Practical Stroke Review for the Hospitalist

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I have no financial disclosures

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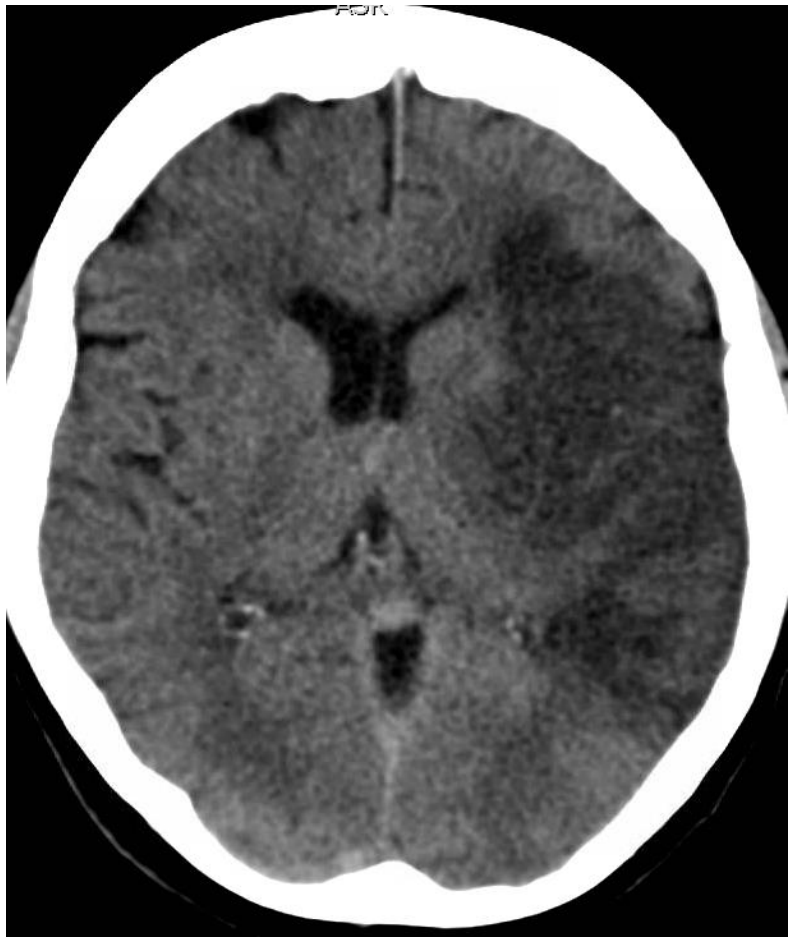
Overview

- Acute ischemic stroke assessment. Answering the time sensitive questions.
  - The right imaging for the job
  - Thrombolysis
  - Endovascular thrombectomy

- Stroke workup particularities

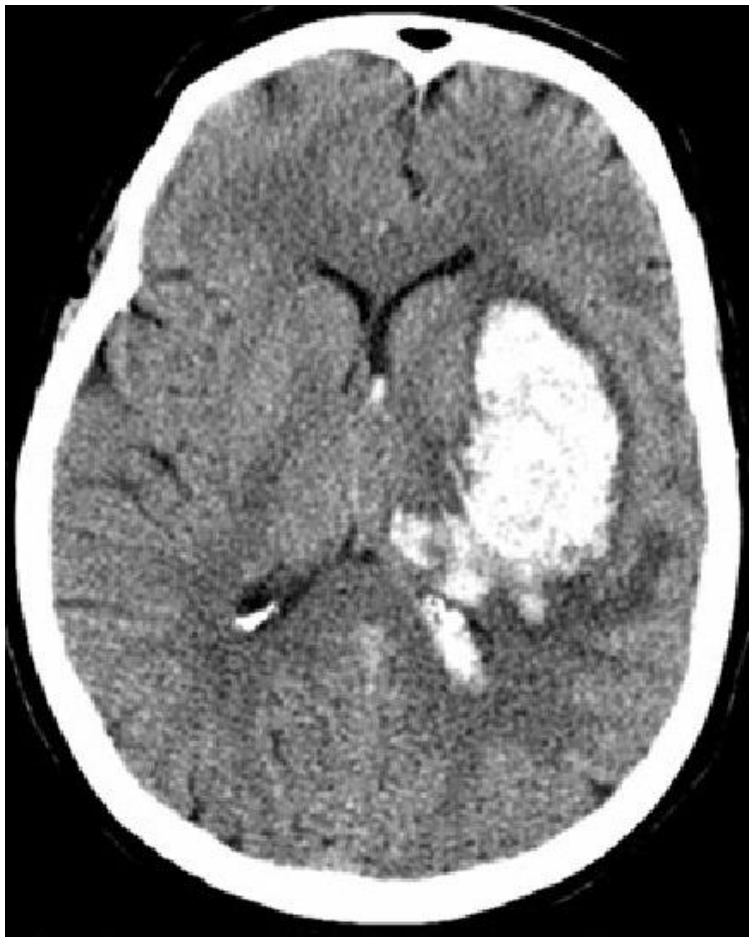
- Secondary stroke prevention
  - Antithrombotics
  - Secondary risk optimization

Ischemic



Due to **blockage** of a vessel
85% of strokes

Hemorrhagic



Due to **rupture** of a vessel
15% of strokes

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Case

68 yr. male admitted for decompensated HFrEF is found by his nurse to have new Right sided weakness, difficulty speaking, and left gaze deviation.

Main goals when concerned for an acute stroke:

1) Rule out intracranial hemorrhage
2) Determine candidacy for **thrombolysis** and/or **endovascular thrombectomy**

Initial Evaluation

1) Last Known Normal
2) Symptoms
3) Examine the patient
    1) NIHSS
    2) Cortical Signs?
4) Is the patient on any anticoagulation?
5) Vitals
6) INR, glucose, CBC

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Last Known Normal

- Important for determining candidacy for acute therapies

- Not always when symptoms started
  - Ex: patient found with left sided arm/leg weakness
    - Last nursing check 3 hrs prior patient was normal
    - LKN ~3 hrs ago

- Seek out anyone who may have interacted with the patient last
  - Witnesses
  - Family members
  - Nursing / techs / providers / etc.

Acute Evaluation

NIHSS

- Very focused neurologic exam designed specifically for acute stroke evaluation.

Figure 2. National Institutes of Health Stroke Scale

Category	Score	Time	Score
1a. Level of Consciousness (LOC) (Alert, drowsy, etc.)	0 = 1 = 2 = 3 =	Alert Drowsy Stuporous Coma	
1b. LOC Questions (Month, age)	0 = 1 = 2 =	Answers both correctly Answers one correctly Incorrect	
1c. LOC Commands (Open/close eyes, make fist & let go	0 = 1 = 2 =	Obeys both correctly Obeys one correctly Incorrect	
2. Best Gaze (Eyes open - pt follows examiner's fingers or face)	0 = 1 = 2 =	Normal Partial gaze palsy Forced deviation	
3. Visual (Introduce visual stimulus/threat to pt's visual field quandrants. Cover 1 eye and hold up fingers in all 4 quadrants.)	0 = 1 = 2 = 3 =	No visual loss Partial hemianopsia Complete hemianopsia Bilateral hemianopsia	
4. Facial Palsy (Show teeth, raise eyebrows and squeeze eyes tightly shut.)	0 = 1 = 2 = 3 =	Normal Minor Partial Complete	
5a. Motor Arm - Left (Elevate extremity to 90 degrees and score drift/ movement. Count to 10 out loud and use fingers for visual cue.)	0 = 1 = 2 = 3 = 4 = NT=	No drift Drift Can't resist gravity No effort against gravity No movement Amputation, joint fusion (Explain)	
5b. Motor Arm - Right (Elevate extremity to 90 degrees and score drift/ movement. Count to 10 out loud and use fingers for visual cue.)	0 = 1 = 2 = 3 = 4 = NT=	No drift Drift Can't resist gravity No effort against gravity No movement Amputation, joint fusion (Explain)	
6a. Motor Leg - Left (Elevate extremity to 30 degrees and score drift/ movement. Count to 5 out loud and use fingers for visual cue.)	0 = 1 = 2 = 3 = 4 = NT=	No drift Drift Can't resist gravity No effort against gravity No movement Amputation, joint fusion	
6b. Motor Leg - Right (Elevate extremity to 30 degrees and score drift/ movement. Count to 5 out loud and use fingers for visual cue.)	0 = 1 = 2 = 3 = 4 = NT=	No drift Drift Can't resist gravity No effort against gravity No movement Amputation, joint fusion (Explain)	
7. Limb ataxia (Finger to nose, heal down shin)	0 = 1 = 2 =	Absent Present in one limb Present in two limbs	
8. Sensory (Pin prick to face, arms, trunk, and legs -compare sharpness side to side, or no feeling at all.)	0 = 1 = 2 =	Normal Partial loss Severe loss	
9. Best Language (Name items, describe picture, and read sentences. Don't forget glasses if they normally wear them.)	0 = 1 = 2 = 3 =	No aphasia Mild to moderate aphasia Severe aphasia Mute	
10. Dysarthria (Evaluate speech clarity by pt reading or repeating words on list.)	0 = 1 = 2 = NT	Normal articulation Mild to moderate dysarthria Near to unintelligible or worse Intubated or other physical barrier	
11. Extinction and Inattention (Use information from prior testing or double simultaneous stimuli testing to identify neglect. Face, arms, legs and visual fields.)	0 = 1 = 2 =	No neglect Partial neglect Complete neglect	
NT= Not Testable acceptable as noted above			
TOTAL SCORE:			

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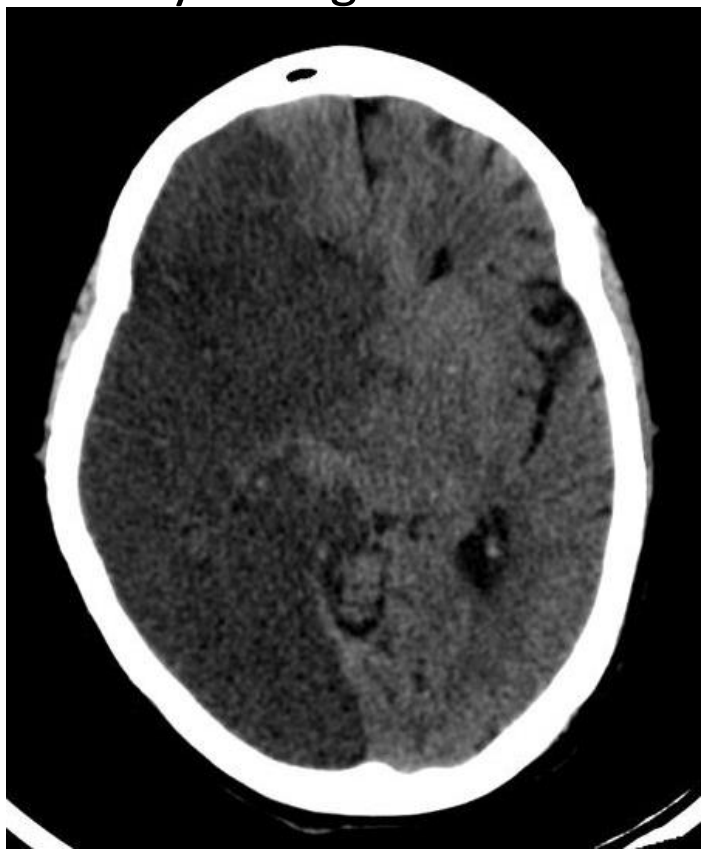
Get CT Head and CT angiogram Head and Neck for anyone you're concerned potentially is having an acute stroke.

