
Tenecteplase Implementation & Blood Pressure Management

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RESEARCH
MEDICAL CENTER



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Disclosures

Emily Lampe

Title: Tenecteplase Implementation & Blood Pressure Management

No relevant financial relationships exist.

Objective

- Discuss the history of tenecteplase in acute stroke
- Explore the latest research and evidence around Tenecteplase
- Tenecteplase and Blood pressure management: A lesson learned

What is tenecteplase?



Thrombolytic

- Engineered/ modified variant of alteplase
- Greater fibrin specificity
- Longer $T^{1/2}$ allows bolus administration



Benefits

- Quicker preparation
- Single bolus administered intravenously over 5 seconds
- No infusion dose
- Less fibrinogen consumption



Outcomes

- As effective and safe as alteplase*
- Better early reperfusion and functional outcome than alteplase**

*Burgos & Saver, Stroke 2019

** Campbell et al. NEJM 2018

Case: Randal, 64 yo man

At home when left leg became weak. Within minutes he was paralyzed, L hemibody. Family found him on the kitchen floor 45 min later and called 911.

EMS Findings: Randal

- Vitals:
 - 168/92
 - RR 12
 - O2 96% RA
 - HR 86
 - Blood sugar: 92
 - NO blood thinners
 - + Cincinnati Stroke Scale (face, arm, speech)
 - Started 18 gauge IV while enroute
 - EMS transported him efficiently
 - Pre-alerted ER
-

ER: Randal

- ER grateful to get pre-alert
 - ER agreed with stroke concern
 - Rapidly taken to CT
 - Evaluated by tele-neurology at sister facility

 - NIHSS: 18: L face, arm and leg weakness, not answer questions and neglect of the left
-



What intervention does Randal need?

- + Cincinnati Score, NIHSS: 18
- Blood sugar is within range
- NO bleed on head CT
- No blood thinners
- Acute symptoms within 0-3 (4.5) hr

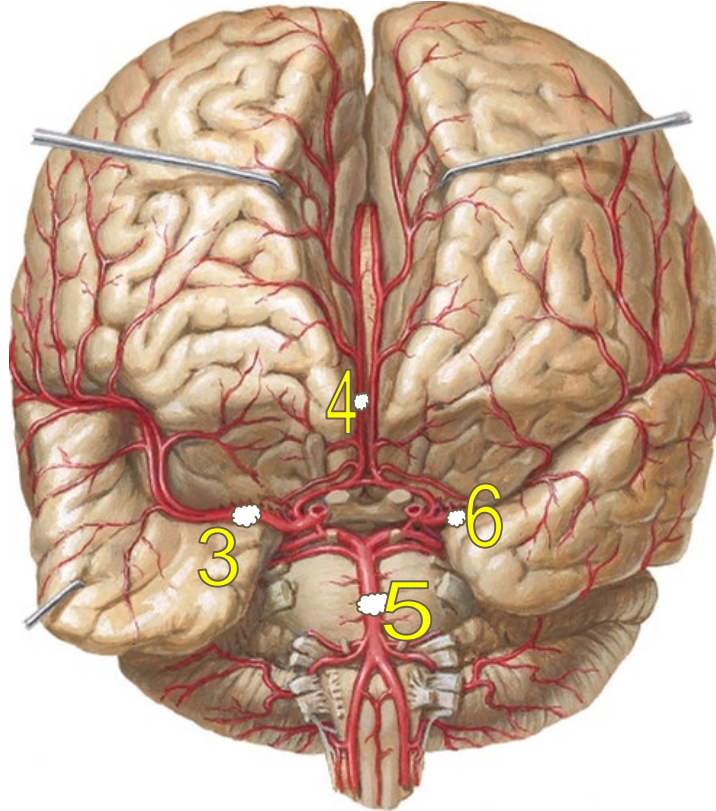
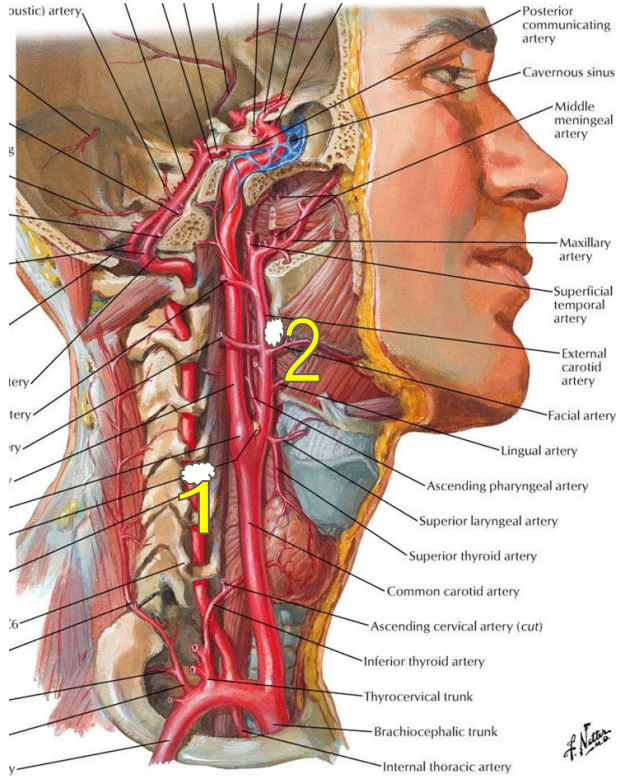
SURVEY: WHAT IS THE NEXT STEP?

- A. Await lab results
- B. IV Thrombolytic
- C. CTA head/neck
- D. Thrombectomy
- E. MRI brain
- F. B, C, possible D

Clot buster- intravenous tPA?



Thrombectomy?



