

Updates in Inpatient Stroke Care, 2024

Andy Treister MD

Department of Neurology

Division of Comprehensive Neurology

Section of Neurocritical Care

Oregon Health and Science University

Disclosures

+ None!

Objectives

- + Review landmark trials in acute stroke care
- + Provide updates in recent clinical trials and how they influence current practice patterns
 - Thrombolytics
 - Endovascular thrombectomy
 - Other acute and post-acute management

Thrombolytics

In the beginning, there was nothing, then there was...

+ **TPA**

NINDS Trial (1995):

333 patients

ICH rate of 6.4% (tPA) compared to 0.4% (placebo)

tPA patients were 30% more likely to have minimal or no disability (at 90 days)

ECASS-III (2008):

821 patients, 3-4.5 hours from symptom onset

MRS Score 0-1 in 52% (tPA) vs 45% (placebo) at 90 days (p=0.04)

Tenecteplase (TNK)

- + NOR-TEST (2017): tPA vs Tenecteplase within 4.5 hours

1100 patients (Norway)

No difference in 90-day independence, adverse events/mortality

TNK is non-inferior to TPA

- + EXTEND-IA TNK (2018): tPA vs TNK in patients who ultimately underwent thrombectomy

202 patients

22% (TNK) vs 10% (tPA) had lysis of clot prior to thrombectomy

Functional independence at 90 days: 65% (TNK) vs 52% (tPA) (p=0.04)

Should we give TNK beyond 4.5 hours?

+ TIMELESS (Feb 2024)

458 pts w/ LVO, 77% underwent thrombectomy

MRS 0-2 at 90 days 46% (TNK+EVT), 42% (EVT alone) ($p>0.05$)

sICH 3% (TNK+EVT) vs 2% (EVT), mortality 19.7% and 18% resp ($p>0.05$)

+ TRACE-III (July 2024)

516 pts w/ LVO where *thrombectomy is unavailable*

TNK vs standard medical treatment

MRS 0-1 at 90 days in **33% (TNK) vs 24% (SMT) ($p=0.03$)**

sICH 3% (TNK) vs 0.8% (SMT), mortality 13% in both

Should we give TNK beyond 4.5 hours?

+ What's the difference?

Access to a thrombectomy center!