- May be bundled
  - Ex: @ OHSU when CTA head/neck is ordered, it comes with a CTH without contrast.

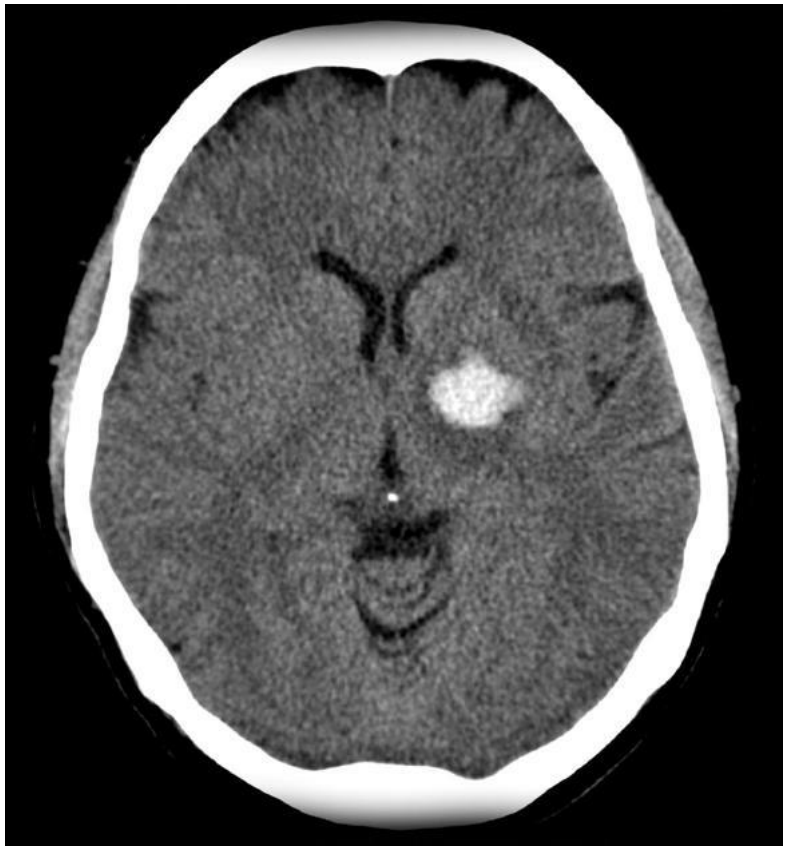
- The two most important images to determine acute intervention.

Acute stroke imaging

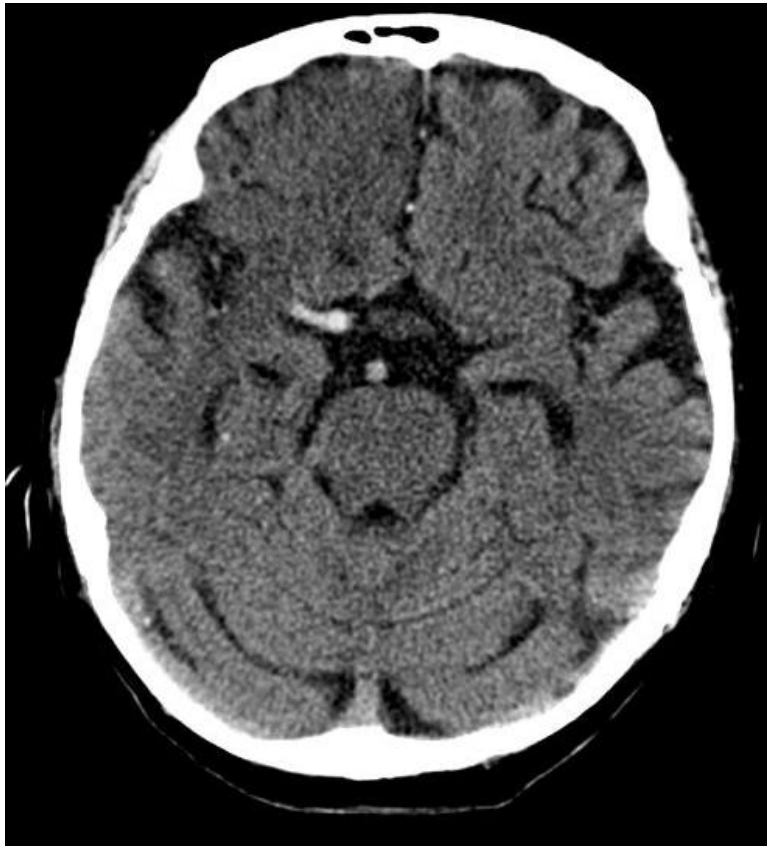
What you might see



Hypodensity = ischemia



Hyperdensity = hemorrhage



Hyperdense vessel = intraluminal thrombus

Avoid MRI in your initial evaluation.*

- Good utility in determining stroke size and complete involvement, at some point during admission.

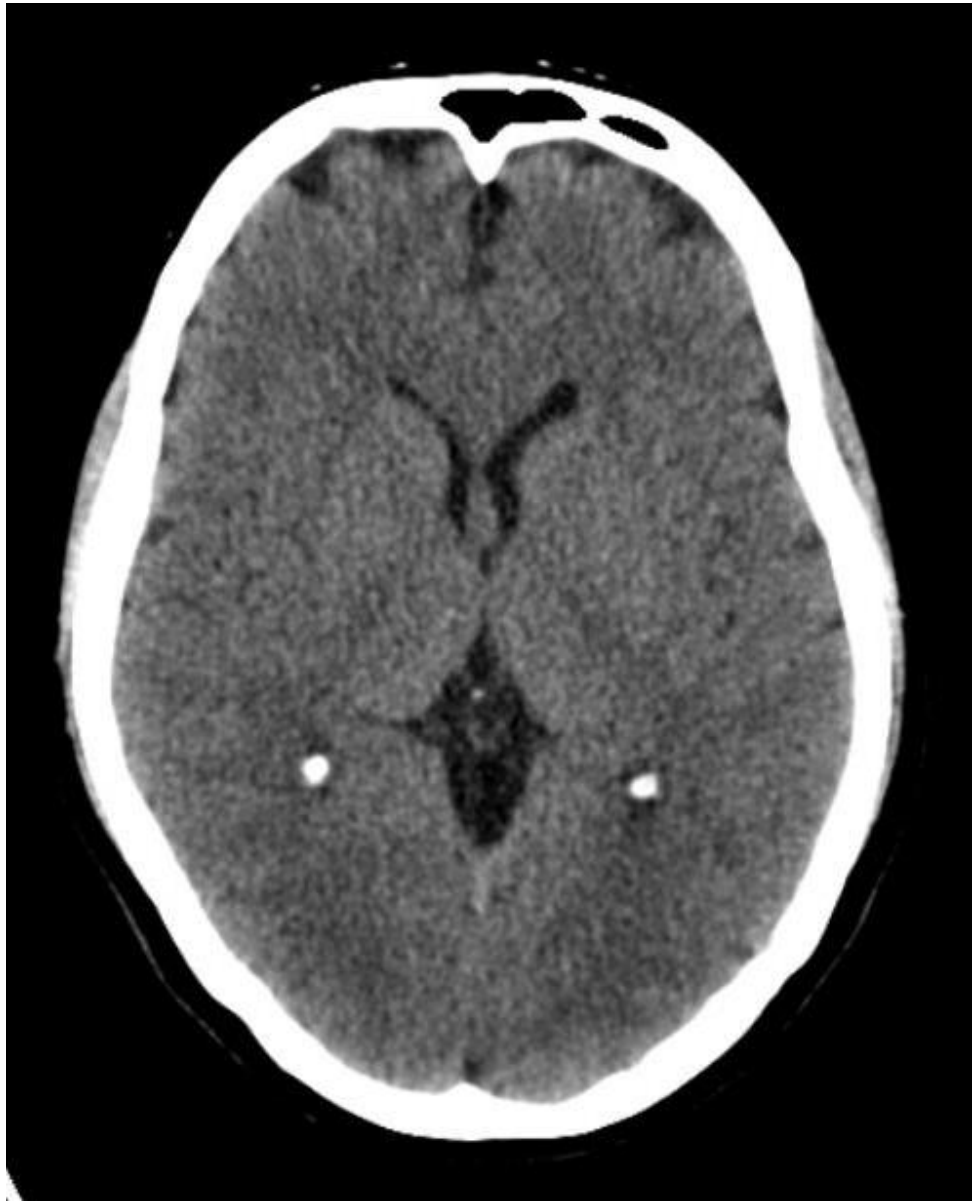
- Slow
- Exception: Less common, but some institutions use rapid MRI based imaging for acute stroke evaluations.
  - Most places are CT based.

Case

Initial History reveals
- LKN: 2 hrs prior
- Not currently anticoagulated
- NIHSS 19
  - RUE, RLE, right facial weakness
  - Left gaze deviation
  - Global aphasia
    - Not following commands
    - Unable to name objects
    - Unable to repeat words

Vitals
BP 161/90
HR 86

Lab Data
INR 1.1
Platelets 210,000
Glucose 160



Noncontrast head CT

Is the patient a candidate for acute stroke treatment?