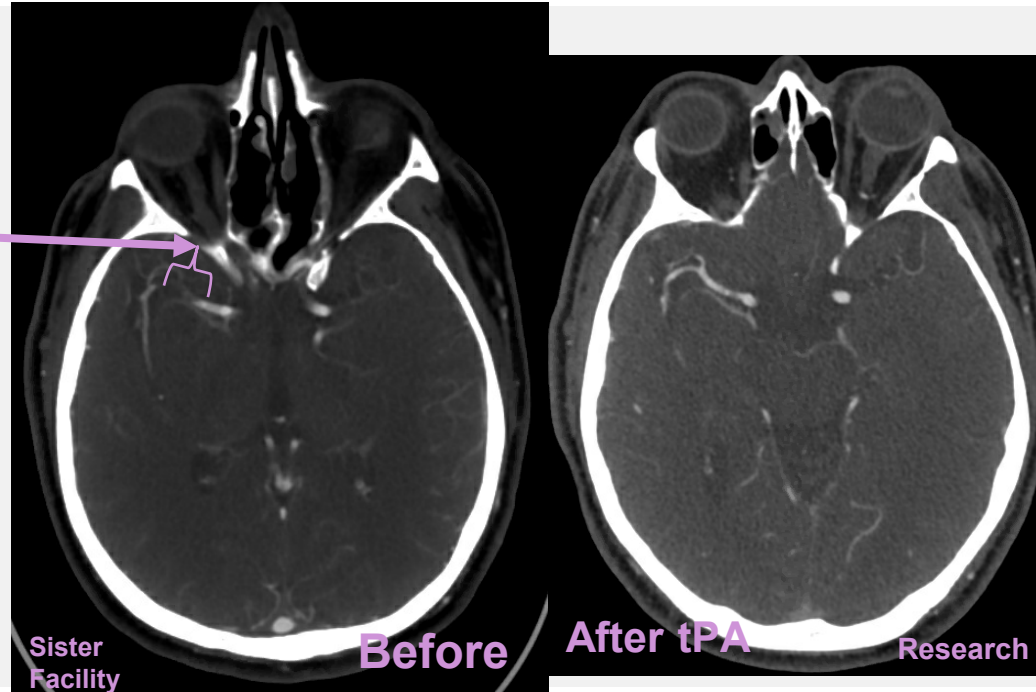
Which vessel?

- 1
- 2
- 3
- 4
- 5
- 6

1. Right Vertebral Artery
2. Right external Carotid Artery
- 3. Right Middle Cerebral Artery**
4. Right Anterior Cerebral Artery
5. Basilar Artery
6. Left Middle Cerebral Artery

Randal

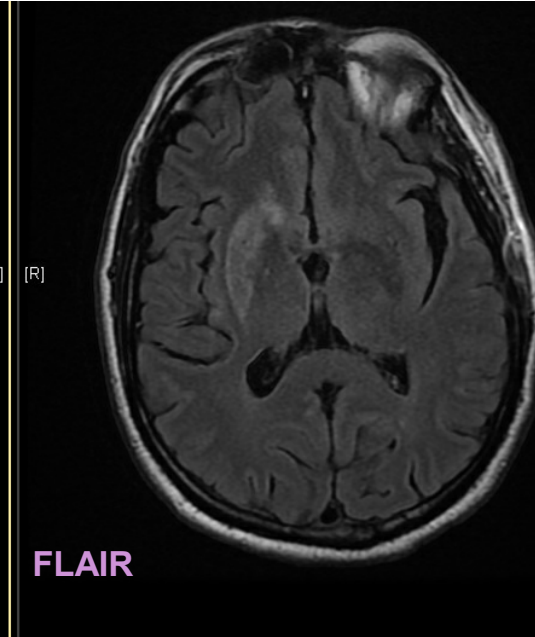
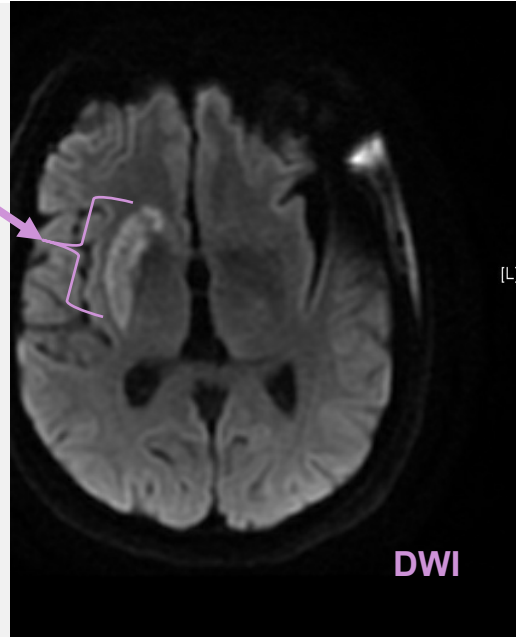
- DTN: 27 minutes
- CT Angiogram: Right MCA (M1) occlusion
- To St. Marks for thrombectomy
- On arrival- resolved L sided weakness and speech changes, ONLY mild L facial droop



Randal

- Brain MRI
- Next day, home without deficits

Small
Infarct



Quiz

Acute Ischemic Stroke Treatment

- Is Tenecteplase a type of tPA?
- What national stroke organization lists tenecteplase (TNKase) as a “reasonable alternative to alteplase”?
- If TNK has more data behind it than NINDS, why is it not FDA approved to treat stroke?

