focal neurological symptoms that are explainable by a vascular cause (i.e. arterial occlusion of a single or group of arteries adequately explain the patient's signs and symptoms) and these signs and symptoms resolve within 24 hours (most TIA's resolve in a much shorter period of time). If the patient's symptoms clear by 24 hours but an acute infarct is observed on brain imaging, this is defined as a stroke and no longer TIA.