Main goal of acute treatment is to save areas of brain that are effected, but not yet infarcted.

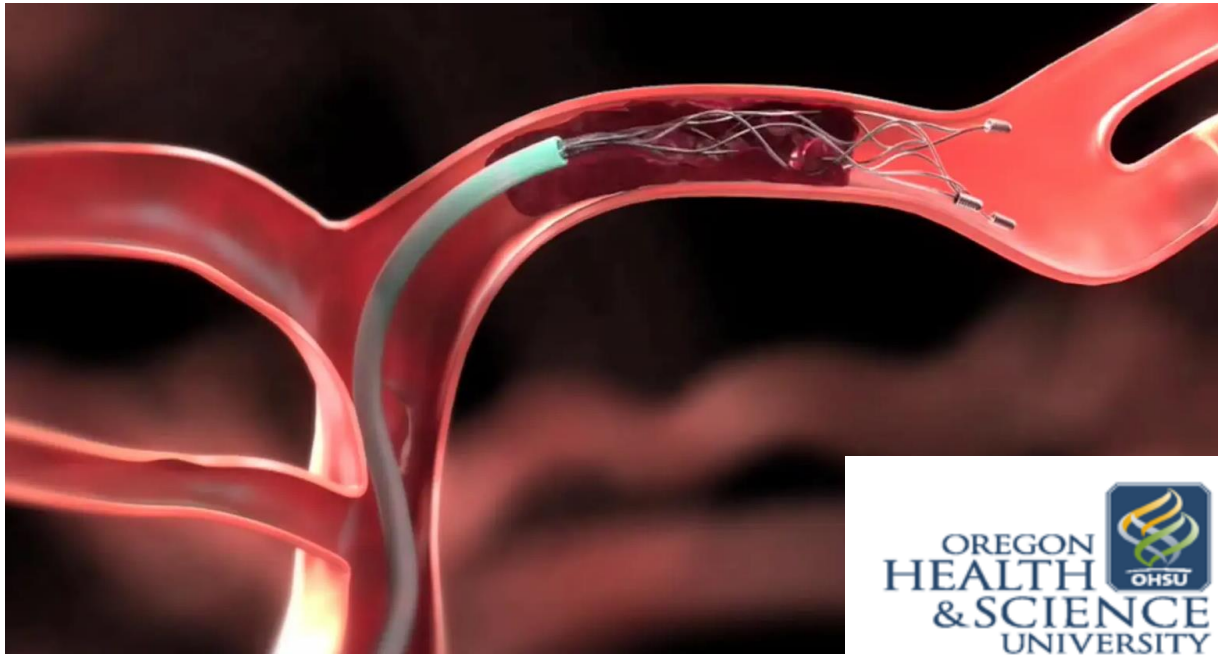
How?

Recanalization and Reperfusion

Two major options

Chemical thrombolysis
- Alteplase (tPA)
- Tenecteplase (TNK)

Endovascular thrombectomy (EVT)



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Recanalization and Reperfusion

Which one(s) do we use and how to we decide?

Thrombolysis

Candidacy

When is thrombolysis appropriate?

Sounds like an ischemic stroke

<4.5 hours from last known normal / witnessed symptom onset

NIHSS generally ~≥ 3-4*

Age >= 18**

No hemorrhage on CT head scan

No contraindications

Candidacy

TNK/tPa contraindications

- Neurosurgery, head trauma, or ischemic stroke in last 3 months
- SBP >185, DBP >110
- Any history of or current intracranial hemorrhage
- Known intracranial AVM, aneurysm, malignancy*
- Suspected/confirmed active endocarditis
- Platelets <100k
- INR >1.7
- Any therapeutic anticoagulation
- Glucose <50
- GI bleed in last 21 days
- Active internal bleeding
- CT Head showing extensive hypodensity > 1/3 of cerebral hemisphere

Imaging

CT Head WO contrast

- Technically, this is all you need to get for thrombolysis

2.2. Head and Neck Imaging

2.2.1. Initial Imaging	COR	LOE	New, Revised, or Unchanged
3. Noncontrast CT (NCCT) is effective to exclude ICH before IV alteplase administration.	I	A	Recommendation revised from 2013 AIS Guidelines.

Often we get more imaging concurrently (CT angio, CT Perfusion) for other purposes

Options

IV Thrombolysis in acute ischemic stroke has two drugs in use

Alteplase (tPA)

Tenecteplase (TNK)

tPA

Alteplase (tPA)

- Only thrombolytic used for acute stroke for >20 years
- The first major evolution in acute stroke treatment

Efficacy

tPA effectively improves functional longterm outcomes in eligible patients with acute ischemic strokes

NINDS 1995

- AIS patients treated with tPA within 3 hrs of last known normal
- **30% more likely to have minimal or no disability @ 90 days**

ATLANTIS 2002

tPA vs placebo in acute stroke patients with last known well **<3 hrs** ago

- 1◦ endpoint: NIHSS ≤1 @ 90 days post stroke
- Significant difference favoring tPA group achieving 1◦ endpoint (60.9% tpa vs 26.3% placebo; p=0.01)

ECASS III

tPA vs placebo in acute stroke patients with last known well **3-4.5 hrs** prior

- 1◦ endpoint: mRS 0-1 @ 90 days post stroke
- significant difference favoring tPA group compared to placebo in achieving primary en
- Significant increase in **sICH** in tPA group 2.4% vs 0.2%; P=0.008

AHA guidelines 2019

<3 hrs from onset / LKN

1. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute) is recommended for selected patients who can be treated within 3 hours of ischemic stroke symptom onset or patient last known well or at baseline state. Physicians should review the criteria outlined in Table 8 to determine patient eligibility.	I	A	Recommendation reworded for clarity from 2013 AIS Guidelines. COR and LOE unchanged. See Table XCV in online Data Supplement 1 for original wording.

The safety and efficacy of this treatment when administered within the first 3 hours after stroke onset are solidly supported by combined data from multiple RCTs[155–157] and confirmed by extensive community experience in many countries.[158] The eligibility criteria for IV alteplase have evolved over time as its usefulness and true risks have become clearer. A recent AHA statement provides a detailed discussion of this topic.[14] Eligibility recommendations for IV alteplase in patients with AIS are summarized in Table 8. The benefit of IV alteplase is well established for adult patients with disabling stroke symptoms regardless of age and stroke severity.[78,159] Because of this proven benefit and the need to expedite treatment, when a patient cannot provide consent (eg, aphasia, confusion) and a legally authorized representative is not immediately available to provide proxy consent, it is justified to proceed with IV alteplase in an otherwise eligible adult patient with a disabling AIS. In a recent trial, a lower dose of IV alteplase (0.6 mg/kg) was not shown to be noninferior to standard-dose IV alteplase for the reduction of death and disability at 90 days.[160]

See Table XX in online Data Supplement 1.

AHA guidelines 2019

<4.5 hrs from onset / LKN

2. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute) is also recommended for selected patients who can be treated within 3 and 4.5 hours of ischemic stroke symptom onset or patient last known well or at baseline state. Physicians should review the criteria outlined in Table 8 to determine patient eligibility.	**I**	**B-R**	Recommendation reworded for clarity from 2013 AIS Guidelines. COR unchanged. LOE amended to conform with ACC/AHA 2015 Recommendation Classification System. See Table XCV in online Data Supplement 1 for original wording.
One trial (ECASS III) specifically evaluating the efficacy of IV alteplase within 3 and 4.5 hours after symptom onset[49] and pooled analysis of multiple trials testing IV alteplase within various time windows[155–157] support the efficacy of IV alteplase up to 4.5 hours after symptom onset. ECASS III excluded octogenarians, patients taking warfarin regardless of international normalized ratio, patients with combined history of diabetes mellitus and previous ischemic stroke, and patients with very severe strokes (NIHSS score >25) because of a perceived excessive risk of intracranial hemorrhage in those cases. However, careful analysis of available published data summarized in an AHA/American Stroke Association (ASA) scientific statement indicates that these exclusion criteria from the trial may not be justified in practice (Table 8).[14]			See Table XX in online Data Supplement 1.

Efficacy is Time Dependent

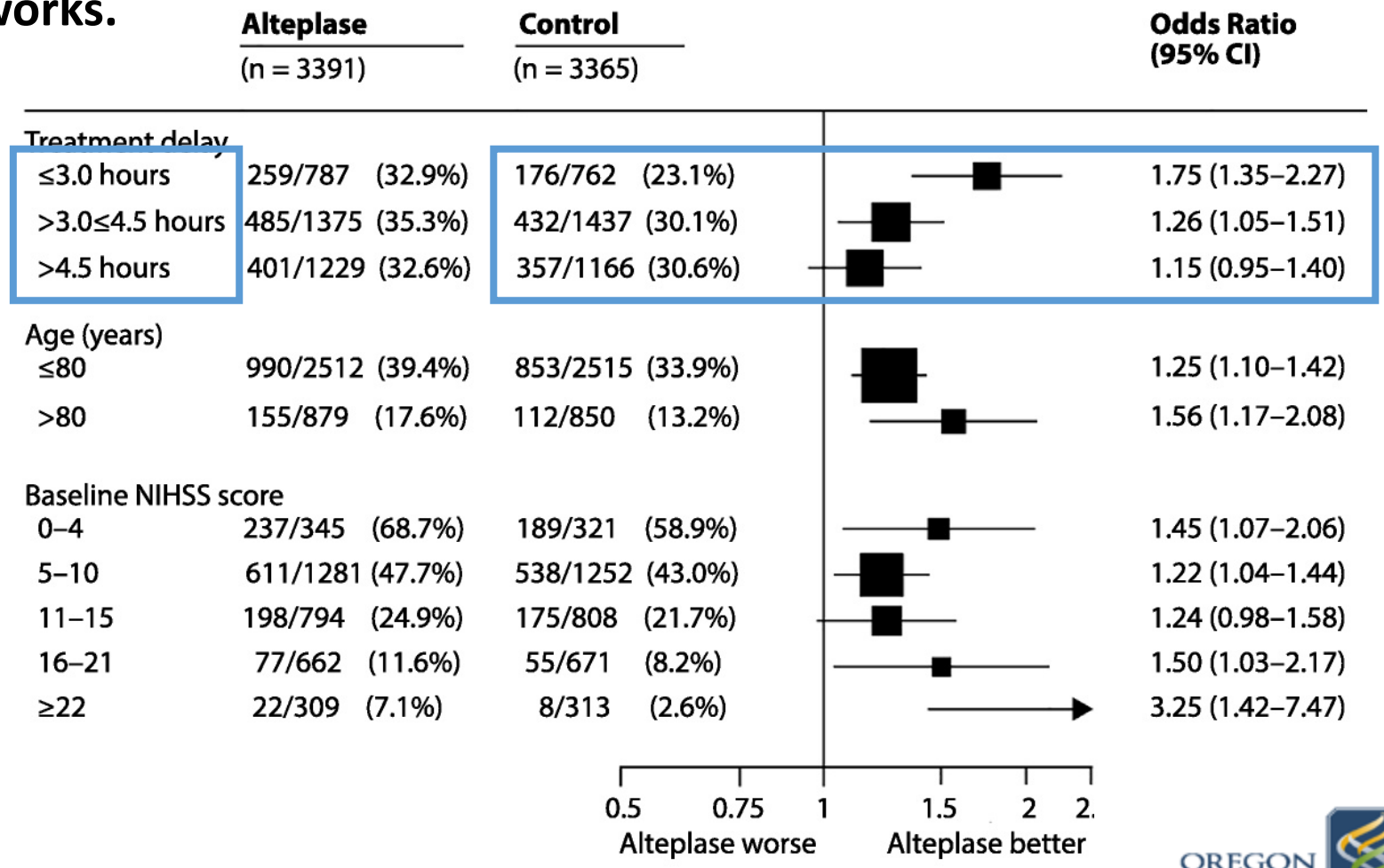
The earlier it is given, the better it works.