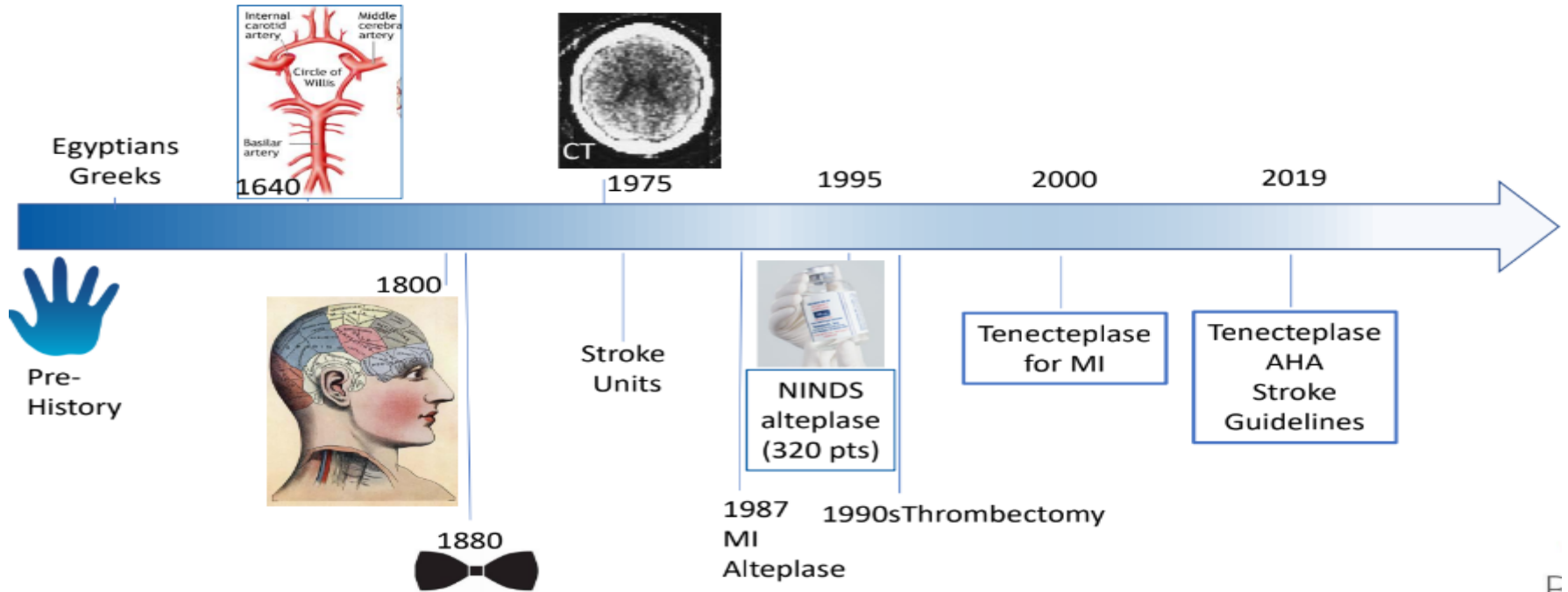
Indications

Tenecteplase is indicated as off label use in the treatment of ischemic strokes with a Last Known Well (LKW) of 0-4.5 hours and is a new recommendation supported by the **AHA 2019 Guidelines**.

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.
2. Tenecteplase administered as a 0.4-mg/kg single IV bolus has not been proven to be superior or noninferior to alteplase but might be considered as an alternative to alteplase in patients with minor neurological impairment and no major intracranial occlusion.	IIb	B-R	New recommendation.

Objective 1: History of Tenecteplase in Acute Stroke

History of Stroke



What is tenecteplase?



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- Engineered/ modified variant of alteplase
- Greater fibrin specificity
- Longer $T^{1/2}$ allows bolus administration



Benefits

- Quicker preparation
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- No infusion dose
- Less fibrinogen consumption



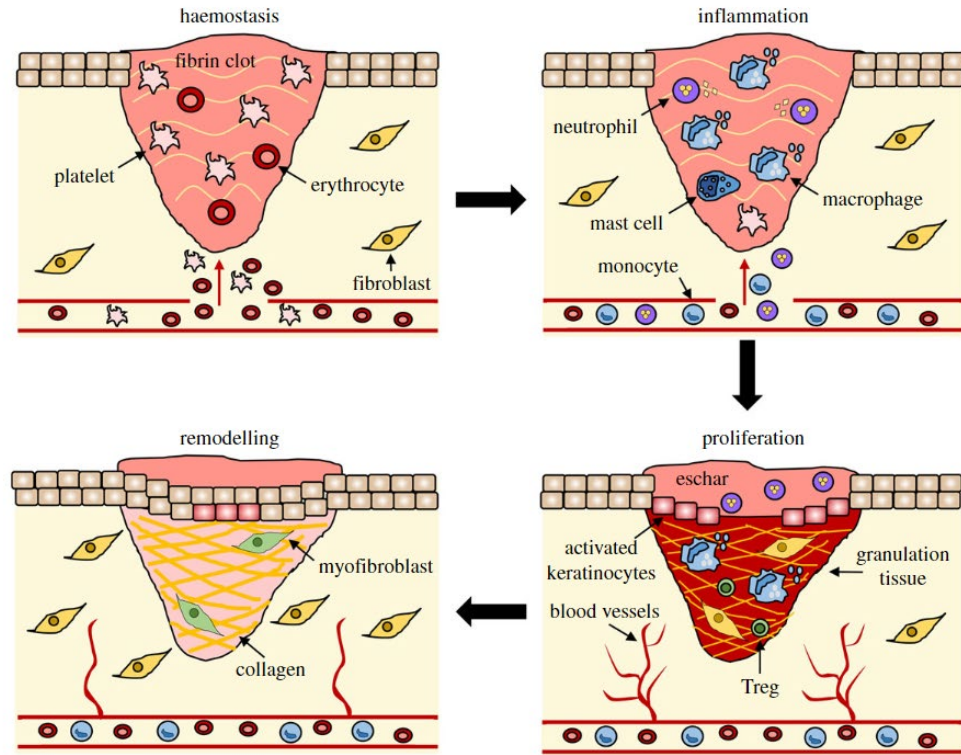
Outcomes

- As effective and safe as alteplase*
- Better early reperfusion and functional outcome than alteplase**

