Acute Stroke Management

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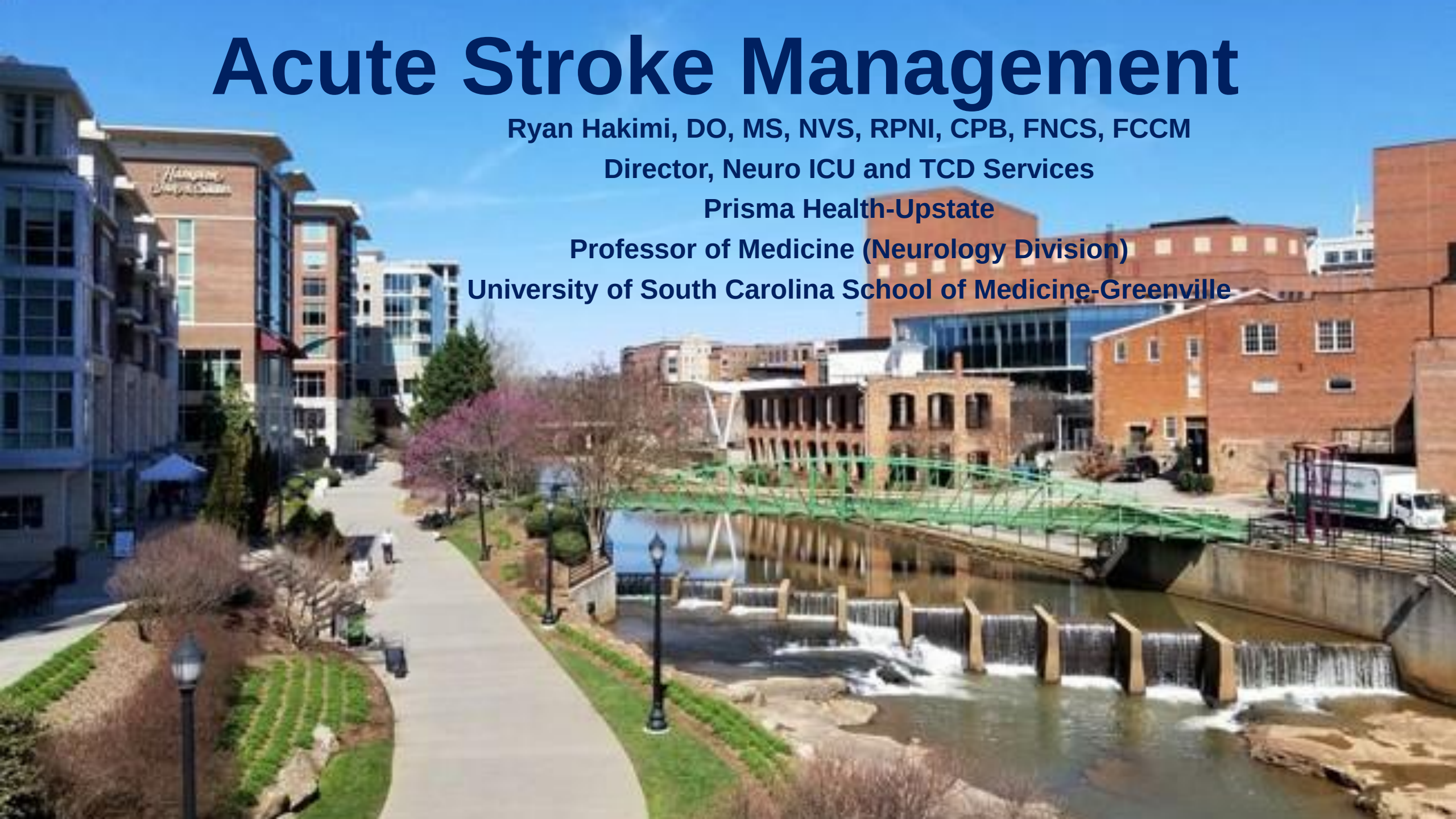


Disclosures

- No relevant conflicts of interest
- Though scientifically proven to be effective for acute ischemic stroke, tenecteplase is not FDA-approved for this indication.