NNT for functional independence (mRS 0-1)

- Given <1.5 hrs → 3.6
- Given between 2 – 3 hrs → 4.3
- Given between 3 – 4.5 hrs → 5.9

Efficacy is Time Dependent

The earlier it is given, the better it works.



Odds ratio for likelihood to achieve mRS 0 or 1 @ 90 days post stroke

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Risks

It is not without risk

Symptomatic ICH; rates vary
- 6% risk in all-comers *Miller DJ, et al. 2011*
- 3-4% risk in patients with minor, non-disabling stroke *PRISMS 2018*
- 1.8 – 21.2% depending on risk stratification *NINDs subsequent analysis 2004*

Orolingual angioedema – rare, but life threatening

TNK

Tenecteplase (TNK)

- Thrombolytic agent long used in myocardial infarction patients
- Single bolus dosing (no additional infusion required)
- Higher fibrin selectivity

TNK

Tenecteplase (TNK)

- Thrombolytic agent long used in myocardial infarction patients
- Single bolus dosing (no additional infusion required)
- Higher fibrin selectivity
- Now being considered and used for acute ischemic strokes in many centers

3.6. Other IV Fibrinolytics and Sonothrombolysis	COR	LOE	New, Revised, or Unchanged
1. It may be reasonable to choose tenecteplase (single IV bolus of 0.25-mg/kg, maximum 25 mg) over IV alteplase in patients without contraindications for IV fibrinolysis who are also eligible to undergo mechanical thrombectomy.	**IIb**	**B-R**	New recommendation.
IV tenecteplase (0.25 mg/kg bolus, maximum 25 mg) was compared with IV alteplase (usual dose of 0.9 mg/kg over 60 minutes, maximum 90 mg) in the EXTEND-IA TNK trial (Tenecteplase Versus Alteplase Before Endovascular Therapy for Ischemic Stroke).[178] This multicenter trial randomized 202 patients without previous severe disability and with documented occlusion of the internal carotid artery, proximal MCA (M1 or M2 segments), or basilar arteries presenting within 4.5 hours of symptom onset to receive 1 of these 2 fibrinolytic agents. Primary end point was reperfusion of >50% of the involved ischemic territory or an absence of retrievable thrombus at the time of the initial angiographic assessment. The trial was designed to test for noninferiority and, if noninferiority proven, for superiority. Secondary outcomes included the mRS score at 90 days. Median NIHSS score was 17. The primary end point was achieved by 22% of patients treated with tenecteplase versus 10% of those treated with alteplase (P=0.002 for noninferiority and 0.03 for superiority). In an analysis of secondary end points, tenecteplase resulted in better functional outcomes at 90 days on the basis of the ordinal shift analysis of the mRS score (common OR [cOR], 1.7 [95% CI, 1.0–2.8]; P=0.04) but less robustly for the proportion who achieved an mRS score of 0 to 1 (P=0.23) or 0 to 2 (P=0.06). sICH rates were 1% in both groups.			See Table XLIII in online Data Supplement 1.

TNK

Tenecteplase (TNK)

- Newer means less data overall
- ~7 randomized trials comparing TNK to tPA

TNK

Tenecteplase (TNK)

sICH Rates

- No study found any significant difference between TNK and tPA

Functional Outcomes @ 90 days

- No significant difference found

Thrombolysis

Options

Alteplase (tPA)	NINDS 1995 ECASS 1995 ECASS II 1998 ATLANTIS B 1999 ATLANTIS A 2000 ATLANTIS sub-group 2002 ECASS III 2008 EPITHET 2008	Many other studies (retrospective, prospective, meta-analyses, etc.) over the years. These are the landmark RCTs
Tenecteplase (TNK)	Australian TNK Trial 2012 ATTEST 2015 NOR-TEST 2017 EXTEND IA–TNK Part 1 2018 EXTEND IA-TNK Part 2 2020	Less study rigor compared to tPA since newer. Mostly phase II trials. Two major phase III RCTs. Clear evidence for non-inferiority. Pretty good evidence that it may be better than tPA in some scenarios.

Candidacy for thrombolysis?

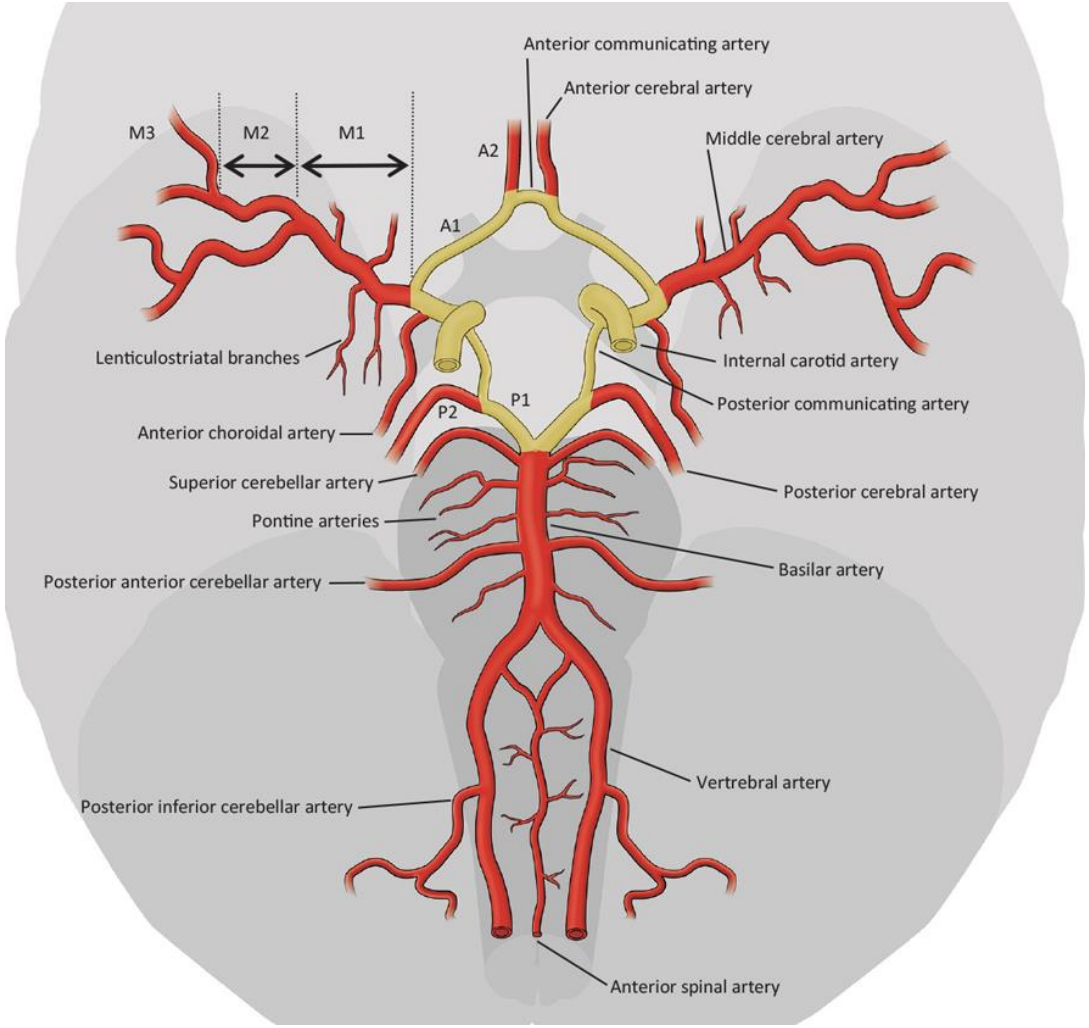
- Onset <4.5 hrs
- NIHSS >= 3-4
- No hemorrhage on CT Head
- Platelets >100,000
- No anticoagulation; INR <1.7
- Blood pressure @ goal (SBP <185 and DBP <110)

If no LVO after tPA/TNK, then post thrombolysis precautions

- ICU monitoring; q1h neurochecks and vital signs
- No antiplatelet or anticoagulation for 24 hrs
- Avoid placing lines or foley
- Permissive HTN; SBP goal <185 and DBP goal <110
- CT Head non-contrast 24 hrs post thrombolysis
- Low threshold for repeating CT Head scan for any new symptoms to rule out intracranial blood.

If there is an LVO seen on vessel imaging…

Candidate for mechanical thrombectomy?