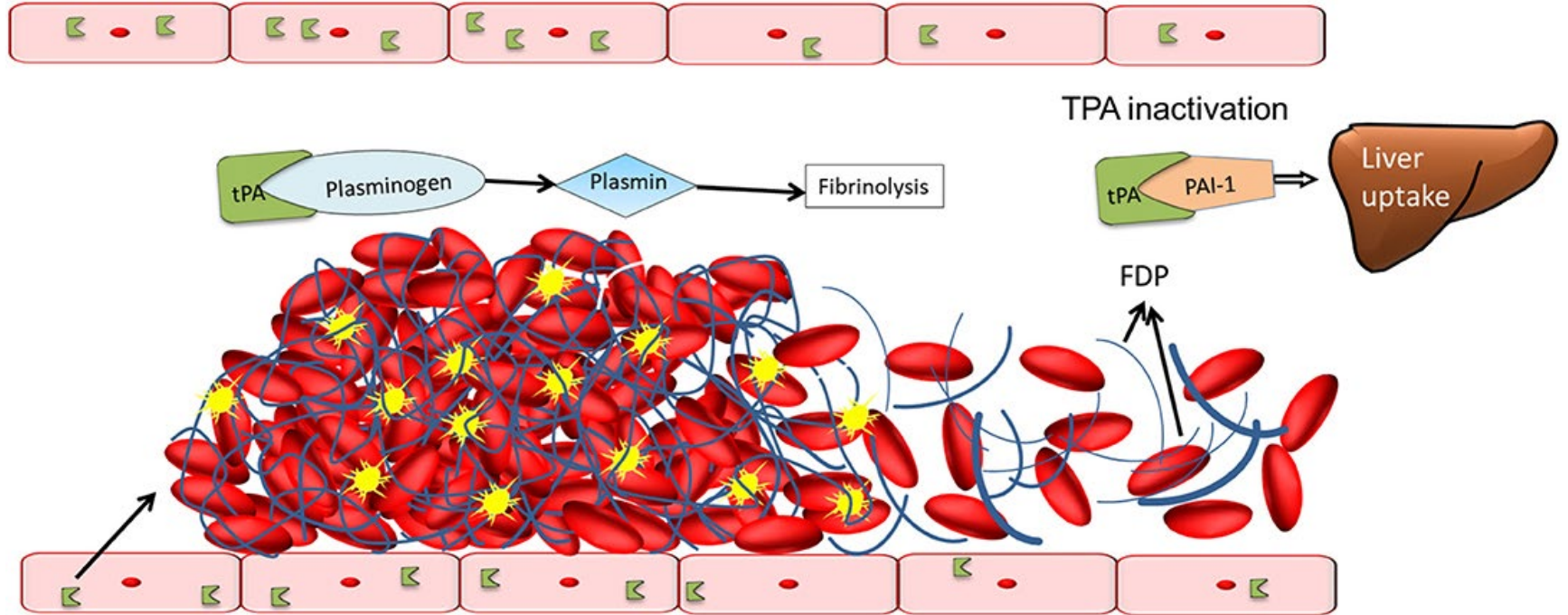
*Burgos & Saver, Stroke 2019

** Campbell et al. NEJM 2018

Tissue Injury and Healing



Clot Lysis



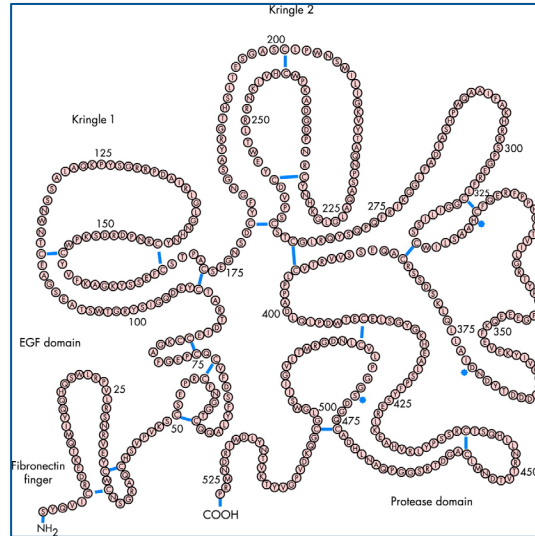
- Endothelial Cell
- Red blood Cell
- Fibrin
- Activated Platelets
- Tissue-type plasminogen activator (tPA)
- Plasminogen
- Plasminogen activator inhibitor-1 / Neuroserpine

Thrombolysis, choose the best option?

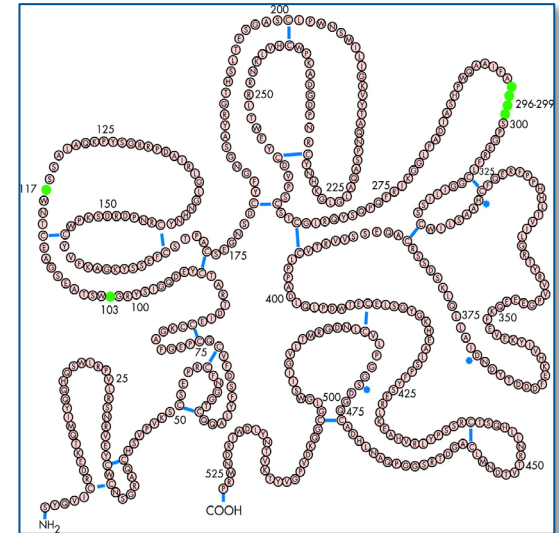
- Agent with 72 hr infusion, need to check fibrinogen levels



- Agent with 1 min bolus and 60 min infusion



- Agent with 5 sec bolus



Tenecteplase



Thrombolytic

- Engineered/ modified variant of alteplase
- Greater fibrin specificity
- Longer $T^{1/2}$ allows bolus administration

Alteplase (ALT) Vs. Tenecteplase (TNK)

Alteplase

Half-life	<5 minutes ¹
Circulating fibrinogen	16–36% decrease ¹
Clearance	Liver ¹
Indication	AMI ¹ , AIS ¹ , PE ¹ , CC ²
Administration	Combined bolus, infusion dose ¹

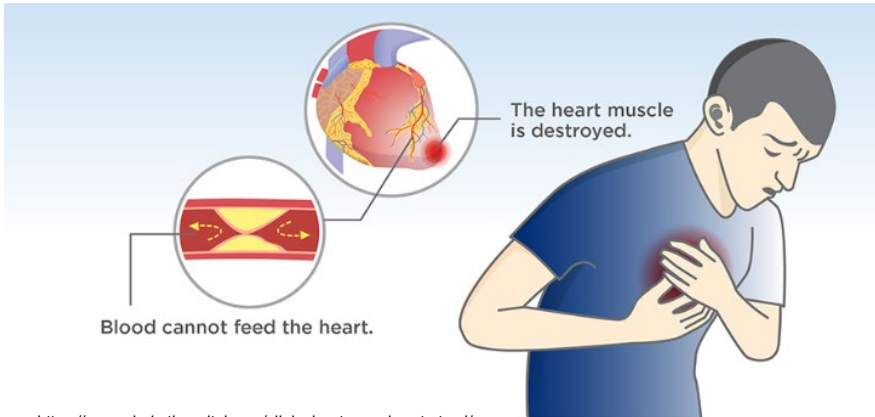
Tenecteplase

Half-life	20–24 minutes
Circulating fibrinogen	4–15% decrease
Clearance	Liver
Indication	AMI, AIS (ASA Guidelines)
Administration	Single weight-based bolus

Tenecteplase: Lessons from Cardiology

ASSENT-2 STEMI Trial (N=16,949)

- Serious bleeding side effects: 1.4% TNK vs 7% alteplase
- ICH rates were rare similar between TNK and alteplase
 - Healthy brains do not bleed (0.9%)
- TNK Bolus instead of 90 min alteplase infusion

