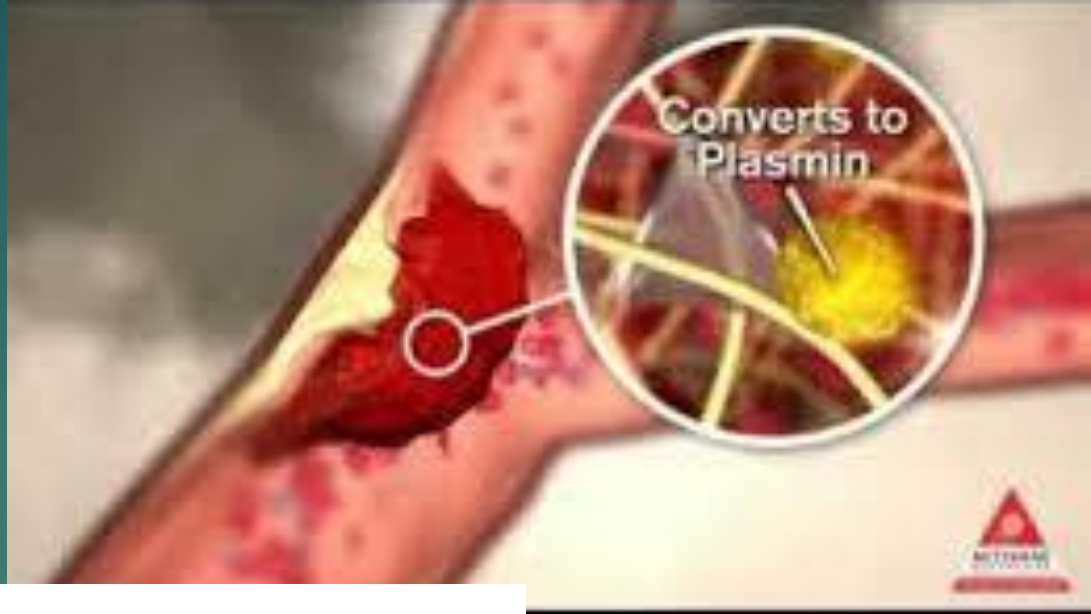

tPA

Dissolves blood clots in the brain

AHA/ASA Guideline

2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

Reviewed for evidence-based integrity and endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons

Endorsed by the Society for Academic Emergency Medicine

William J. Powers, MD, FAHA, Chair; Alejandro A. Rabinstein, MD, FAHA, Vice Chair; Teri Ackerson, BSN, RN; Opeolu M. Adeoye, MD, MS, FAHA; Nicholas C. Bambakidis, MD, FAHA; Kyra Becker, MD, FAHA; José Biller, MD, FAHA; Michael Brown, MD, MSc; Bart M. Demaerschalk, MD, MSc, FAHA; Brian Hoh, MD, FAHA; Edward C. Jauch, MD, MS, FAHA; Chelsea S. Kidwell, MD, FAHA; Thabele M. Leslie-Mazwi, MD; Bruce Ovbiagele, MD, MSc, MAS, MBA, FAHA; Phillip A. Scott, MD, MBA, FAHA; Kevin N. Sheth, MD, FAHA; Andrew M. Southerland, MD, MSc; Deborah V. Summers, MSN, RN, FAHA; David L. Tirschwell, MD, MSc, FAHA; on behalf of the American Heart Association Stroke Council

Eligibility Recommendations for IV Alteplase in Patients With AIS

Within 3 h* :
IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 min with initial 10% of dose given as bolus over 1 min) is recommended for selected patients who may be treated within 3 h of ischemic stroke symptom onset or patient last known well or at baseline state.

Age:

For otherwise medically eligible patients ≥18 y of age, IV alteplase administration within 3 h is equally recommended for patients <80 and >80 y of age.

Severity:

- ✓ For severe stroke symptoms, IV alteplase is indicated within 3 h from symptom onset of ischemic stroke. Despite increased risk of hemorrhagic transformation, there is still proven clinical benefit for patients with severe stroke symptoms.
- ✓ For patients with mild but disabling stroke symptoms, IV alteplase is indicated.
- ✓ There should be no exclusion for patients with mild but nonetheless disabling stroke symptoms, in the opinion of the treating physician, from treatment with IV alteplase because there is proven clinical benefit for those patients.

3–4.5 h* :
IV alteplase is also recommended for selected patients who can be treated within 3 and 4.5 h of ischemic stroke symptom onset or patient last known well.