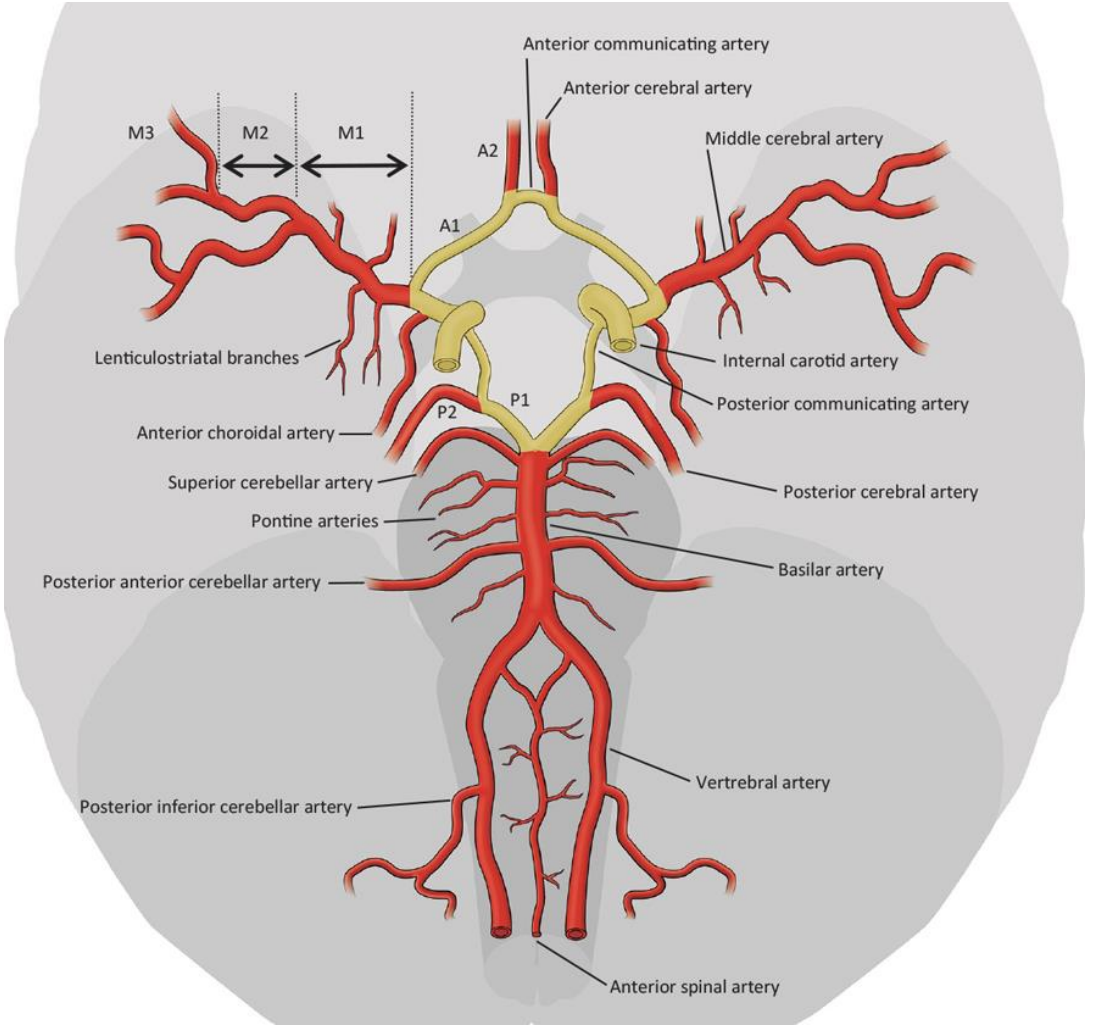
Candidacy

A. LVO?

Look for on vessel imaging (typically CT angio H/N)

- Classically include
  - Internal carotid artery (ICA)
  - Middle cerebral artery (MCA)
    - M1
  - Anterior cerebral artery (ACA)
    - A1

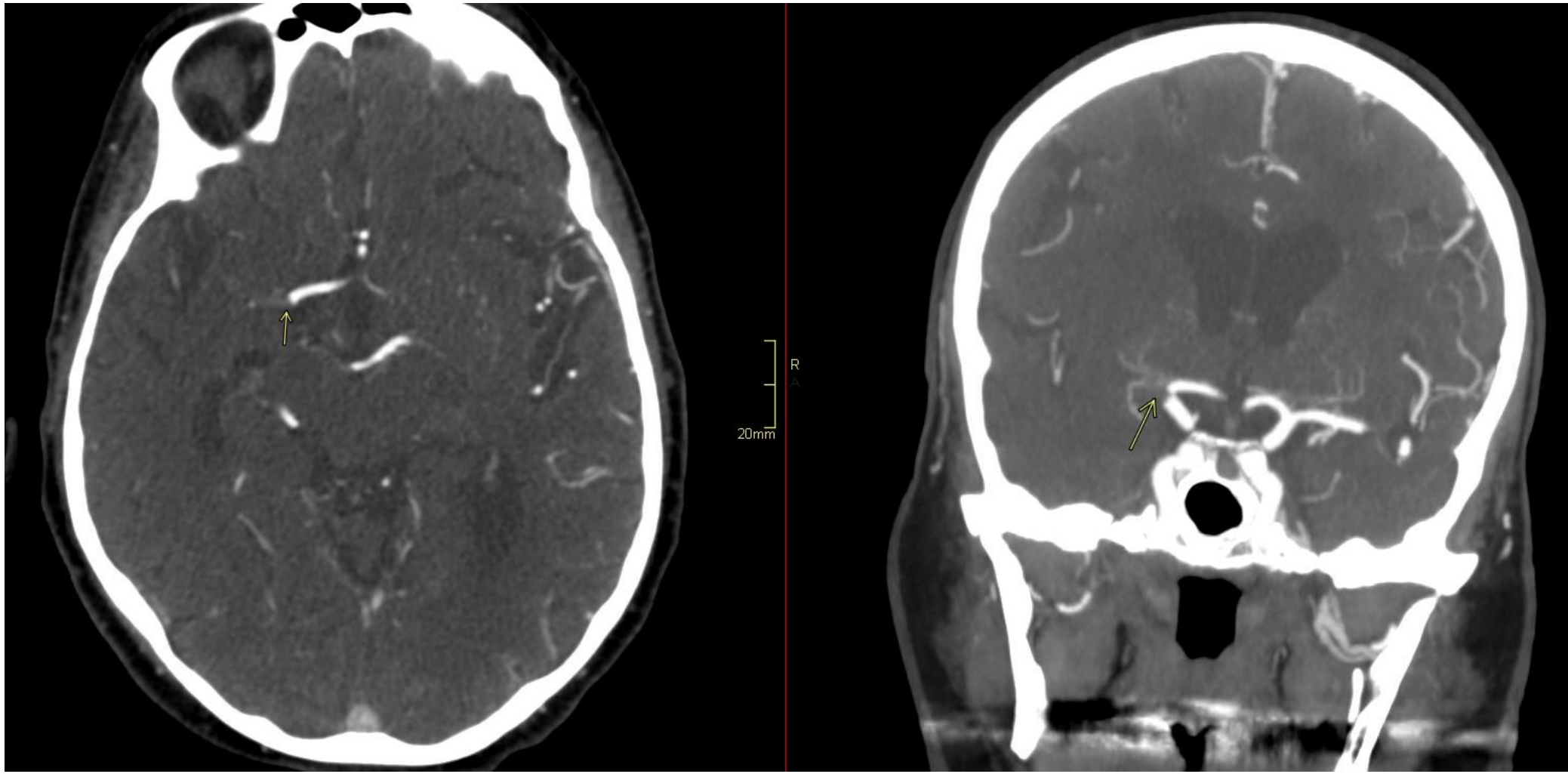
*All **anterior circulation**.*
*There is significantly less data for **posterior** circulation thrombectomy.*



Candidacy

LVO Examples

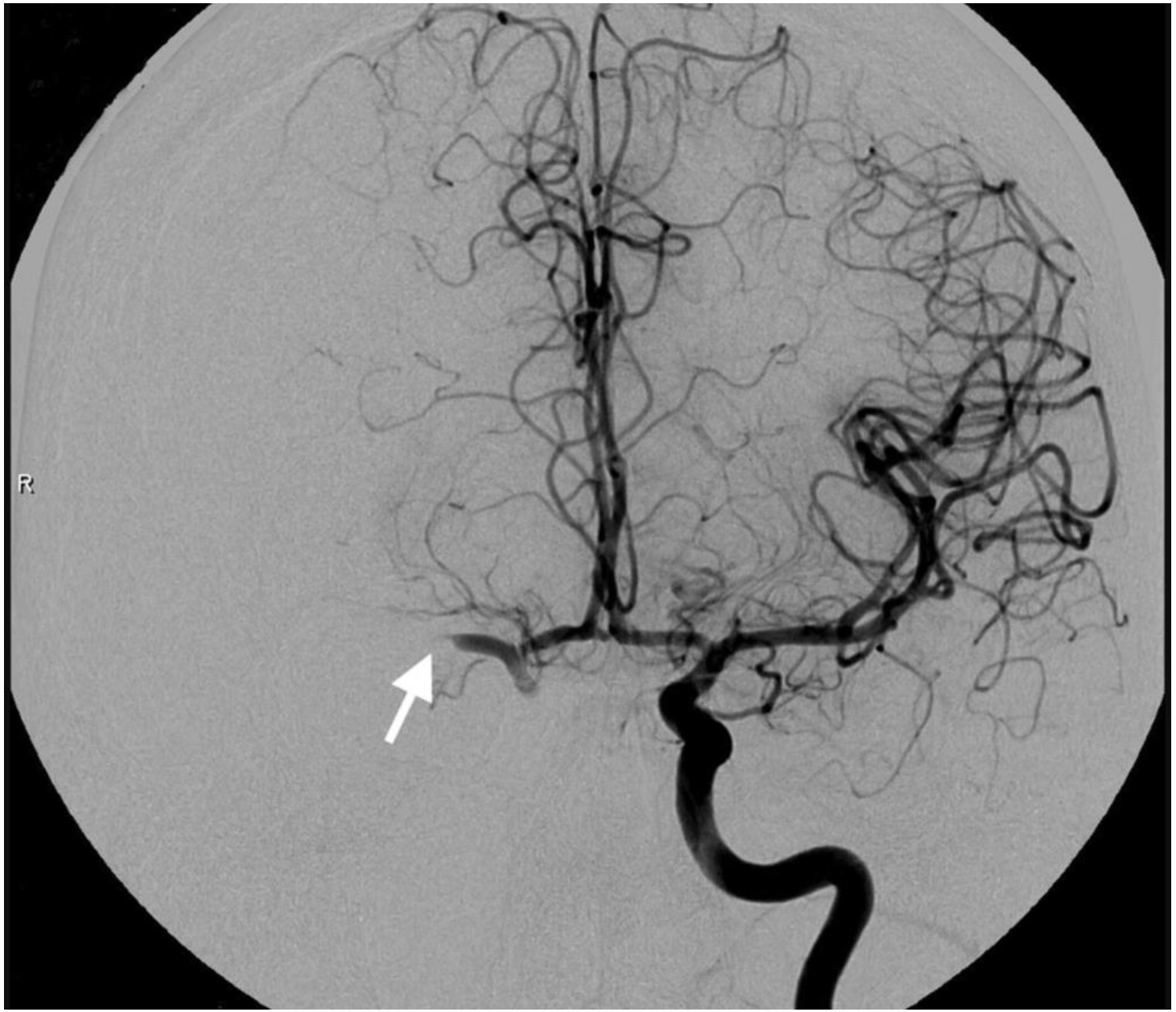
CT Angiogram
Right M1



Candidacy

LVO Examples

Diagnostic cerebral angiogram
Right M1 occlusion



Powerful intervention for treatment of acute strokes with **Large Vessel Occlusion within 6 hrs**