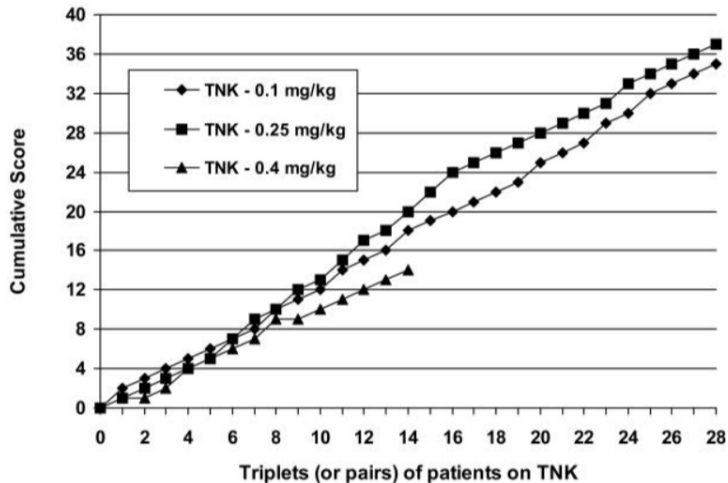


Objective 2: Tenecteplase Research and Evidence





Phase IIB/III Trial of Tenecteplase in acute ischemic stroke



- Dose Finding Study

- Randomized,
double-blind

- <3hr

- 0.1,0.25,0.4 mg/kg

TNK vs. ALT

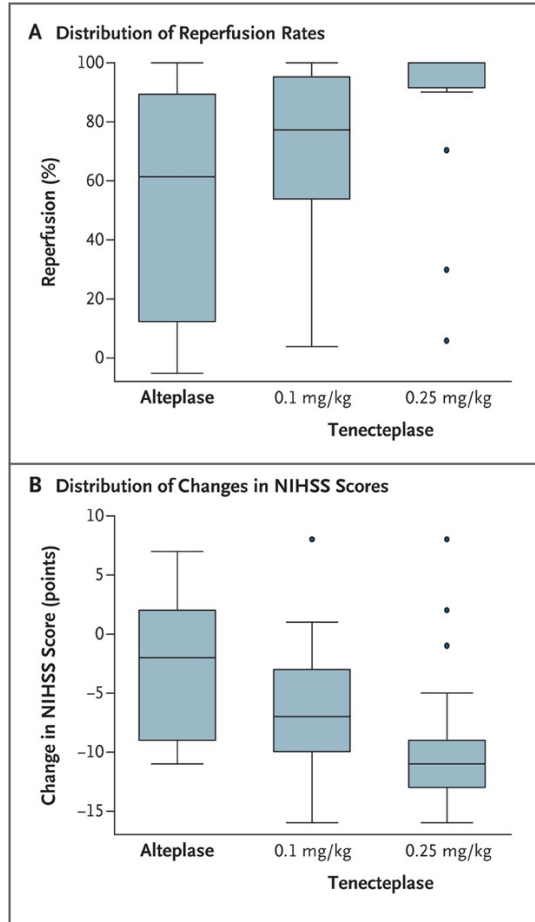
- N (TNK)= 81

- Composite Outcome

24 hr

- 0.4mg/kg inferior

A Randomized Trial of Tenecteplase vs Alteplase for Acute ischemic stroke



- Phase 2
- Randomized
- <6hr; LVO with penumbra by CTA/CTP
- 0.1,0.25mg/kg TNK vs. ALT
- N (TNK)= 50
- Reperfusion and clinical improvement at 24 hr
- Combined TNK superior to ALT

Alteplase versus tenecteplase for thrombolysis after ischaemic stroke (ATTEST)

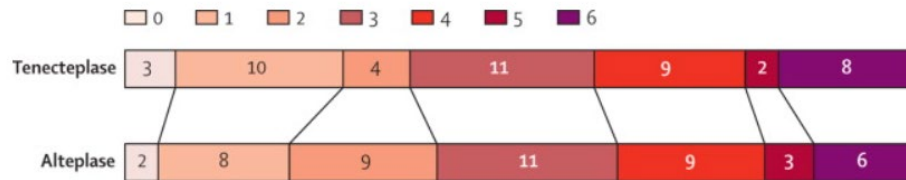


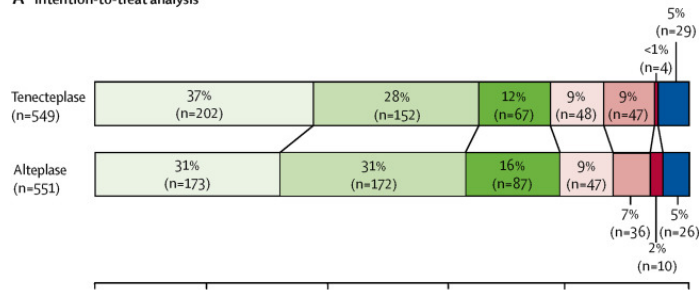
Figure 3 Distribution of modified Rankin scale scores at 90 days

- Phase 2
- Randomized
- <4.5hr; penumbra by CTA/CTP
- 0.25mg/kg TNK vs. ALT
- N (TNK)= 52
- Penumbral Salvage 24-48 hr
- No diff, non-inferior

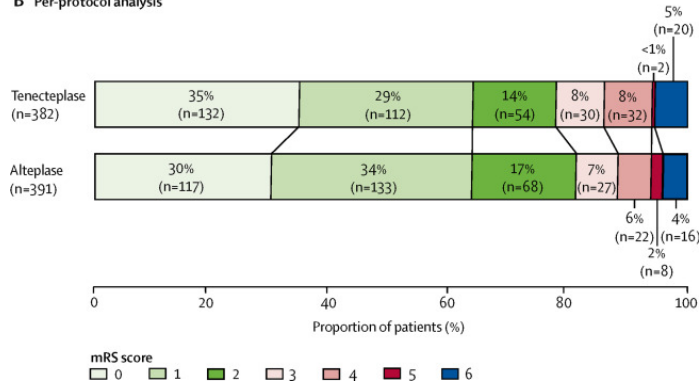
Tenecteplase versus alteplase for management of acute ischaemic stroke (NOR-TEST)

- Phase 3
- Randomized, PROBE
- <4.5hr (+Wake-up), All thrombolytic/thrombectomy
- 0.4mg/kg TNK vs. ALT
- N (TNK)= 549
- mRS at 3 months
- No diff, mRS or sICH
- NIHSS>15, TNK worse mortality