IV alteplase treatment in the 3- to 4.5-h time window is recommended for those

- ✓ patients ≤80 y of age,
- ✓ without a history of both diabetes mellitus and prior stroke,
- ✓ NIHSS score ≤25,
- ✓ not taking any OACs,
- ✓ and without imaging evidence of ischemic injury involving more than one third of the MCA territory

Urgency Treatment should be initiated as quickly as possible within the above listed time frames because time to treatment is strongly associated with outcomes.

BP:

IV alteplase is recommended in patients whose BP can be lowered safely (to <185/110 mm Hg) with antihypertensive agents, with the physician assessing the stability of the BP before starting IV alteplase.

Blood glucose IV alteplase is recommended in otherwise eligible patients with initial glucose levels >50 mg/dL.

CT:

IV alteplase administration is recommended in the setting of early ischemic changes on NCCT of mild to moderate extent (other than frank hypodensity).

Prior antiplatelet therapy

IV alteplase is recommended for patients taking antiplatelet drug monotherapy before stroke on the basis of evidence that the benefit of alteplase outweighs a possible small increased risk of sICH.

IV alteplase is recommended for patients taking antiplatelet drug combination therapy (eg, aspirin and clopidogrel) before stroke on the basis of evidence that the benefit of alteplase outweighs a probable increased risk of sICH.

End-stage renal disease:

In patients with end-stage renal disease on hemodialysis and normal aPTT, IV alteplase is recommended.

However, those with elevated aPTT may have elevated risk for hemorrhagic complications.

Contraindications

Time of onset IV alteplase is not recommended in ischemic stroke patients who have an unclear time and/ or unwitnessed symptom onset and in whom the time last known to be at baseline state is >3 or 4.5 h.

IV alteplase is not recommended in ischemic stroke patients who ***awoke with stroke*** with time last known to be at baseline state >3 or 4.5 h.

CT

- ✓ IV alteplase should not be administered to a patient whose CT reveals an acute intracranial hemorrhage.
- ✓ There remains insufficient evidence to identify a threshold of hypoattenuation severity or extent that affects treatment responseto alteplase.
- ✓ However, administering IV alteplase to patients whose CT brain imaging exhibits extensive regions of clear hypoattenuation is not recommended.
- ✓ These patients have a poor prognosis despite IV alteplase, and severe hypoattenuation defined as obvious hypodensity represents irreversible injury.

Ischemic stroke within 3 mo
Use of IV alteplase in patients presenting with AIS who have had a prior ischemic stroke within 3 mo may be harmful.

Severe head trauma within 3 mo

In AIS patients with recent severe head trauma (within 3 mo), IV alteplase is contraindicated.
Given the possibility of bleeding complications from the underlying severe head trauma, IV alteplase should not be administered in posttraumatic infarction that occurs during the acute in-hospital phase.
(Recommendation wording modified to match Class III stratifications.)

Intracranial/intraspinal surgery within 3 mo:

For patients with AIS and a history of intracranial/spinal surgery within the prior 3 mo, IV alteplase is potentially harmful.

History of intracranial hemorrhage
IV alteplase administration in patients who have a history of intracranial hemorrhage is potentially harmful.
Subarachnoid hemorrhage
IV alteplase is contraindicated in patients presenting with symptoms and signs most consistent with an SAH.

GI malignancy or GI bleed within 21 d
Patients with a structural GI malignancy or recent bleeding event within 21 d of their stroke event should be considered high risk,and IV alteplase administration is potentially harmful.

Coagulopathy :

IV alteplase for acute stroke patients with platelets <100 000/mm_3, INR >1.7, aPTT >40 s, or PT >15 s should not be administered.

*In patients without history of thrombocytopenia, treatment with IV alteplase can be initiated before availability of platelet countbut should be discontinued if platelet count is <100 000/mm_3.

*In patients without recent use of OACs or heparin, treatment with IV alteplase 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.

LMWH

IV alteplase should not be administered to patients who have received a treatment dose of LMWH within the previous 24 h.

Thrombin inhibitors or factor Xa inhibitors

IV alteplase should not be administered to patients taking direct thrombin inhibitors or direct factor Xa inhibitors unless laboratory tests such as aPTT, INR, platelet count, ecarin clotting time, thrombin time, or appropriate direct factor Xa activity assays are normal or the patient has not received a dose of these agents for >48 h (assuming normal renal metabolizing function).

