Commonly Asked Questions in Patients with Acute Ischemic Stroke Considered for Intravenous Thrombolysis

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Disclosure Statement

All content in my presentation and material are free of commercial interest input and hold no commercial bias.

Learning Objectives

- To discuss commonly posed questions in thrombolytic management in the treatment of acute ischemic stroke within 4.5 hours and beyond
- To review safety and efficacy of thrombolytic therapy in specific situations with ambiguous guidance from the literature

Acute ischemic st[illegible] of symptom onset

Time is Brain

Should thrombolytic therapy be withheld from patients with acute ischemic stroke older than 80 years of age? Due to the fear of an increased bleeding risk, thrombolytic therapy is withheld from many patients with AIS > 80 years of age. The European license for rt-PA is restricted to patients between 18 and 80 years of age.

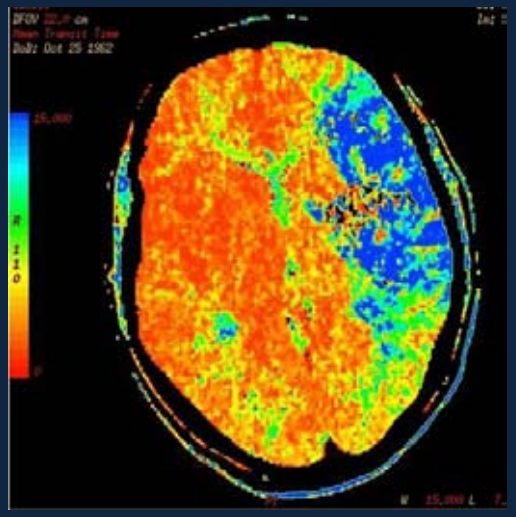
Octogenarians or older patients should be part of the target population for thrombolysis.

Is the NIHSS a substitute for the neurologic examination? No.

The NIHSS is a well validated 15-item scale used to assess the severity of an acute stroke. The NIHSS yields a score between 0 (normal) and 42 (maximum score). Lower scores with right hemispheric strokes. Underpowered for assessing severity of right hemispheric damage in the acute phase.

A score of 0 in the NIHSS does not exclude a stroke (eg; cerebellar infarction).

Is penumbral imaging clinically useful for patient selection for thrombolysis following acute ischemic stroke?



The penumbral neuroimaging pattern to select patients for thrombolysis or embolectomy has not been shown to lead to improved clinical outcomes.

Kidwell CS, et al. A Trial of Imaging Selection and Endovascular Treatment for Ischemic Stroke. N Engl J Med 2013;368:914

Is it safe to use thrombolytic therapy for acute ischemic stroke following an acute or recent myocardial infarction? There is no evidence to support the 3 month window for recent MI as a contraindication for IV stroke thrombolysis in many guidelines. Indirect histopathologic evidence indicates that the risk of cardiac rupture is highest within 7 weeks of MI. After 7 weeks risk for cardiac rupture can be stratified and IV stroke thrombolysis may be considered for younger patients with MI without transmural involvement.

Neurology. 2011 (76):1838-1840

- Is a seizure at onset of stroke symptoms an exclusion? NO, provided the persistent deficits are due to the stroke and are not post-ictal
- Are mild or rapidly improving symptoms an exclusion? NO, approximately 20% of patients in the “too good to treat” category end up with a poor outcome.
- What is an isolated mild neurological deficit? Ataxia alone, sensory loss alone, dysarthria alone, or minimal weakness
- Is a recent TIA with manifestations similar to the current symptoms a contraindication? NO (reset the clock!)
- Should I wait for laboratory coagulation tests in patients without a suspected coagulopathy? NO
- Are active menses at the time of stroke symptoms an exclusion? NO

Is prior use of antiplatelet therapy a contraindication to IV tPA in acute ischemic stroke? No.

Antiplatelet therapy not associated with a significant increased risk of symptomatic ICH, mortality, or poor functional outcome. Antiplatelet therapy is not to be given within the first 24 hours after IV tPA.