MR CLEAN 2015

Thrombectomy vs standard care in patients with acute stroke + anterior LVO + symptoms onset <6 hrs

- Primary outcome: mRS @ 90 days post stroke
- EVT superior to standard of care for:
  - Better mRS @ 90 days
  - Small final infarct volume
  - Lower NIHSS at 1 week
- No different in symptomatic ICH

Powerful intervention for treatment of acute strokes with **Large Vessel Occlusion** ***in extended perfusion guided windows up to 24 hrs***

DEFUSE III 2018

Standard care +/- thrombectomy in acute stroke + anterior LVO + LKN 6-16 hrs + favorable perfusion

- Good functional outcome (mRS 0-2)
  - Favored EVT group. 45% vs 17%; $p<0.001$
- No significant difference in sICH
  - 7% (EVT) vs 4% (control); $p=0.75$

DAWN 2017

Standard care +/- thrombectomy in acute stroke + anterior LVO + LKN 6-24 hrs + favorable perfusion

- Favored EVT group over standard of care alone →Functional independence in 49% (EVT) vs 13% (control)
  - **NNT 2.8**
- No significant difference in sICH. 6% (EVT) v 3% (control); $p=0.5$

Candidacy

<6 hrs from LKN / symptom onset

3.7.2. 0 to 6 Hours From Onset	COR	LOE	New, Revised, or Unchanged
1. Patients should receive mechanical thrombectomy with a stent retriever if they meet all the following criteria: (1) prestroke mRS score of 0 to 1; (2) causative occlusion of the internal carotid artery or MCA segment 1 (M1); (3) age ≥18 years; (4) NIHSS score of ≥6; (5) ASPECTS of ≥6; and (6) treatment can be initiated (groin puncture) within 6 hours of symptom onset.	I	A	Recommendation revised from 2015 Endovascular.
3.7.2. 0 to 6 Hours From Onset (Continued)	**COR**	**LOE**	**New, Revised, or Unchanged**
2. Direct aspiration thrombectomy as first-pass mechanical thrombectomy is recommended as noninferior to stent retriever for patients who meet all the following criteria: (1) prestroke mRS score of 0 to 1; (2) causative occlusion of the internal carotid artery or M1; (3) age ≥18 years; (4) NIHSS score of ≥6; (5) ASPECTS ≥6; and (6) treatment initiation (groin puncture) within 6 hours of symptom onset.	I	B-R	Recommendation revised from 2015 Endovascular.

Candidacy

6 – 24 hrs from LKN / symptom onset

3.7.3. 6 to 24 Hours From Onset	COR	LOE	New, Revised, or Unchanged
1. In selected patients with AIS within 6 to 16 hours of last known normal who have LVO in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended.	I	A	New recommendation.
2. In selected patients with AIS within 16 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable.	IIa	B-R	New recommendation.
The DAWN trial used clinical-core mismatch (a combination of NIHSS score and imaging findings on CTP or DW-MRI) as eligibility criteria to select patients with large anterior circulation vessel occlusion for treatment with mechanical thrombectomy between 6 and 24 hours from last known normal. This trial demonstrated an overall benefit in function outcome at 90 days in the treatment group (mRS score 0–2, 49% versus 13%; adjusted difference, 33% [95% CI, 21–44]; posterior probability of superiority >0.999).[51] In DAWN, there were few strokes with witnessed onset (12%). The DEFUSE 3 trial used perfusion-core mismatch and maximum core size as imaging criteria to select patients with large anterior circulation occlusion 6 to 16 hours from last seen well for mechanical thrombectomy. This trial showed a benefit in functional outcome at 90 days in the treated group (mRS score 0–2, 44.6% versus 16.7%; RR, 2.67 [95% CI, 1.60–4.48]; $P<0.0001$).[52] Benefit was independently demonstrated for the subgroup of patients who met DAWN eligibility criteria and for the subgroup who did not. DAWN and DEFUSE 3 are the only RCTs showing benefit of mechanical thrombectomy >6 hours from onset. Therefore, only the eligibility criteria from one or the other of these trials should be used for patient selection. Although future RCTs may demonstrate that additional eligibility criteria can be used to select patients who benefit from mechanical thrombectomy, at this time, the DAWN or DEFUSE 3 eligibility should be strictly adhered to in clinical practice.[51,52]			See Table XVII in online Data Supplement 1.

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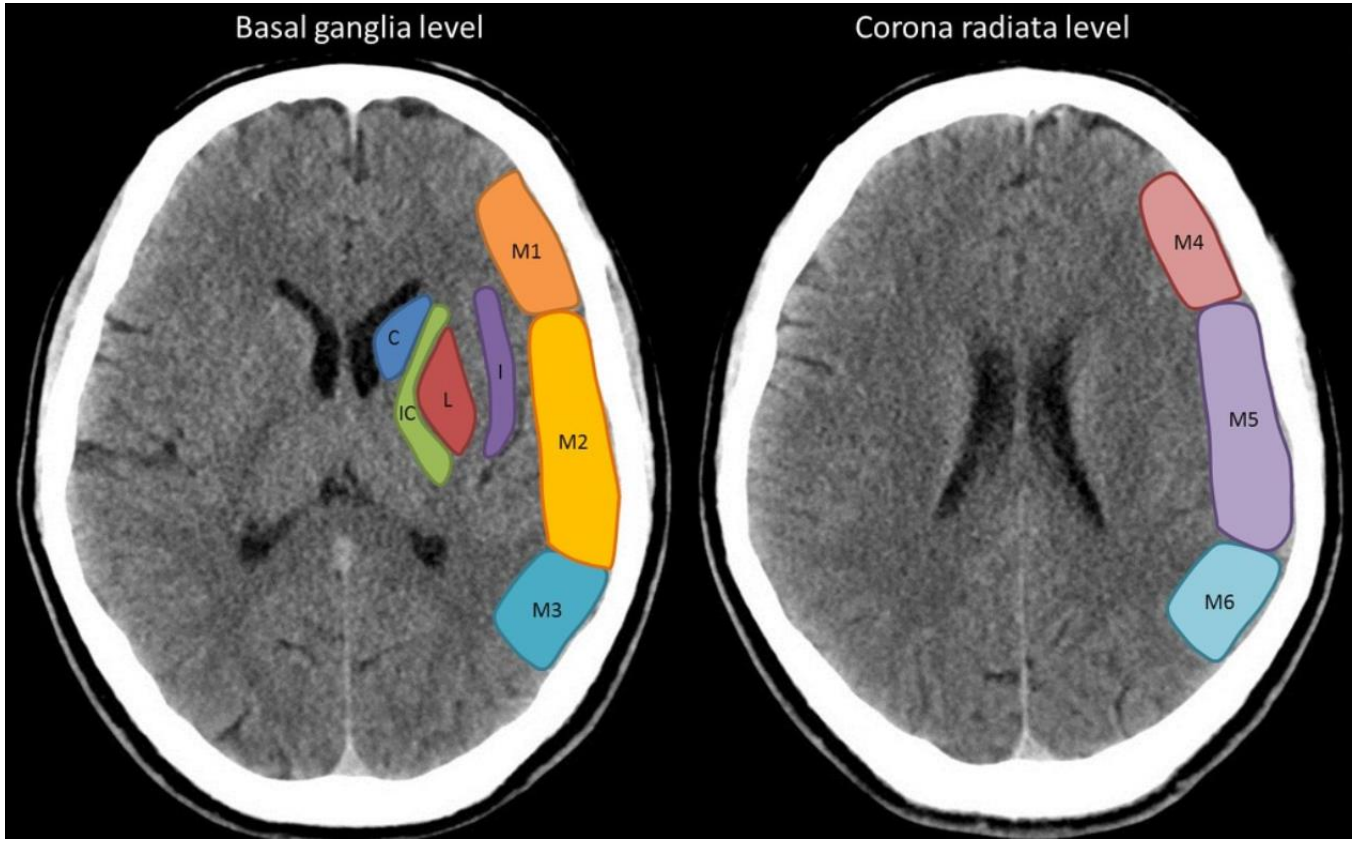
Candidacy