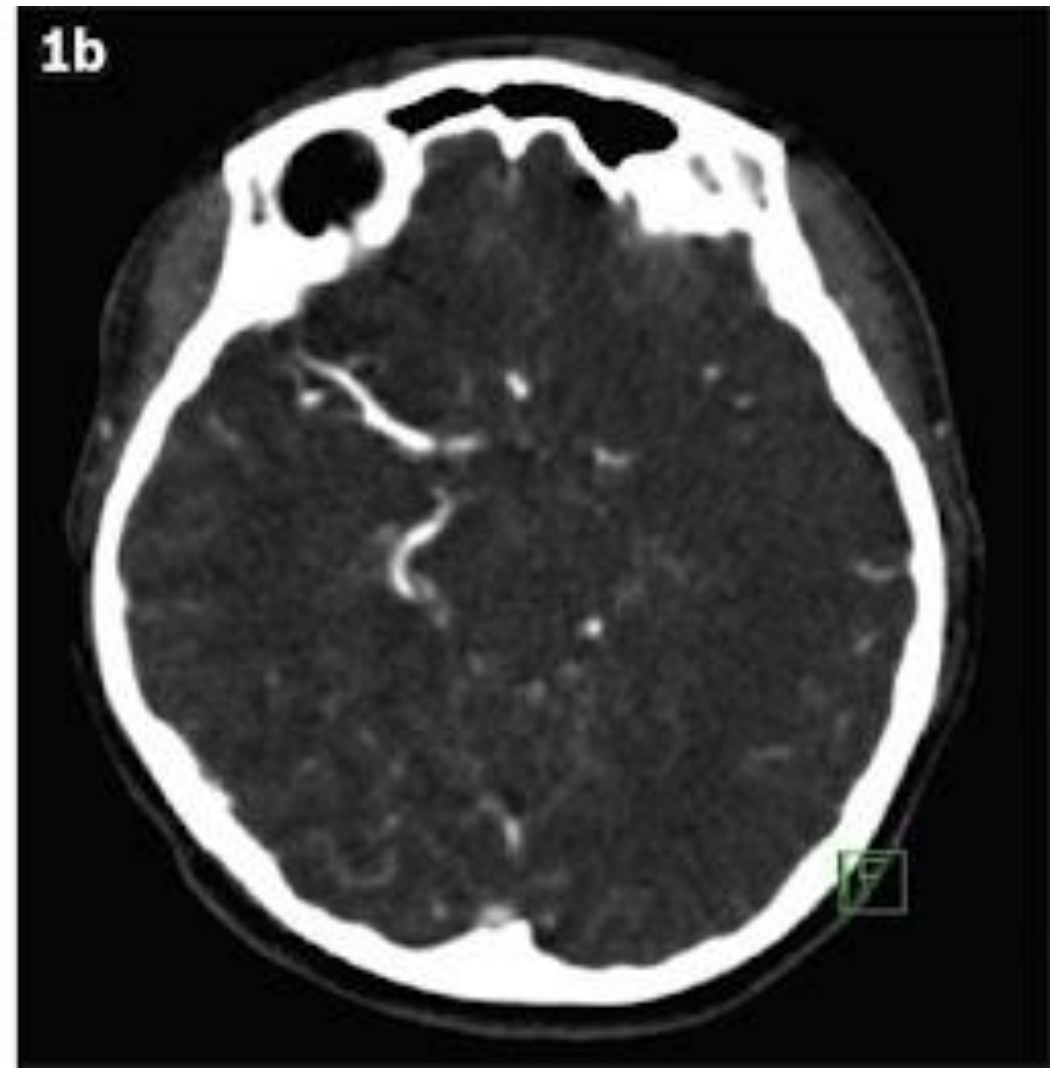
TRACE-III shows that TNK without thrombectomy is better than nothing.

EXTEND-IA TNK showed that TNK lyses a clot much better than TPA.

Risk of giving TNK at 4.5-24 hours is low and there is some benefit.

Recap!

- + 77 year old female with history of AFib, not on anticoagulation is found down at home by her husband with right hemiplegia and aphasia.
- + She was last seen well when he left to run errands 5 hours ago.



Recap!

- + Is she a candidate for Tenectaplastase?

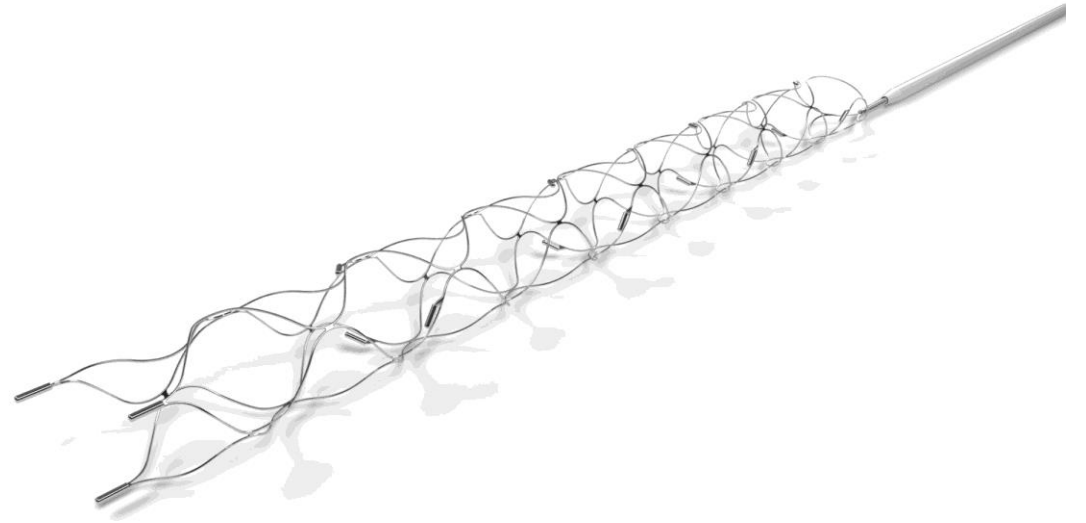
It Depends.