A Intention-to-treat analysis

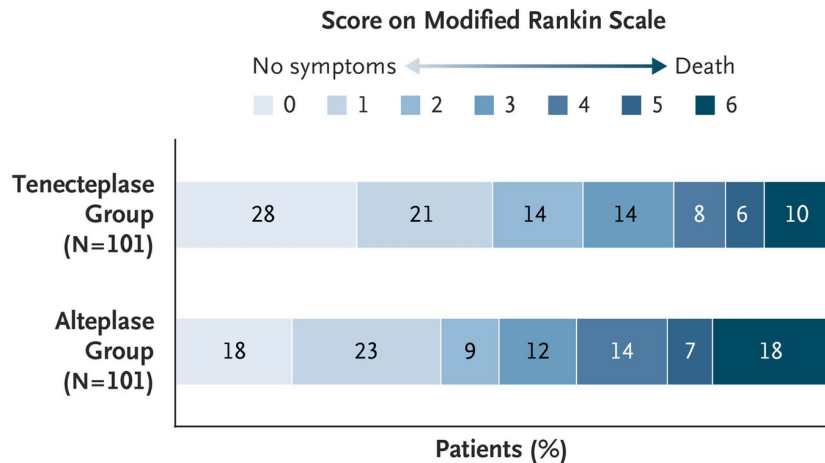


B Per-protocol analysis



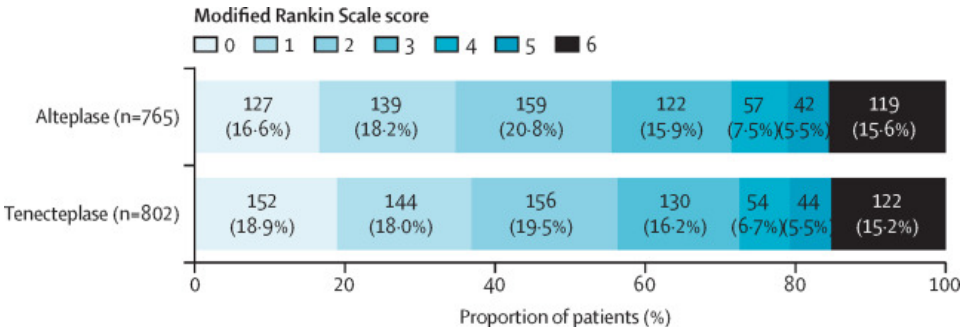
Logallo N, Novotny V, et al. Tenecteplase versus alteplase for management of acute ischaemic stroke (NOR-TEST): a phase 3, randomised, open-label, blinded endpoint trial. *Lancet Neurol.* 2017 Oct;16(10):781-788.

Tenecteplase vs Alteplase before thrombectomy



- Phase 3
- Randomized, PROBE
- <4.5hr LVO by CTA and planned thrombectomy
- 0.25mg/kg TNK vs. ALT
- N (TNK)= 101
- Substantial reperfusion on angiogram prior to thrombectomy (2x !!)
- Improved mRS at 3 months

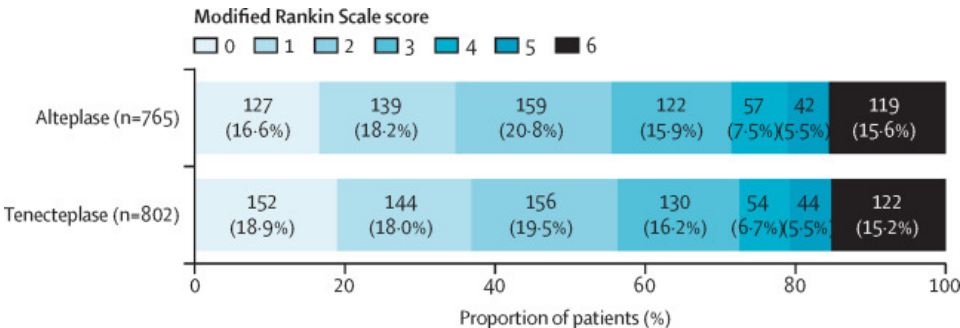
Intravenous tenecteplase compared with alteplase for acute ischaemic stroke in Canada (AcT)



- Randomized
- 1577 patients
- (36.9%) of 802 patients in the tenecteplase group and 266 (34.8%) of 765 in the alteplase group had an mRS score of 0-1 at 90-120 days
- 27 (3.4%) of 800 patients in the tenecteplase group and 24 (3.2%) of 763 in the alteplase group had 24 h symptomatic intracerebral haemorrhage
- Tenecteplase is noninferior to Alteplase

Menon BK, Buck BH, et al. Intravenous tenecteplase compared with alteplase for acute ischaemic stroke in Canada (AcT): a pragmatic, multicentre, open-label, registry-linked, randomised, controlled, non-inferiority trial. *Lancet*. 2022 Jul 16;400(10347):161-169.

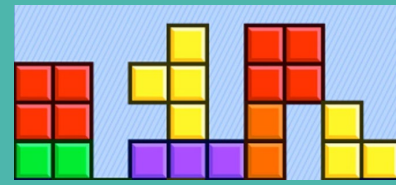
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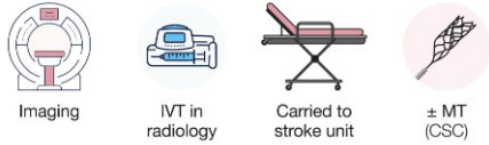
Treatment times, functional outcome, and hemorrhage rates after switching to tenecteplase for stroke thrombolysis



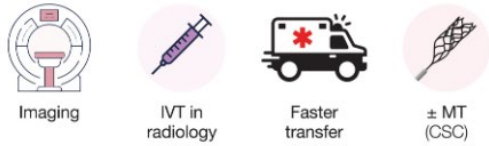
- Tetris Registry
- Retrospective study
- TNK vs Alteplase in CSC vs PSC
- 795 patients
- TNK with shorter imaging-to-thrombolysis times at CSC
- TNK with shorter thrombolysis-to-puncture times at PSC

Whole cohort	TNK (n=395)							tPA (n=358)						
	23	21	19	14	7	3	12	20	20	13	17	8	5	17

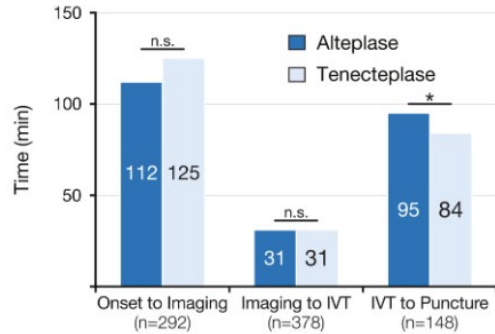
(b) Saint-Antoine PSC
Code stroke protocol with alteplase



Code stroke protocol with tenecteplase

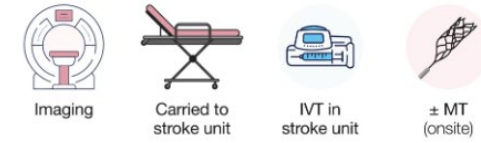


Treatment time metrics

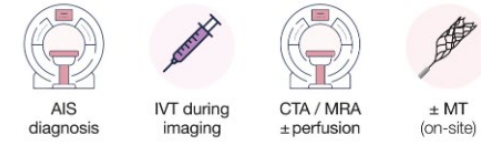


PSC	Alteplase (n=395)						
	27	19	20	11	6	4	13
tPA (n=358)	24	21	12	14	6	4	19

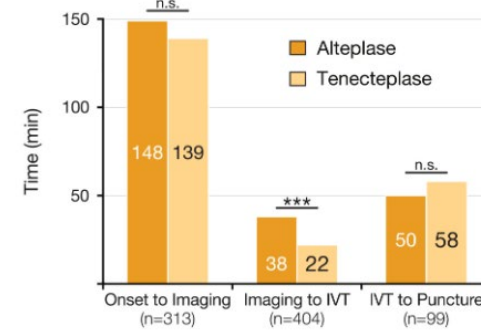
(a) Bordeaux University CSC
Code stroke protocol with alteplase



Code stroke protocol with tenecteplase



Treatment time metrics



CSC	Alteplase (n=395)						
	18	23	19	18	8	2	12
tPA (n=358)	17	19	14	20	9	6	15

Gerschenfeld G, Liegry JS, et al Treatment times, functional outcome, and hemorrhage rates after switching to tenecteplase for stroke thrombolysis: Insights from the TETRIS registry. Eur Stroke J. 2022 Dec;7(4):358-364.