Thanks to our Neuro ICU Team

- 5 physicians
- 4 NPs, 1 DNP, 2 PAs

Neuro ICU Provider Team

TCD Sonographers

Objectives

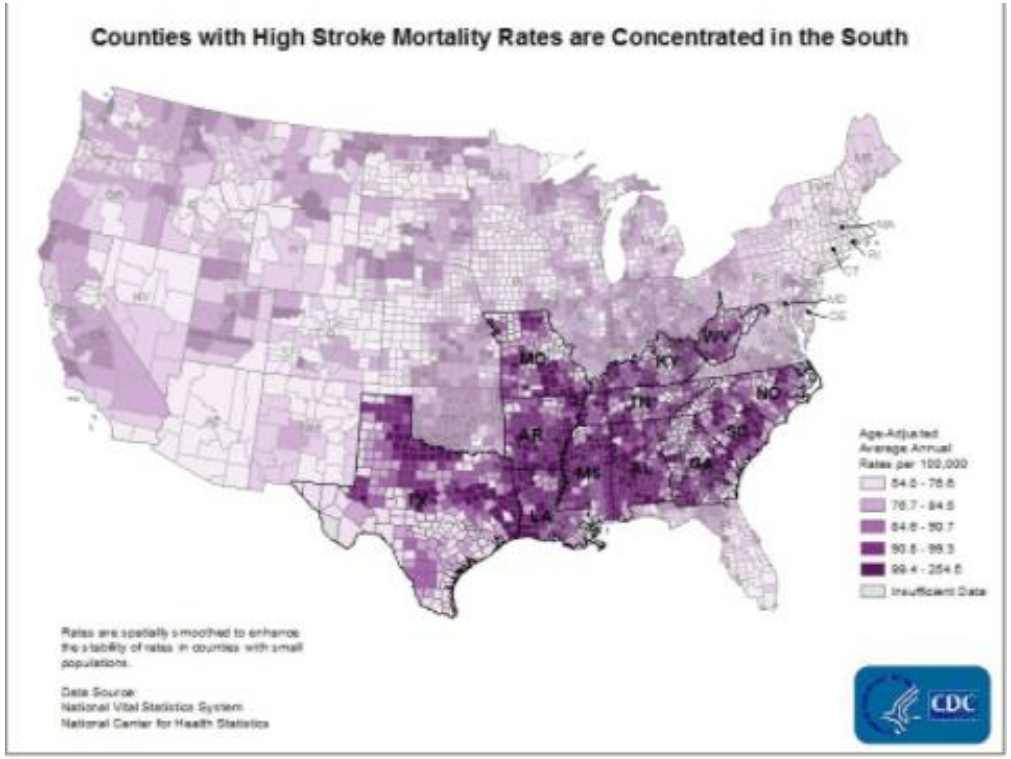
- Describe the modern evaluation and management of patients presenting with acute stroke-like symptoms
- Identify inclusion and exclusion criteria for IV thrombolytics
- Illustrate the use of mechanical thrombectomy in acute ischemic stroke for improved patient outcomes
- Compare alteplase and tenecteplase for treatment of acute ischemic stroke

Stroke in the United States 2021

- Affects > 795,000 people per year
- Someone in the United States has a stroke every 40 seconds. Every 4 minutes, someone dies of stroke
- About 185,000 strokes—**nearly 1 of 4**—are in people who have had a previous stroke
- About 87% of all strokes are ischemic strokes, in which there is lack of blood flow to a particular part of the brain