She is a candidate for thrombectomy; the addition of TNK adds no significant benefit or risk (TIMELESS)

- + What if she can't get to the thrombectomy center?

TNK results in a greater chance at functional independence with a 3% risk of symptomatic ICH (TRACE-III)

Thrombectomy



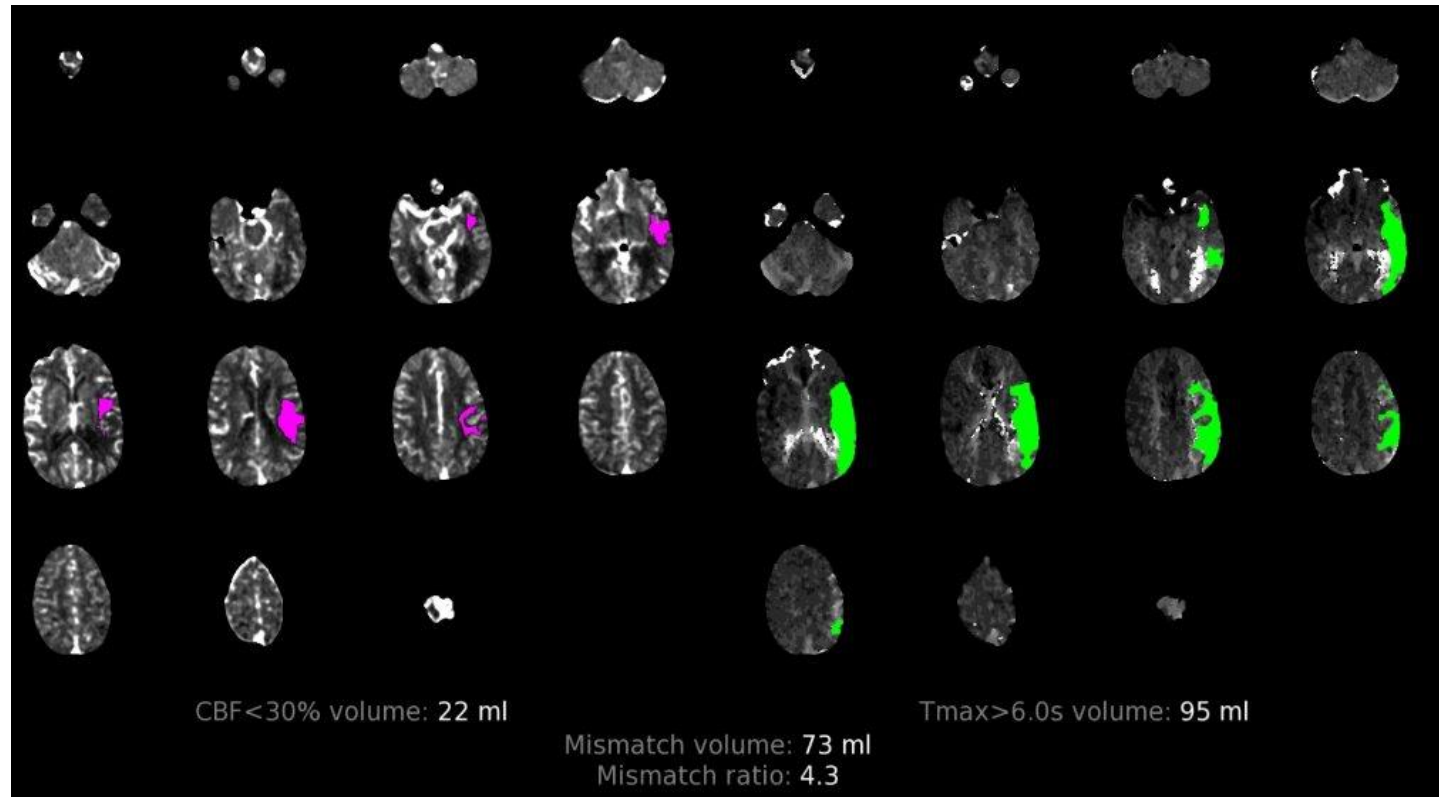
A brief history of thrombectomy for stroke...