Treatment times, functional outcome and hemorrhage rates after switching to tenecteplase for stroke thrombolysis

Encouraging efficacy and safety data and its practical advantages motivated our centers to switch from alteplase to tenecteplase in all patients (with and without large vessel occlusion).

Methods

- Retrospective analysis of all patients treated with alteplase or tenecteplase
- 2 centers (1 CSC, 1 PSC) from the TETRIS registry

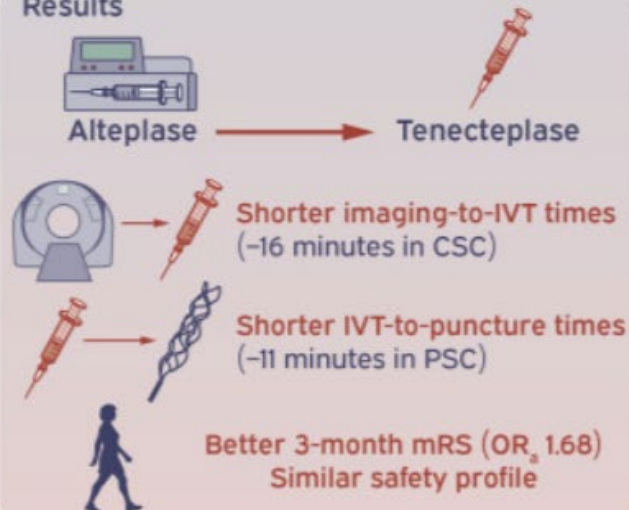
Main outcomes:

- Imaging-to-thrombolysis
- Thrombolysis-to-puncture

Secondary outcomes:

- 3-month mRS score
- Parenchymal hemorrhage

Results



Conclusion

Switch to tenecteplase:

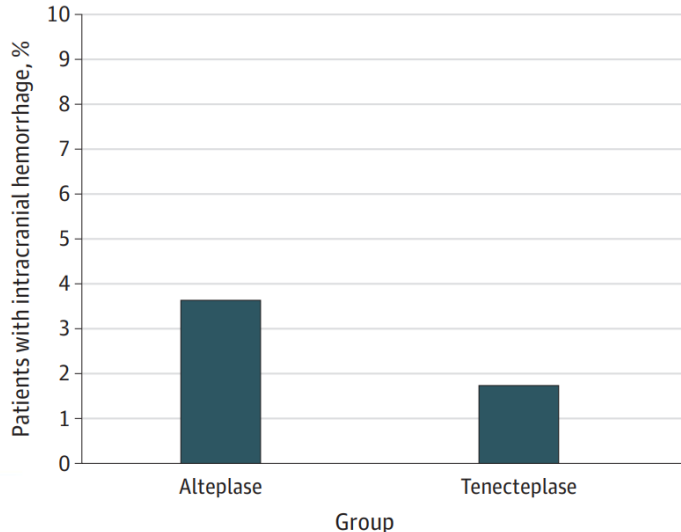
- ✓ Reduced process times
- ✓ Associated with better functional outcome
- ✓ With similar safety profile

Abbreviations:

CSC: comprehensive stroke center
PSC: primary stroke center
mRS: modified Rankin scale
IVT: intravenous thrombolysis

Symptomatic Intracranial Hemorrhage With Tenecteplase vs Alteplase in Patients With Acute Ischemic Stroke

Figure. Rates of Intracranial Hemorrhage



- Retrospective study
- Comparative Effectiveness of Routine Tenecteplase vs Alteplase in Acute Ischemic Stroke (CERTAIN) collaboration
- 9238 patients
- The proportion of patients with sICH was 1.8% for tenecteplase and 3.6% for alteplase ($P < .001$)

Tenecteplase Stroke Literature Summary

- Single bolus injection- workflow advantages
- Higher rates of recanalization- better outcomes
- Reduced bleeding complications- better safety

So... Why did the case of AG happen?

HPI

History:

67 yo M presenting the ED at 18:42 with Right sided weakness.

Patient took a nap but awoke feeling normal. He was able to ambulate, make a sandwich. Then at 15:45 he noticed the sudden right sided weakness. Unable to ambulate.

Possible Thrombolytic candidate:

not on warfarin or NOACs

no intracranial hemorrhage history

no recent major surgery

no known active major internal bleeding

no known blood disorders

Case Review: AG

Scores

Time of exam and NIHSS (Mountain Time): 06/07/2022, 18:45

Level of Consciousness 1a: [0] = Alert; keenly responsive

LOC Questions 1b: [0] = Answers both questions correctly

LOC Commands 1c: [0] = Performs both tasks correctly

Best Gaze 2: [0] = Normal

Visual 3: [0] = No visual loss

Facial Palsy 4: [2] = Partial paralysis

Motor Arm Left 5a: [0] = No drift

Motor Arm Right 5b: [2] = Some effort against gravity

Motor Leg Left 6a: [0] = No drift

Motor Leg Right 6b: [2] = Some effort against gravity

Limb Ataxia 7: [0] = Absent

Sensory 8: [0] = Normal

Best Language 9: [0] = No aphasia

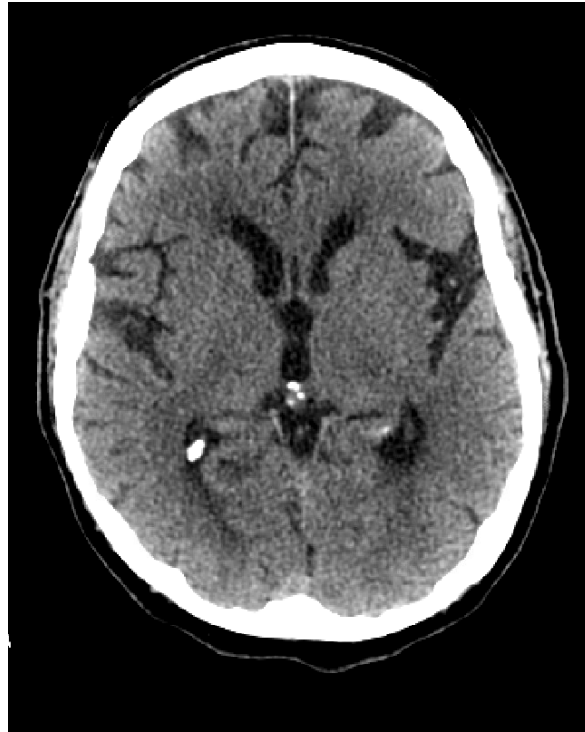
Dysarthria 10: [1] = Mild-to-moderate dysarthria