Acute ischemic strok  s of symptom onset

Time is Brain

Exclusion Criteria: Historical/Clinical/Laboratory/Imaging

- ECASS III excluded patients >80 years old and patients with a combination of previous stroke and diabetes mellitus.
- ECASS III additionally excluded patients with an NIHSS score of >25.
- ECASS III additionally excluded any anticoagulant therapy regardless of INR value
- ECASS III additionally excluded evidence of major infarct signs (>1/3 of the MCA territory)

Acute ischemic strok  of symptom onset

Time is Brain

What is the effectiveness of IV tPA administered from 4.5 to 6 hrs after stroke onset? Neither established, nor excluded. In the IST-3 Trial, 3035 patients with ischemic stroke within 6 hours of onset were studied. At 6 months there was a non-significant trend for a favorable outcome (alive or independent) with IV tPA compared to placebo (37% vs 35 %). Patients given tPA within 6 hours were more likely to have a good quality of life 18 months afterwards.

What is the NNT to obtain a favorable outcome with IV tPA for acute ischemic stroke in each of the following four time windows?

- *4.5* for 0-90 minutes
- *9.0* for 91-180 minutes
- *14.1* for 181-270 minutes
- *21.4* for 271-360 minutes

Time is Brain
Primum non tardar

Which of the following - 1) spontaneous, 2) IV tPA, 3) IA tPA, 4) IV + IA tPA, or 5) mechanical thrombectomy has the highest rate of recanalization?

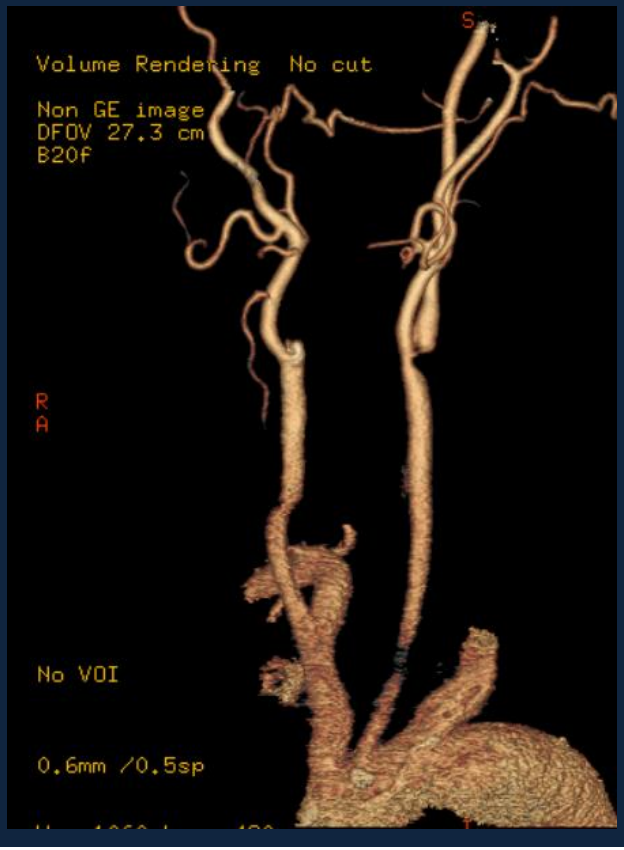
1) 24.1 %
2) 46.2%
3) 63.2 %
4) 67.5 %
5) 83.6 %

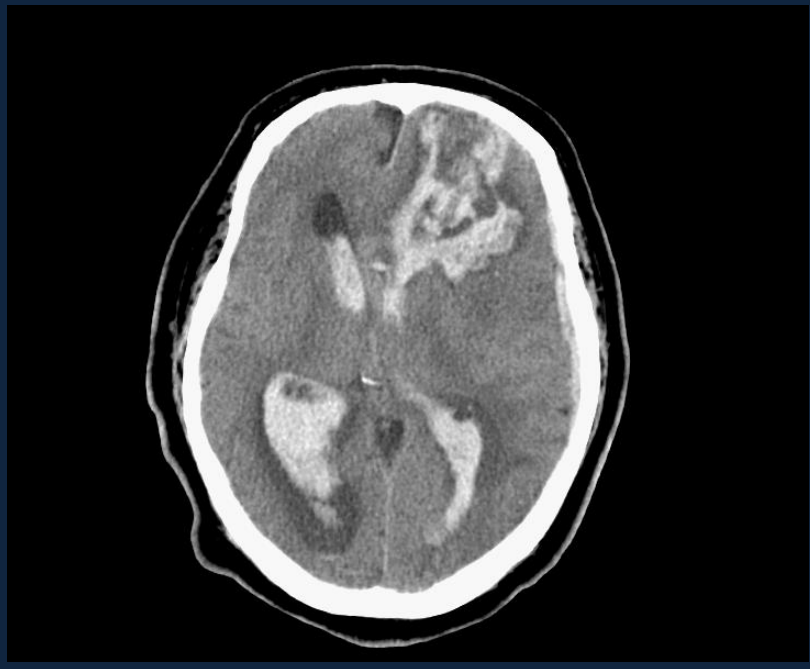
What is the risk of ICH among patients with *stroke mimics* treated with iv rtPA? Very Low (<1% chance in patients who do not have a mass visible on CCT)