https://www.cdc.gov/stroke/facts.htm, accessed 2.2.21

Stroke Death Rates



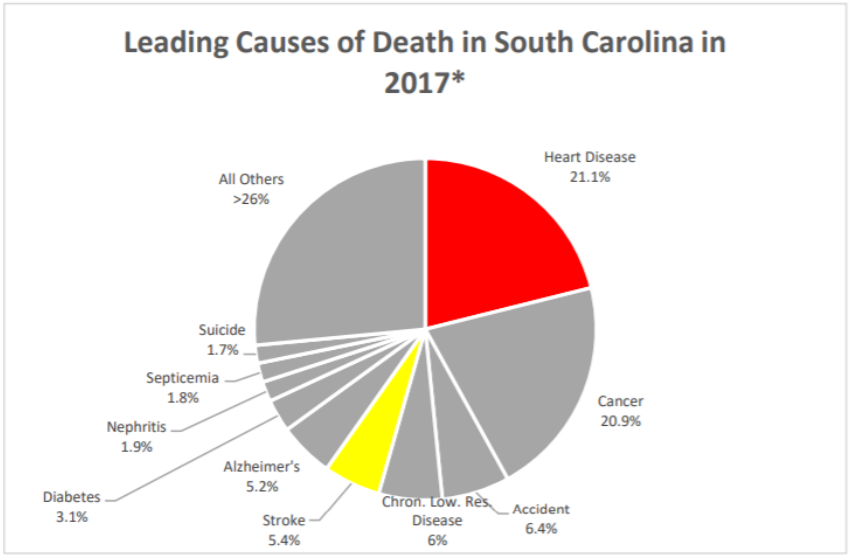
The country's highest death rates from stroke are in the southeastern United States.[2]

https://www.cdc.gov/stroke/facts.htm, accessed 2.2.21

South Carolina Statistics

South Carolina Fact Sheet

American Heart Association.



South Carolina has the 15th highest death rate from cardiovascular disease in the country.**

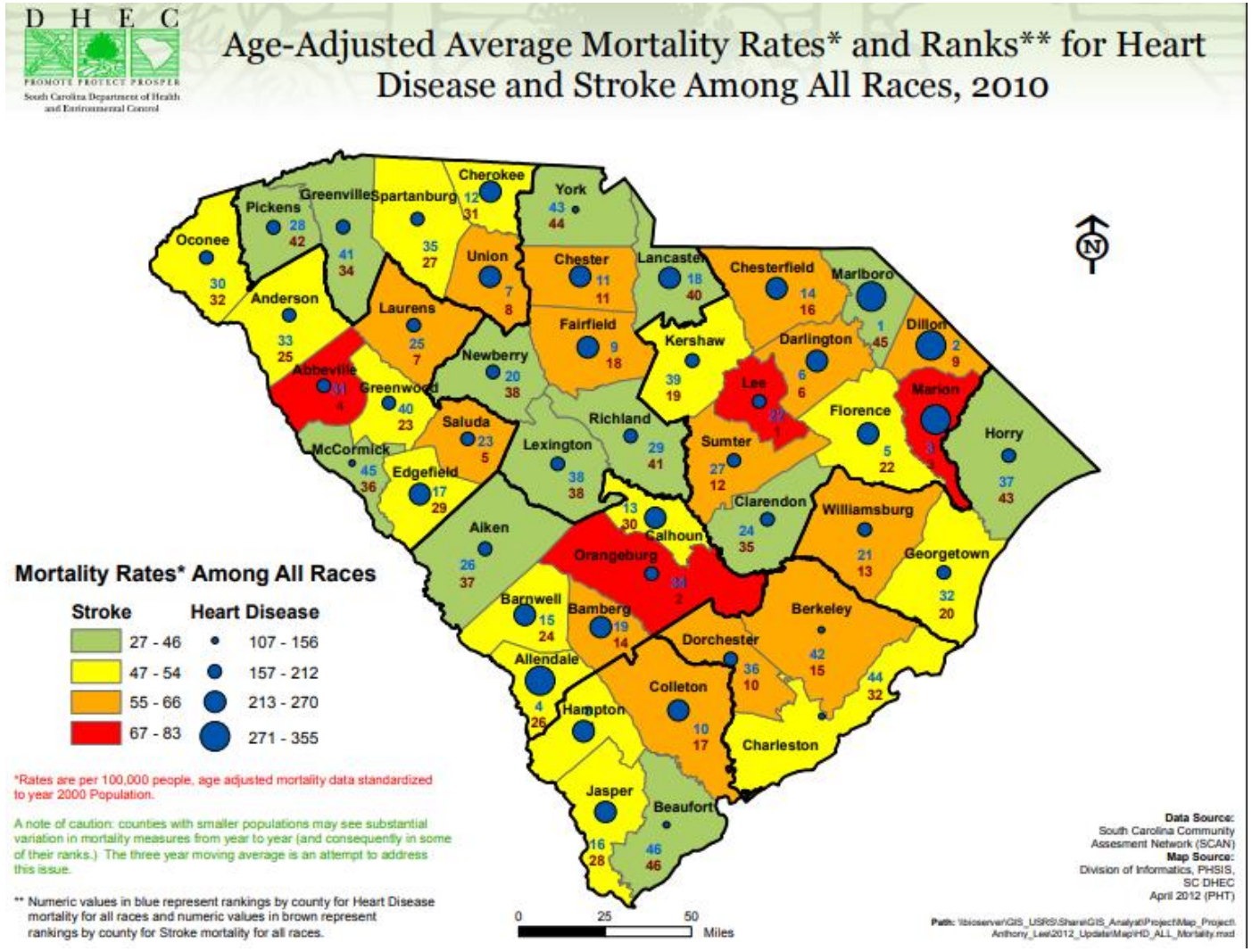
- Heart disease is the no. 1 killer in South Carolina*
- 10,418 people in SC died of heart disease in 2017*
- Stroke is the no. 5 killer in South Carolina*
- 2,691 in South Carolina died of stroke in 2017*