Extinction and Inattention 11: [0] = No abnormality

NIHSS Total: 7

Case of AR

Initial CTH



TNK administered at: 17:07

Case of AR

Documented Blood pressures:

Jun 07,22	23:01	169/84	
Jun 07,22	22:00	147/71	Non-invasive monitor Arm upper left
Jun 07,22	20:16	262/126	Monitor Arm upper left
Jun 07,22	19:34	174/84	Monitor
Jun 07,22	19:25	193/92	Monitor
Jun 07,22	19:00	208/100	Monitor

Case of AR

“Reevaluation: 1930

Patient had a mental status change and is diaphoretic pale and feeling achy all over his body. Nursing unable to get a blood pressure. Stat head CT ordered. Updated intensivist who is in ED”

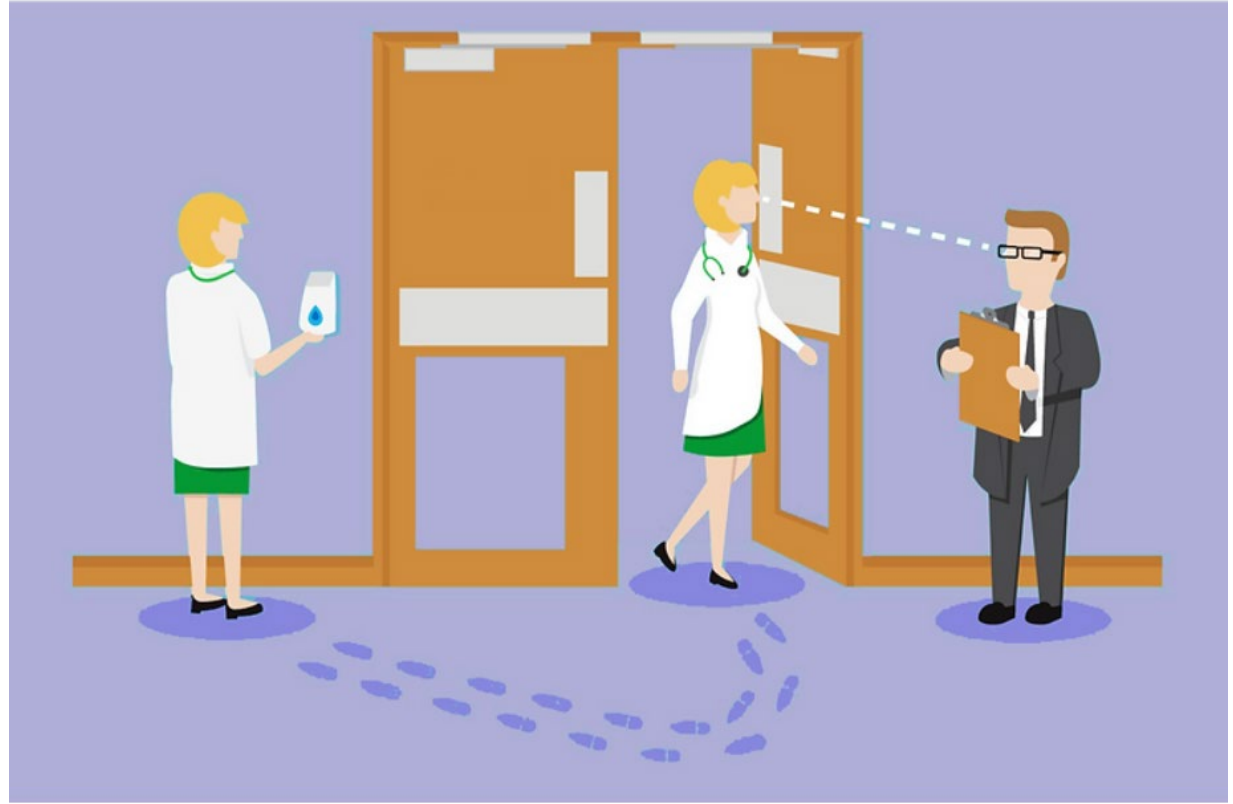


“Reevaluation

Patient continues to decline. CT head shows a bleed in the right pons and subarachnoid. Updated Dr. Lampe who has not had a chance to review scans. Patient needing cryoprecipitate and reversal. This has been ordered. Along with TXA. Concerns that patient is not protecting his airway and will likely decline further. We will plan to intubate patient”

How did this happen?

Hawthorne Effect



Case AG

Jun 07,22 22:00	147/71
Jun 07,22 20:16	262/126
Jun 07,22 19:34	174/84
Jun 07,22 19:25	193/92
Jun 07,22 19:00	208/100

Nicardipine HCl (CARDENE)	25 MG	X1ED ONE IV	Jun 07,22 19:30 Jun 07,22 19:31	DC	Jun 07,22 19:28 250 MLS
Sodium Chloride (NACL-0.9%)	250 ML				
Miscellaneous ... (NO Anticoagul)	See Detail	Q24H -	Jun 07,22 19:30 Jun 08,22 19:31	DC	
Labetalol HCl (LABETALOL HCL)	10 MG	X1ED ONE IV	Jun 07,22 19:30 Jun 07,22 19:31	DC	Jun 07,22 19:28 10 MG
Tenecteplase (TNKASE)	18.5 MG	ONCE ONE IV	Jun 07,22 19:07 Jun 07,22 19:08	DC	Jun 07,22 19:07 18.5 MG
Sodium Chloride	10 ML	DDN DDN	Jun 07,22 19:12	DC	Jun 07,22 19:12

What did I learn?

1. Don't mess around with Blood pressure control
 - a. Go right to cardene

Our Providers Think	
S Stroke Scale	Communicate your NIH
T Thrombolytic Decision	Yes/No/Not sure yet
A Antihypertensives	BP Parameters Medication Recommendations
T Tests/Imaging	CTA: Yes/No and urgency CTP: Yes/No and urgency
At The Pad	

2. Follow Through:



Stay involved from start to finish

Thank you!



Special thanks to:

- Jana Braklow
- Becky VanVliet
- Matthew Grantz, MD



Questions:
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MEDICAL CENTER**