- + MERCI (2005)
- + MULT MERCI (2008)
- + Penumbra (2009)
- + 2013:
MR RESCUE, IMS III, SYNTHESIS
- + 2015:
MR CLEAN, ESCAPE, EXTEND-IA,
SWIFT-PRIME, REVASCAT



A brief history of thrombectomy for stroke...

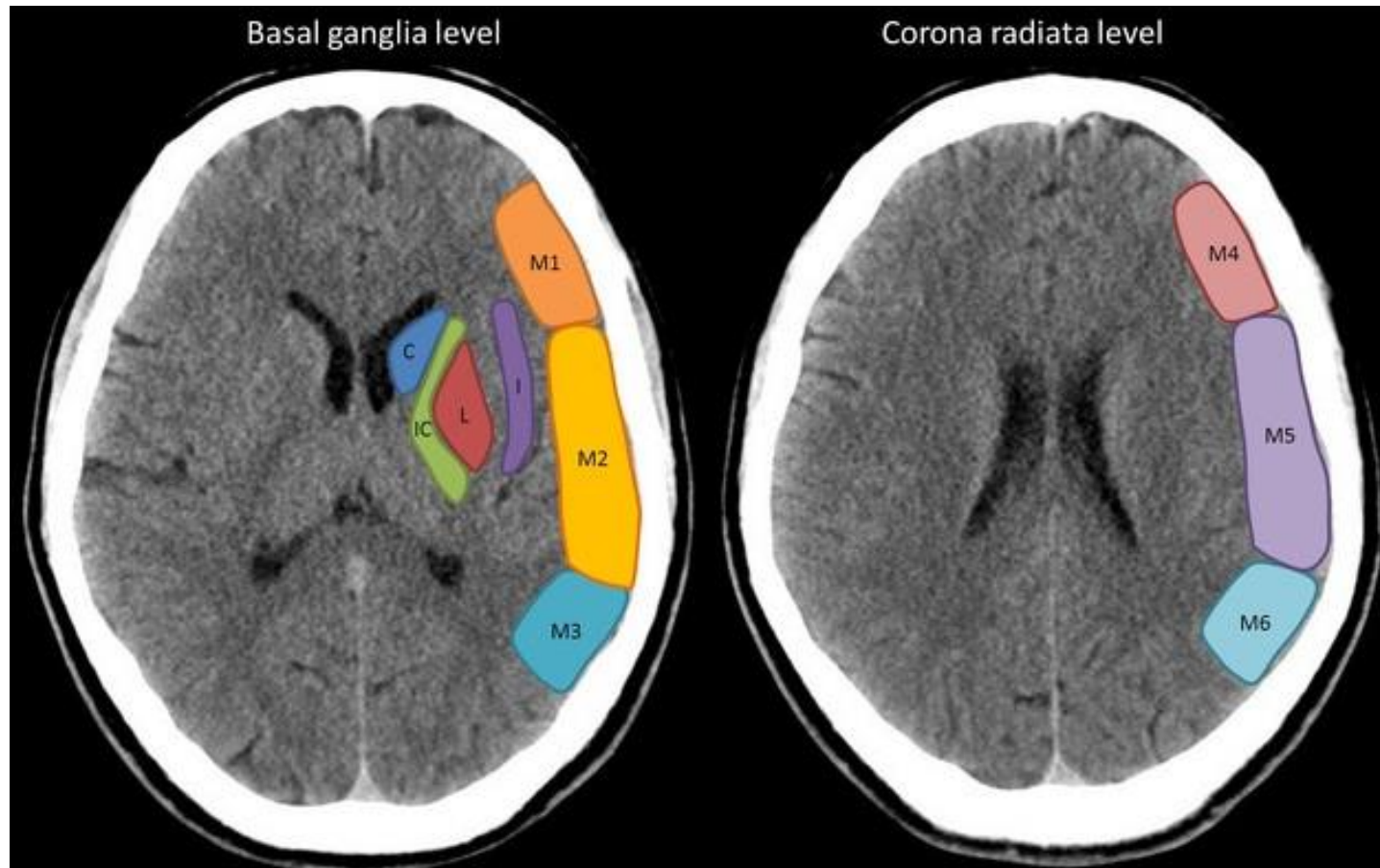
+ 2018: DAWN and DEFUSE 3



Perfusion imaging: it had a good run

- + DAWN and DEFUSE: thrombectomy outside of 6 hours is ok **IF** a CT Perfusion tells us there is enough brain to save