B. Assessment of ischemic change volumes

Two Ways:
1) ASPECTS on CTH
2) CT Perfusion imaging



Candidacy

B. Assessment of ischemic change volumes

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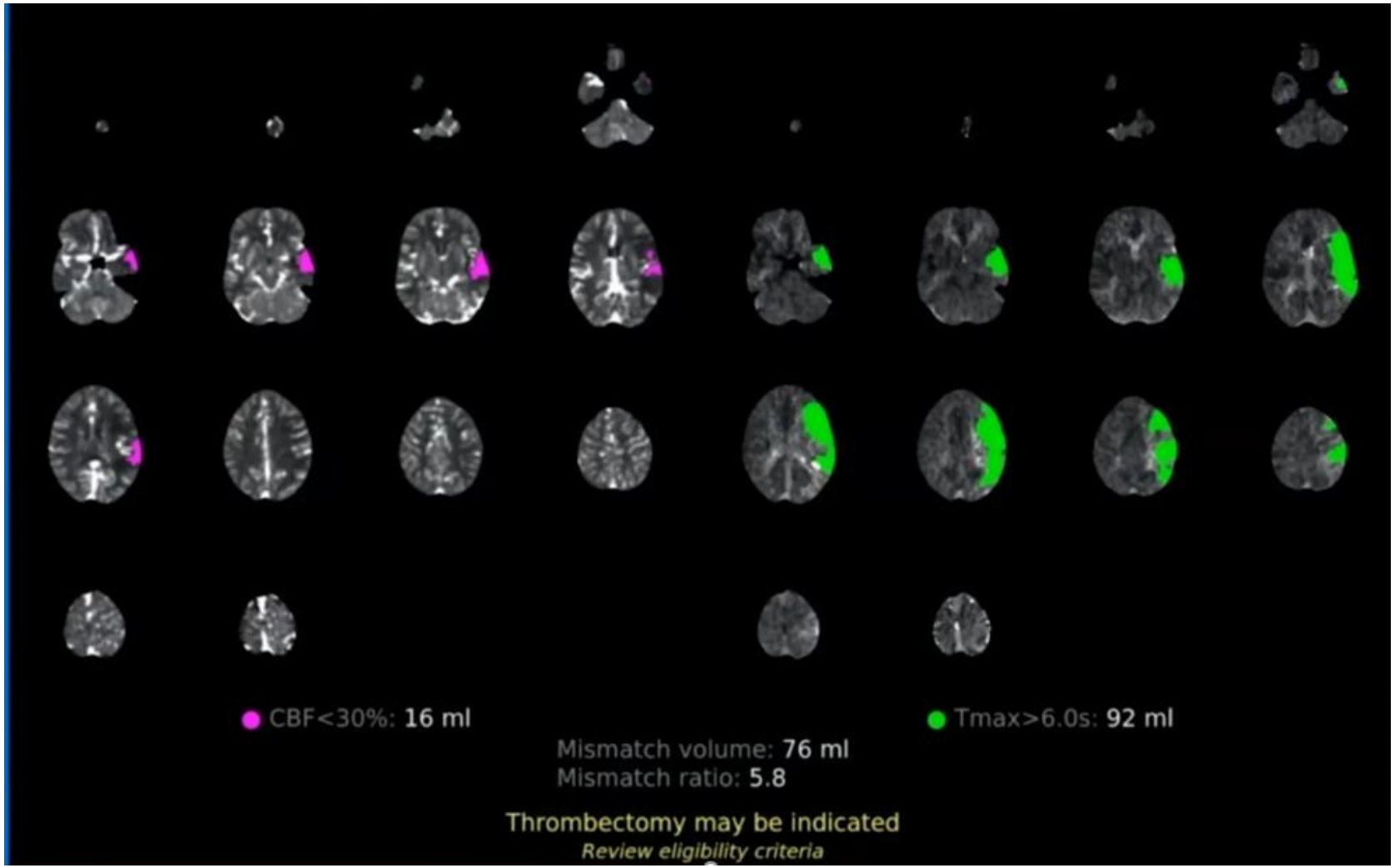


In general, **TNK** and **thrombectomy** interventions should be thought of *in parallel*.

- Not mutually exclusive.

Thrombolysis alone

OR

Endovascular thrombectomy alone

OR

Thrombolysis + Endovascular thrombectomy

Etiologic evaluation during admission

Stroke Workup

- Vessel Imaging (CTA, MRA, carotid US)
- MRI brain WO
- TTE w/ bubble
- A1c
- LDL (doesn’t have to be fasting)
- Telemetry (while in-house)
- Cardiac monitor on discharge (holter or ziopatch)
- Rehabilitation: PT / OT / SLP

Echocardiography

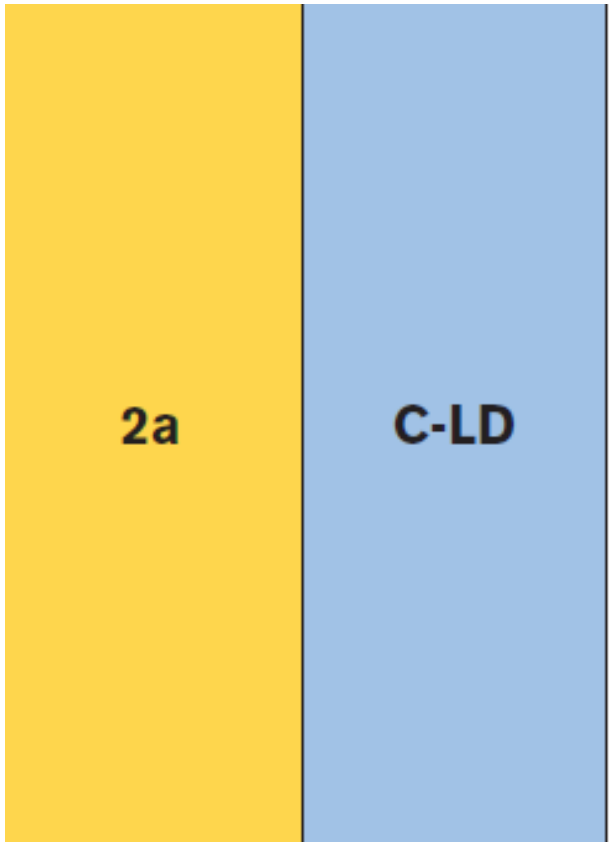
2a	B-R

6. In patients with cryptogenic stroke, echocardiography with or without contrast is reasonable to evaluate for possible cardiac sources of or transcardiac pathways for cerebral embolism.[56,57]

Cardiac monitoring

7. In patients with cryptogenic stroke who do not have a contraindication to anticoagulation, long-term rhythm monitoring with mobile cardiac outpatient telemetry, implantable loop recorder, or other approach is reasonable to detect intermittent AF.[58–60]

Thrombophilia Evaluation



10. In patients with cryptogenic stroke, tests for inherited or acquired hypercoagulable state, bloodstream or cerebral spinal fluid infections, infections that can cause central nervous system (CNS) vasculitis (eg, HIV and syphilis), drug use (eg, cocaine and amphetamines), and markers of systemic inflammation and genetic tests for inherited diseases associated with stroke are reasonable to perform as clinically indicated to identify contributors to or relevant risk factors for stroke.[70–72]

Thrombophilia Evaluation

Prothrombin 20210A gene mutation
Protein C activity
Protein S antigen
Factor VIII activity
Antithrombin III activity

B2 glycoprotein IgG/IgM
Cardiolipin IgG/IgM
Lupus inhibitor panel

Secondary Prevention

Antithrombotics in Stroke Prevention

Antithrombotics

Dual antithrombotics: Acute

Antithrombotics

Short term Dual Antiplatelet Use

Do consider **dual antiplatelet (aspirin + Clopidogrel) x21 days** for patients with **low NIHSS ischemic stroke** or **high risk TIA** (ABCD2 score ≥4).

Ideally starting within 12-24 hrs of LKN/onset.

Followed by single antiplatelet longterm thereafter.

Assuming no thrombolysis. if tPA or TNK given, then can consider starting after the 24 hr thrombolytic period.

Antithrombotics

Short term Dual Antiplatelet Use

CHANCE Trial (China)
ASA+Plavix x21 days → Plavix alone x69 days
Vs
ASA alone x90 days

- Less ischemic stroke recurrence and less/similar hemorrhagic stroke in DAPT group.

Questions of generalizability

Antithrombotics

Short term Dual Antiplatelet Use

POINT Trial (U.S)

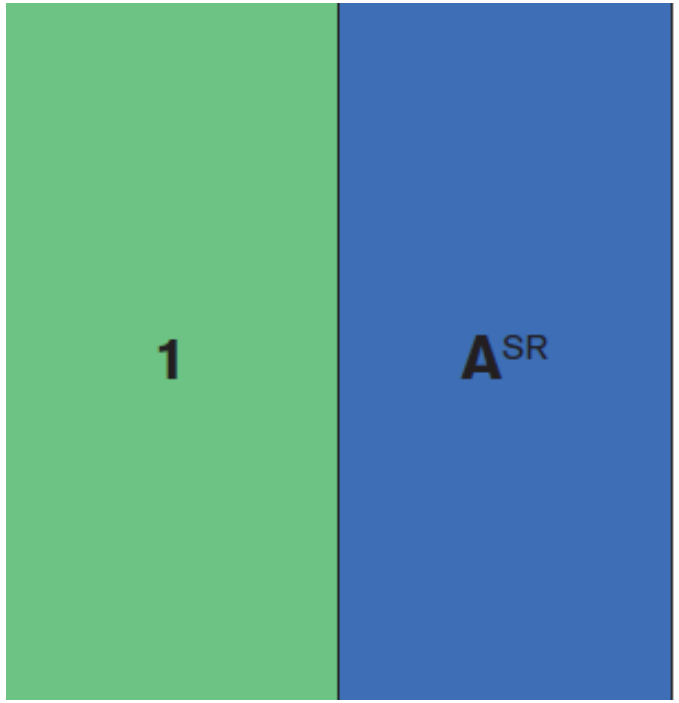
- Minor stroke or high risk (ABCD2 ≥4) TIA
- ASA + Clopidogrel vs ASA alone for 90 days
- Less ischemic stroke recurrence with DAPT
- Small increased risk of hemorrhage

Treating 1000 patients

→ prevents 15 ischemic strokes and causes 5 major hemorrhages.