Glycoprotein IIb/IIIa receptor inhibitors

Antiplatelet agents that inhibit the glycoprotein IIb/IIIa receptor should not be administered concurrently with IV alteplase outside a
clinical trial.

Infective endocarditis

For patients with AIS and symptoms consistent with infective endocarditis, treatment with IV alteplase should not be administered because of the increased risk of intracranial hemorrhage.

Aortic arch dissection IV alteplase in AIS known or suspected to be associated with aortic arch dissection is potentially harmful and should not be administered.

Intra-axial intracranial neoplasm
IV alteplase treatment for patients with AIS who harbor an intra-axial intracranial neoplasm is potentially harmful.

Additional recommendations for treatment with IV alteplase for patients with AIS

Preexisting disability

Preexisting disability does not seem to independently increase the risk of sICH after IV alteplase, but it may be associated with less neurological improvement and higher mortality.

Thrombolytic therapy with IV alteplase for acute stroke patients with preexisting disability (mRS score ≥2) may be reasonable, but decisions should take into account relevant factors, including quality of life, social support, place of residence, need for a caregiver, patients' and families' preferences, and goals of care.

Patients with preexisting dementia may benefit from IV alteplase. Individual considerations such as life expectancy and premorbid level of function are important to determine whether alteplase may offer a clinically meaningful benefit.

Early improvement

IV alteplase treatment is reasonable for patients who present with moderate to severe ischemic stroke and demonstrate early improvement but remain moderately impaired and potentially disabled in the judgment of the examiner.

Seizure at onset IV alteplase is reasonable in patients with a seizure at the time of onset of acute stroke if evidence suggests that residual impairments are secondary to stroke and not a postictal phenomenon.

Blood glucose Treatment with IV alteplase in patients with AIS who present with initial glucose levels <50 or >400 mg/dL that are subsequently normalized and who are otherwise eligible may be reasonable.

Coagulopathy

The safety and efficacy of IV alteplase for acute stroke patients with a clinical history of potential bleeding diathesis or coagulopathy are unknown. IV alteplase may be considered on a case-by-case basis.

IV alteplase may be reasonable in patients who have a history of warfarin use and an INR ≤1.7 and/or a PT <15 s.

Dural puncture

IV alteplase may be considered for patients who present with AIS, even in instances when they may have undergone a lumbar dural puncture in the preceding 7 d.

Arterial puncture

The safety and efficacy of administering IV alteplase to acute stroke patients who have had an arterial puncture of a noncompressible blood vessel in the 7 d preceding stroke symptoms are uncertain.

Recent major trauma

In AIS patients with recent major trauma (within 14 d) not involving the head, IV alteplase may be carefully considered, with the risks of bleeding from injuries related to the trauma weighed against the severity and potential disability from the ischemic stroke.

Recent major surgery

Use of IV alteplase in carefully selected patients presenting with AIS who have undergone a major surgery in the preceding 14 d may be considered, but the potential increased risk of surgical-site hemorrhage should be weighed against the anticipated benefits of reduced stroke related neurological deficits.

GI and genitourinary bleeding

Reported literature details a low bleeding risk with IV alteplase administration in the setting of past GI/genitourinary bleeding.

Administration of IV alteplase in this patient population may be reasonable (Note: Alteplase administration within 21 d of a GI bleeding event is not recommended).

Menstruation

IV alteplase is probably indicated in women who are menstruating who present with AIS and do not have a history of menorrhagia.

However, women should be warned that alteplase treatment could increase the degree of menstrual flow.

Because the potential benefits of IV alteplase probably outweigh the risks of serious bleeding in patients with recent or active history of menorrhagia without clinically significant anemia or hypotension, IV alteplase administration may be considered.

When there is a history of recent or active vaginal bleeding causing clinically significant anemia, then emergency consultation with a
gynecologist is probably indicated before a decision about IV alteplase is made.

Extracranial cervical dissections

IV alteplase in AIS known or suspected to be associated with extracranial cervical arterial dissection is reasonably safe within 4.5 h and probably recommended.

Intracranial arterial dissection

IV alteplase usefulness and hemorrhagic risk in AIS known or suspected to be associated with intracranial arterial dissection remain unknown, uncertain, and not well established.

Unruptured intracranial aneurysm

For patients presenting with AIS who are known to harbor a small or moderate-sized (<10 mm) unruptured and unsecured intracranial aneurysm, administration of IV alteplase is reasonable and probably recommended.