- + But what if we offer a thrombectomy anyway?

2023: Large core, don't care







Large core, don't care

+ SELECT-2 (2023)

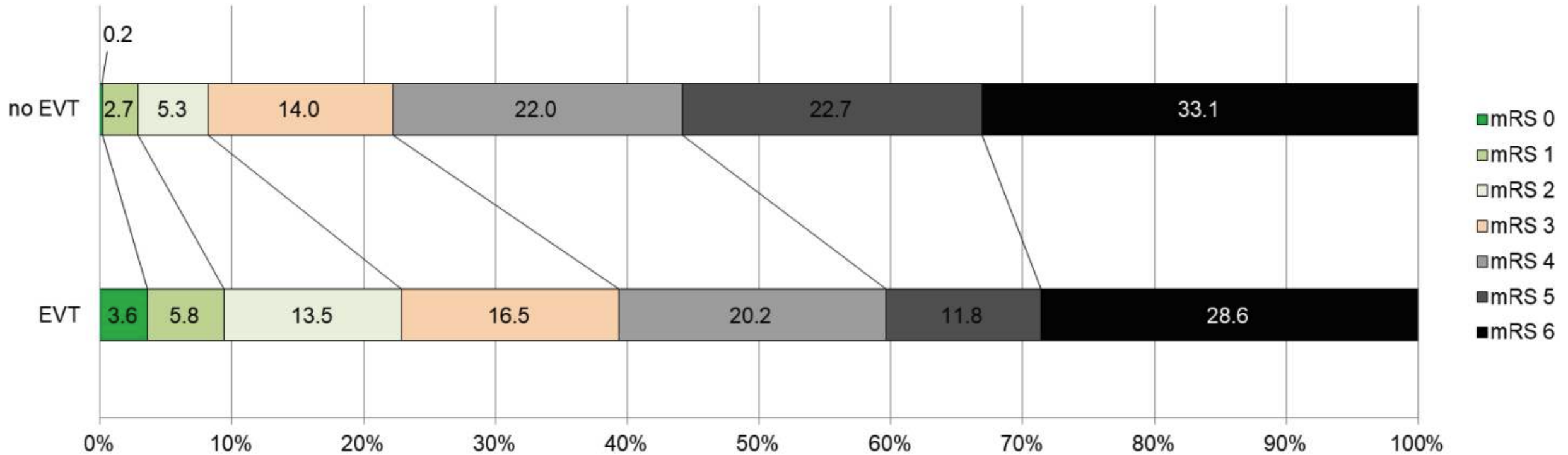
352 patients, endovascular thrombectomy (EVT) within 24 hours despite large core on CT or CTP

Stopped early d/t efficacy:

Functional independence: 20% (EVT) vs 7% (SMT) (**NNT = 5**)

More sICH in the SMT group! (2 vs 1). No difference in mortality.