Antithrombotics

Short term Dual Antiplatelet Use



3. For patients with recent minor (NIHSS score ≤3) noncardioembolic ischemic stroke or high-risk TIA (ABCD² score ≥4), DAPT (aspirin plus clopidogrel) should be initiated early (ideally within 12–24 hours of symptom onset and at least within 7 days of onset) and continued for 21 to 90 days, followed by SAPT, to reduce the risk of recurrent ischemic stroke.[382,384,410,795,796]

Antithrombotics

Short term Dual Antiplatelet Use

POINT Trial (U.S) secondary analyses

- Benefit of ASA + Clopidogrel is predominantly within initial 21 days
- Hemorrhage rate rises linearly over time

Treating 1000 patients with ASA + Clopidogrel

→ prevents 20 major ischemic events and causes 2 major hemorrhages

Antithrombotics

Short term Dual Antiplatelet Use

THALES Trial (U.S)

- Minor stroke or high risk (ABCD2 ≥4) TIA
- ASA + Clopidogrel vs ASA alone for 90 days
- Less ischemic stroke recurrence with DAPT
- Small increased risk of hemorrhage

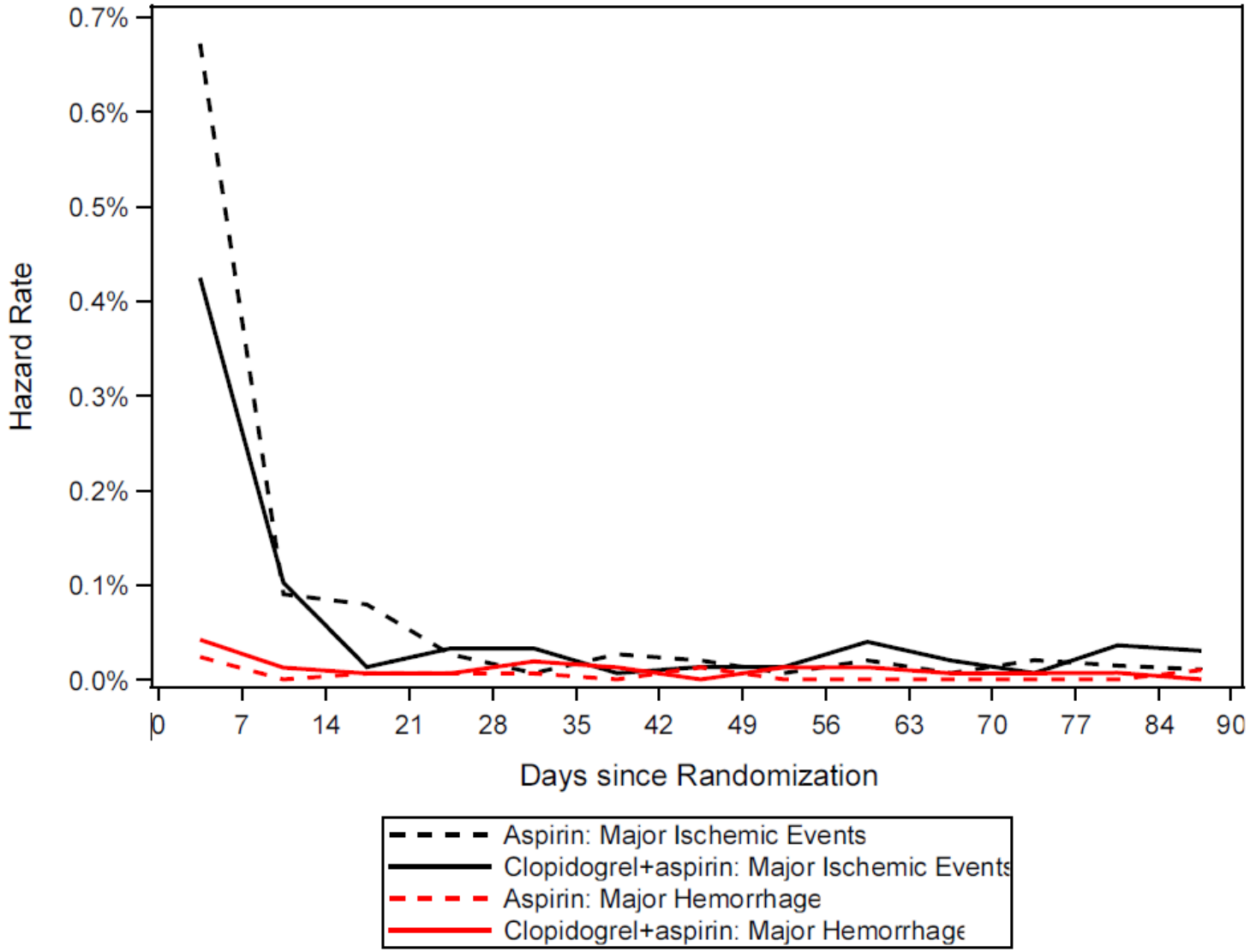
Treating 1000 patients

→ prevents 15 ischemic strokes and causes 5 major hemorrhages.

Antithrombotics

POINT Trial

Hazard Rates By Week After Randomization for Major Ischemic Events, Major Hemorrhage



Antithrombotics

Dual Antiplatelets short term + intracranial vessel stenosis

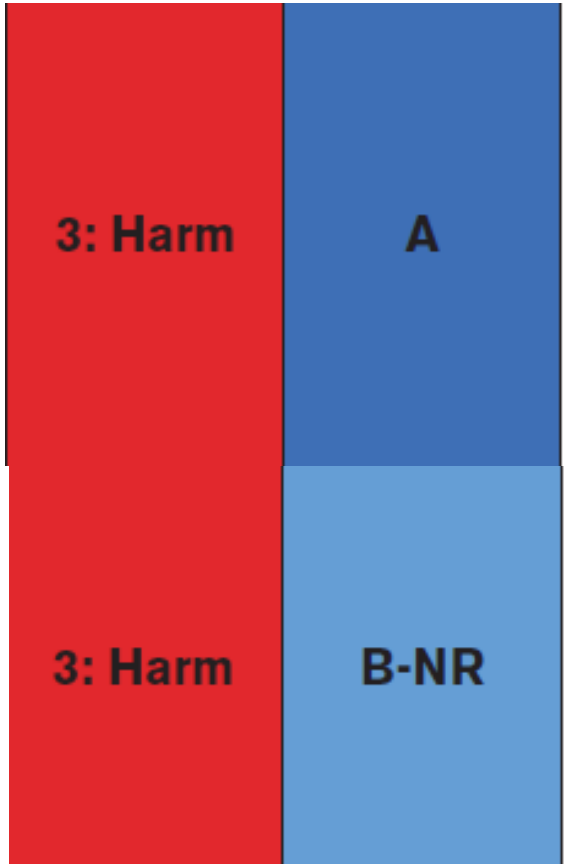
Do consider **dual antiplatelet (Aspirin 325 mg + Clopidogrel 75 mg) x90 days** for patients with stroke/TIA attributable to stenotic (50-99%) vessel.

1. In patients with a stroke or TIA caused by 50% to 99% stenosis of a major intracranial artery, aspirin 325 mg/d is recommended in preference to warfarin to reduce the risk of recurrent ischemic stroke and vascular death.[335,336]

Antithrombotics

Dual Antiplatelets short term + intracranial vessel stenosis

Don't consider stenting for intracranial stenosis.



8. In patients with stroke or TIA attributable to severe stenosis (70%–99%) of a major intracranial artery, angioplasty and stenting should not be performed as an initial treatment, even for patients who were taking an antithrombotic agent at the time of the stroke or TIA.[353–359]

9. In patients with a stroke or TIA attributable to moderate stenosis (50%–69%) of a major intracranial artery, angioplasty or stenting is associated with excess morbidity and mortality compared with medical management alone.[336,354,355,360]

Antithrombotics

Single antiplatelet agent options

Common

- Aspirin 81 mg or 325 mg daily
- Clopidogrel 75 mg daily

Uncommon or off label use

- Ticagrelor 90 mg BID
  newer med; notable cost for many patients.

- Cilostazol 100 mg BID
  uncommon in the US. Standard of care in china and many European countries.

Antithrombotics

Ticagrelor as an *alternative* antiplatelet

Single antiplatelet agent
→ Consider if allergies or "failed" aspirin or Clopidogrel
**Cost

SOCRATES; ASA v Ticagrelor; prevention of recurrent stroke/TIA
- Superiority trial; Ticagrelor not superior to aspirin
- Similar bleeding rates
- Marginally improved %1 ARR for recurrent ischemic stroke of Ticagrelor
  - Not statistically significant

Antithrombotics

Ticagrelor as an *alternative* antiplatelet

Single antiplatelet agent
→ Consider if allergies or “failed” aspirin or Clopidogrel
SOCRATES trial

**Cost

Dual antiplatelet (aspirin + Ticagrelor) short term
THALES trial

Antithrombotics

Dual antithrombotics: Chronic

Antithrombotics

Avoid dual antiplatelet therapy for the longer term.

Previous trials without evidence of benefit / risk reduction

SPS3 Trial – Clopidogrel + aspirin vs aspirin alone *longterm*

- *no additional benefit found*
- *DAPT arm → major hemorrhage doubled (P<0.001). Mortality increased (p = 0.004)*
- *study was stopped early*

6. For patients with noncardioembolic ischemic stroke or TIA, the continuous use of DAPT (aspirin plus clopidogrel) for >90 days or the use of triple antiplatelet therapy is associated with excess risk of hemorrhage.[381,382,801]

Antithrombotics

Triple Antithrombotics?

Antithrombotics

Avoid triple therapy

TARDIS

- ASA/dipyridamole/plavix vs standard
- *No added benefit for stroke outcomes*
- *Significantly more hemorrhage outcomes*

6. For patients with noncardioembolic ischemic stroke or TIA, the continuous use of DAPT (aspirin plus clopidogrel) for >90 days or the use of triple antiplatelet therapy is associated with excess risk of hemorrhage.[381,382,801]

Anticoagulation

Avoid anticoagulation unless there is a specific indication for it.

- Afib
- LV thrombus

Strokes of undetermined source are treated with Antiplatelets

Risk Factor Optimization

HTN
- BP goal <130/80 longterm

Diabetes
- A1c goal <7 longterm

1	B-R

2. In patients with hypertension who experience a stroke or TIA, an office BP goal of <130/80 mm Hg is recommended for most patients to reduce the risk of recurrent stroke and vascular events.[185,190–194]

1	A

1. In patients with an ischemic stroke or TIA who also have diabetes, the goal for glycemic control should be individualized based on the risk for adverse events, patient characteristics and preferences, and, for most patients, especially those <65 years of age and without life-limiting comorbid illness, achieving a goal of HbA1c ≤7% is recommended to reduce risk for microvascular complications.[229,230]

Hyperlipidemia
- LDL goal <100 (typically)
- LDL goal <70 (for those with intracranial atherosclerotic disease.)

Treat Stroke to Target (TST) trial
- Ischemic stroke or high risk TIA
- Evidence of atherosclerotic disease (coronary, intracranial, aortic, carotid)

Comparing LDL goal <70 vs goal <100.
- <70 goal superior for preventing major vascular events*
- 8.5% v 10.9%; p=0.04

* = ischemic stroke, MI, new symptoms necessitating urgent coronary or carotid revascularization.

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Thank You!

OREGON HEALTH & SCIENCE UNIVERSITY