Is rtPA contraindicated in the management of AIS after cardiac catheterization? No defined standard treatment exists for AIS following cardiac catheterization. Limited number of studies of IV vs. IA thrombolysis. Need for additional prospective randomized study to determine which stroke treatment modality is the safer alternative.

Is it safe to perform thrombolysis for an acute ischemic stroke in a patient treated with Dabigatran, Rivaroxaban, Apixaban, or other Direct Factor Xa inhibitors? No, evidence-based data available to answer this question. Relationship of aPTT prolongation and dabigatran concentration is not linear. The aPTT may be normal despite a prolonged TT. A dabigatran concentration of < 10 ng/ml which corresponds to a TT < 38 seconds has been proposed as the upper limit for selective thrombolysis. Future studies are needed.

Can CEA be performed safely after thrombolysis with tPA, and, if so, when? Insufficient data.

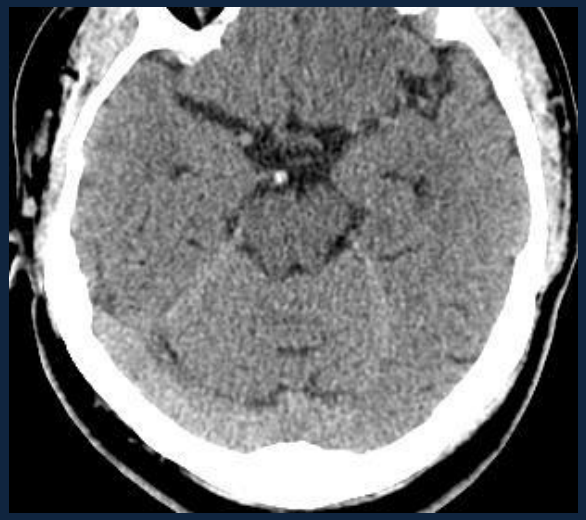


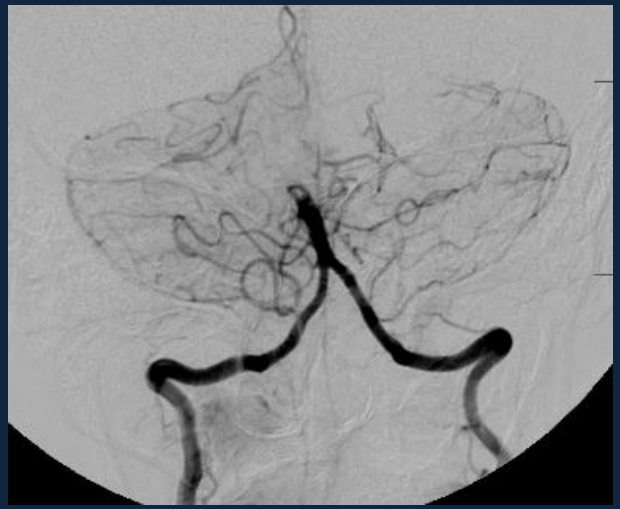


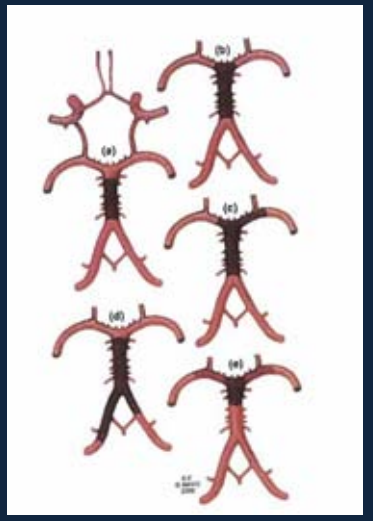
Bartoli MA, et al. Eur J Vasc Endovasc Surg 37:512-518. 2009

Crozier JEM, et al. Br J Surg 2008;95(3):188

What is the optimal management of Basilar Artery Occlusion? No evidence that death or dependency, or survival is improved with intra-arterial thrombolytic therapy when compared to intravenous thrombolytic therapy.