ANGEL ASPECT (2023), IMS-III (2014), Rescue Japan LIMIT (2022), SELECT₂ (2023), TENSION (2023), TESLA (2024)



What else is new in stroke?

+ Zodiac (ahead of pub)

92 patients (stopped early due to efficacy)

0-degrees vs 30-degrees HOB while awaiting thrombectomy

Recorded NIHSS every 10 minutes until thrombectomy; primary endpoint defined as increase in 2 points

Clinical worsening: 55% (30°) vs 2% (0°)

Significant improvements in NIHSS at day 0 and day 7 in 0° group as well



When to start anticoagulation?

- + Prior practice: 10-14 days in large stroke (*source needed*)
- + ELAN (2023)

2013 participates with Afib, (37% minor stroke, 40% moderate, 23% major), early and late groups for each severity group

Minor: early = 48 hours, late = 3-4 days

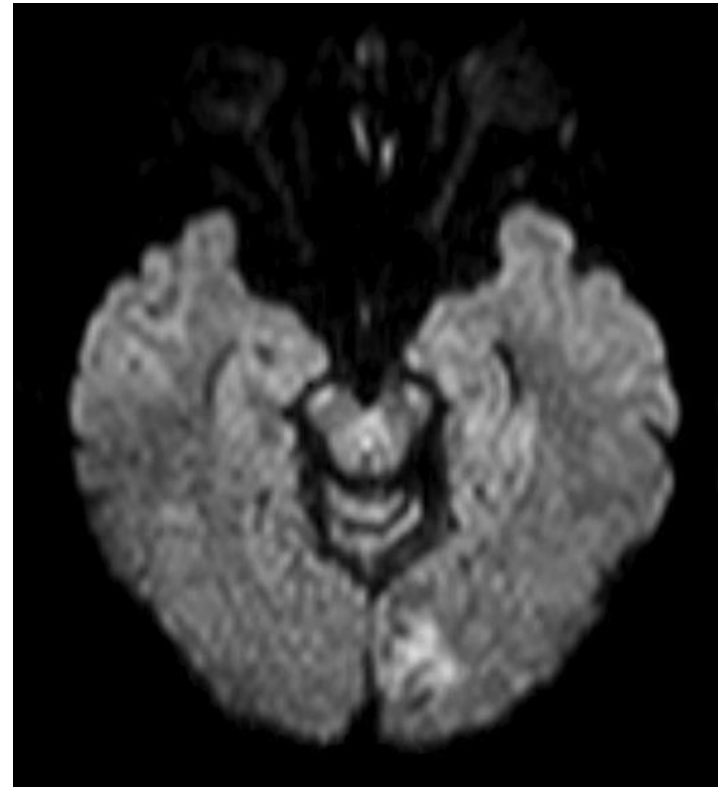
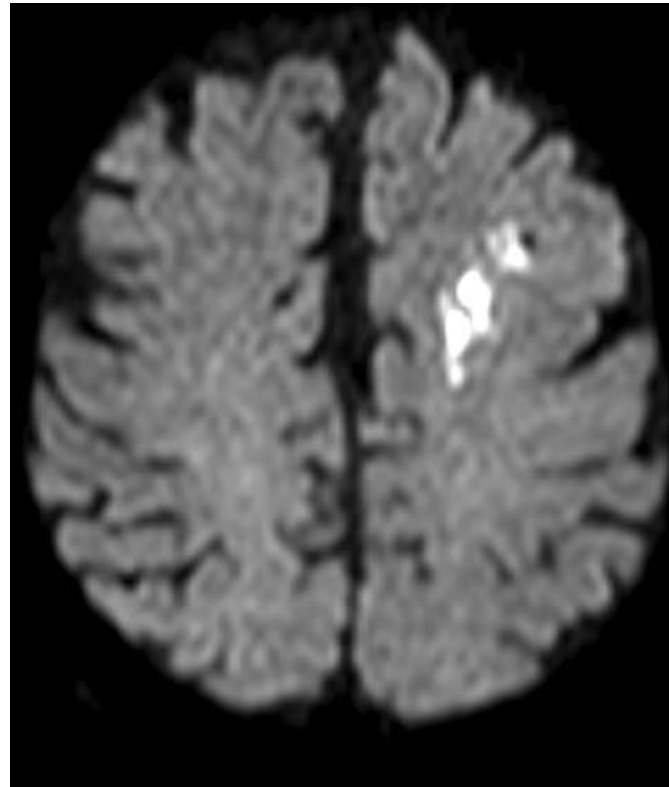
Moderate: early = 48 hours, late = 6-7 days