Usefulness and risk of IV alteplase in patients with AIS who harbor a giant unruptured and unsecured intracranial aneurysm are not well established

Intracranial vascular malformations

For patients presenting with AIS who are known to harbor an unruptured and untreated intracranial vascular malformation the usefulness and risks of administration of IV alteplase are not well established.

Because of the increased risk of ICH in this population of patients, IV alteplase may be considered in patients with stroke with severe neurological deficits and a high likelihood of morbidity and mortality to outweigh the anticipated risk of ICH secondary to thrombolysis.

CMBs

In otherwise eligible patients who have previously had a small number (1–10) of CMBs demonstrated on MRI, administration of IV alteplase is reasonable.

In otherwise eligible patients who have previously had a high burden of CMBs (>10) demonstrated on MRI, treatment with IV alteplase may be associated with an increased risk of sICH, and the benefits of treatment are uncertain. Treatment may be reasonable if there is the potential for substantial benefit.

Extra-axial intracranial neoplasms
IV alteplase treatment is probably recommended for patients with AIS who harbor an extra-axial intracranial neoplasm.

Acute MI

For patients presenting with concurrent AIS and acute MI, treatment with IV alteplase at the dose appropriate for cerebral ischemia, followed by percutaneous coronary angioplasty and stenting if indicated, is reasonable.

Recent MI

For patients presenting with AIS and a history of recent MI in the past 3 mo, treating the ischemic stroke with IV alteplase is reasonable if the recent MI was non-STEMI.

For patients presenting with AIS and a history of recent MI in the past 3 mo, treating the ischemic stroke with IV alteplase is reasonable if the recent MI was a STEMI involving the right or inferior myocardium.

For patients presenting with AIS and a history of recent MI in the past 3 mo, treating the ischemic stroke with IV alteplase may reasonable if the recent MI was a STEMI involving the left anterior myocardium.

Systemic malignancy

The safety and efficacy of alteplase in patients with current malignancy are not well established.

Patients with systemic malignancy and reasonable (>6 mo) life expectancy may benefit from IV alteplase if other contraindications such as coagulation abnormalities, recent surgery, or systemic bleeding do not coexist.

Pregnancy

IV alteplase administration may be considered in pregnancy when the anticipated benefits of treating moderate or severe stroke outweigh the anticipated increased risks of uterine bleeding.

The safety and efficacy of IV alteplase in the early postpartum period (<14 d after delivery) have not been well established.

Ophthalmological conditions
Use of IV alteplase in patients presenting with AIS who have a history of diabetic hemorrhagic retinopathy or other hemorrhagic ophthalmic conditions is reasonable to recommend, but the potential increased risk of visual loss should be weighed against the anticipated benefits of reduced stroke-related neurological deficits.

Sickle cell disease IV alteplase for adults presenting with an AIS with known sickle cell disease can be beneficial.

Illicit drug use Treating clinicians should be aware that illicit drug use may be a contributing factor to incident stroke. IV alteplase is reasonable in instances of illicit drug use–associated AIS in patients with no other exclusions.

Stroke mimics

The risk of symptomatic intracranial hemorrhage in the stroke mimic population is quite low; thus, starting IV alteplase is probably recommended in preference over delaying treatment to pursue additional diagnostic studies.

Inclusion criteria

- Acute ischemic stroke with measurable neurologic deficit
- Onset of symptoms less than 3 h before institution of treatment
- Onset of symptoms between 3 and 4.5 h and patient younger than 80 years, and with NIH stroke score below 25, nondiabetic, and having received no recent anticoagulant medication, regardless of INR'
- Age over 18 years

Exclusion criteria

- Cerebral imaging showing intracerebral hemorrhage
- Cerebral imaging demonstrating large infarction
- Head trauma within 3 months prior to stroke
- History of intracranial hemorrhage
- BP sys >185 mm Hg or dias>110 mm Hg that has not responded to med
- Active bleeding or arterial puncture a t non compressible site
- Platelet count <1 00,000 /mm3
- Heparin administered within 48 h resulting in a PTTabove normal range
- Current use of anticoagulation with INR > 1 .7 or prothrombin time > 1 5 s
- Blood glucose <50 mg/ dL (2. 7 mmol /L)

Relative contraindications

- Minor or resolving stroke
- Seizure at onset
- Major surgery or trauma within 14 days
- Gastrointestinal or urinary bleeding within 21 days
- Myocardial infarction within 3 months