Can thrombolytic therapy be administered in the context of a non-ruptured intracranial aneurysm?

The administration of thrombolytic therapy does not influence the rupture of an intracranial aneurysm. However, the predominance of patients described experienced small aneurysms mostly under 10 mm, and many under 7 mm, sized that are less likely to bleed over the short term. There are insufficient data to recommend in favor of or against thrombolytic therapy in the context of medium and large intracranial aneurysms.

Could thrombolysis with intravenous tPA worsen a cervical artery dissection and patient outcome? Thrombolysis with tPA appears safe in patients with AIS secondary to CAD. No increase in complications, including intracranial hemorrhage were noted in two studies when outcome in patients treated with tPA when compared to controls.

Stroke 2011; 42: 2515-2520 ;
Arch Neurol 2011; 68:1536-1542

Is the combined IV and IA approach to recanalization more effective than standard IV tPA alone for moderate to large (NIHSS ?Å10) stroke, and with a similar safety profile?

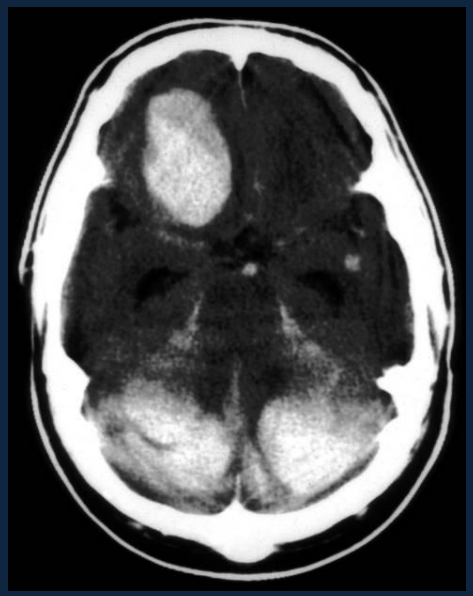
- IV tPA alone (n= 222)
- IV tPA and IA Rx - *either tPA delivered at the site of clot OR device to remove clot* - (n=434)
- 900 planned subjects; study stopped early at 656 due to futility
- Functional Independence
  - combined Rx = 41 %
  - IV tPA group = 39%
  - absolute adjusted difference 1.5 percentage points, 95% CI - 6.1 to 9.1
  - no significant difference in rate of functional independence for any of predefined secondary subgroup analysis
  - no safety concerns

Broderick JP, Palesh YY, Demchuck AM, et al. N Engl J Med. 2013; 368: 913

Is intra-arterial thrombolysis proven therapy for patients with acute ischemic stroke? The SYNTHESIS Expansion trial testing endovascular therapy found no benefit compared with IV tPA treatment. This open label trial with blinded assessment randomly assigned 362 patients with AIS to either IV tPA within 4.5 hours or endovascular treatment (IA tPA, mechanical clot disruption or combination of these methods) within 6 hours of symptom onset. At 3 months, endovascular treatment was no better than IV tPA for the outcome of disability-free survival (30% vs 35%). There was no significant differences between groups in the secondary outcome measures.

N Engl J Med 2013;368:904

How do you manage intracranial bleeding following IV thrombolysis for acute ischemic stroke?



- Stop thrombolytic
- CBC, PT, PTT, platelets, fibrinogen, D-dimer, type and cross match
- Emergency unenhanced head CT
- 10 units of cryoprecipitate
- 6 to 8 units of platelets
- FFP 2 units every 6 hours for 24-hours?
- Hematology and Neurosurgery consultations

How do you manage orolingual angioedema following IV thrombolysis for acute ischemic stroke? ACEIs, diphenhydramine 50 mg IV, H2 blockers, 100 mg of IV methylprednisolone or nebulized epinephrine, endotracheal intubation (fiberoptic techniques)

Thank you for your attention.
Questions? Comments?

References

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- *Neurology, 2011 (76):1838-1840*
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