Major: early = 6-7 days, late = 12-14 days

30-day recurrent stroke: 1.4% (early), 2.5% (late) (not significant)

sICH: 0.2% in both groups

- + A 67 year old female with hx of tobacco use presents with 24 hours of speech changes and clumsiness in the RUE. On exam, you note a patchy right homonymous hemianopsia.



EKG shows normal sinus rhythm, though on cardiac monitoring overnight, she does have occasional multifocal PACs. Her TTE shows moderate dilation of the left atrium.

What would be the best medication for secondary stroke prevention?

What if you think it's Afib but haven't proven it yet...

+ RESPECT ESUS (2019):

5390 patients, dabigatran vs aspirin in cryptogenic stroke

Recurrent stroke in 4.1% per year (dabigatran) vs 4.8% per year (aspirin) ($p=0.1$)

+ ARCADIA (2024):

1015 pts with cryptogenic stroke AND atrial cardiopathy, but NO known Afib

Apixaban vs Aspirin

4.4% recurrent stroke per year in both groups

No difference in major bleeding events

So how do we treat stroke *this year*?

- + Tenectaplastase is better than tPA for large vessel strokes
- + TNK *may* still be an option after 4.5 hours
- + Our threshold for offering thrombectomy is at an all-time low, don't hesitate to call!
- + We still use CT-Perfusion, but not as often
- + Keeping HOB flat while awaiting thrombectomy actually works!
- + Cryptogenic stroke \neq Atrial fibrillation (still, but moreso!)

+ References

Campbell, Mitchell, Churilov, et al. **Tenecteplase versus Alteplase before Thrombectomy for Ischemic Stroke.** *N Engl J Med.* 2018 Apr 26;378(17):1573-1582.

Xiong, Campbell, Schwamm, et al. **Tenecteplase for Ischemic Stroke at 4.5 to 24 Hours without Thrombectomy.** *N Engl J Med.* 2024 Jul 18;391(3):203-212.

Albers, Juma, Purdon, et al. **Tenecteplase for Stroke at 4.5 to 24 Hours with Perfusion-Imaging Selection.** *N Engl J Med* 2024;**390:701-711**

Saraj, Hassan, Abraham et al. **Trial of Endovascular Thrombectomy for Large Ischemic Strokes.** *N Engl J Med* 2023;**388:1259-1271**

Romoli, Princiotta Cariddi, Longoni, et al. **Mechanical Thrombectomy in Ischemic Stroke with a Large Infarct Core: A Meta-Analysis of Randomized Controlled Trials.** *J Clin Med.* 2024 Aug;13(15):4280.

Kamel, Longstreth, Tirschwell, et al. **Apixaban to prevent recurrence after cryptogenic stroke in patients with atrial cardiopathy.** *JAMA.* 2024;331(7):573-581

"ZODIAC trial demonstrates the impact of head-of-bed positioning in LVO stroke care" [vjneurology.com](https://www.vjneurology.com). Accessed 9/7/2024.