Heart Disease and Stroke Risk Factors in SC***

	SC	US
Adults who are current smokers+	18.8%	17.1%
Adults who participate in 150+ min of aerobic physical activity per week	48.6%	50.6%
Adults who are overweight or obese++	68.1%	66.6%
Adults who have been told that they have had a heart attack	4.8%	4.2%
Adults who have been told that they have had a stroke	3.8%	3%
Adults who have been told that they have angina or coronary heart disease	4.9%	3.9%
Population of adults (18-64) who have some kind of health care coverage	86%	89.5%
High school Students who are obese+++	17.2%	14.8%
Percentage of population covered by Medicaid/Chip++++	19%	19%

https://www.heart.org/-/media/files/about-us/policy-research/fact-sheets/quality-systems-of-care/quality-systems-of-care-south-carolina.pdf?la=en, accessed 2.2.21

South Carolina Heart Disease and Stroke Data by County



https://scdhec.gov/sites/default/files/docs/Health/docs/Heart%20Disease%20and%20Stroke%20Mortality%20by%20SC%20County.pdf, accessed 2.2.21

Modifiable Stroke Risk Factors

CLINICAL STATEMENTS AND GUIDELINES

Figure. AHA's My Life Check – Life's Simple 7. Seven approaches to staying heart healthy: be active, keep a healthy weight, learn about cholesterol, don't smoke or use smokeless tobacco, eat a heart-healthy diet, keep blood pressure healthy, and learn about blood sugar and diabetes mellitus.[1] AHA indicates American Heart Association; HDL, high-density lipoprotein cholesterol; and LDL, low-density lipoprotein cholesterol. Copyright © 2019, American Heart Association, Inc.

https://www.ahajournals.org/doi/epub/10.1161/CIR.0000000000000757, accessed 2.2.21

Stroke Sub-types

- Ischemic stroke
  - **Acute ischemic stroke management**
    - **Our focus today**
  - Chronic ischemic stroke
    - Secondary stroke prevention

- Hemorrhagic Stroke

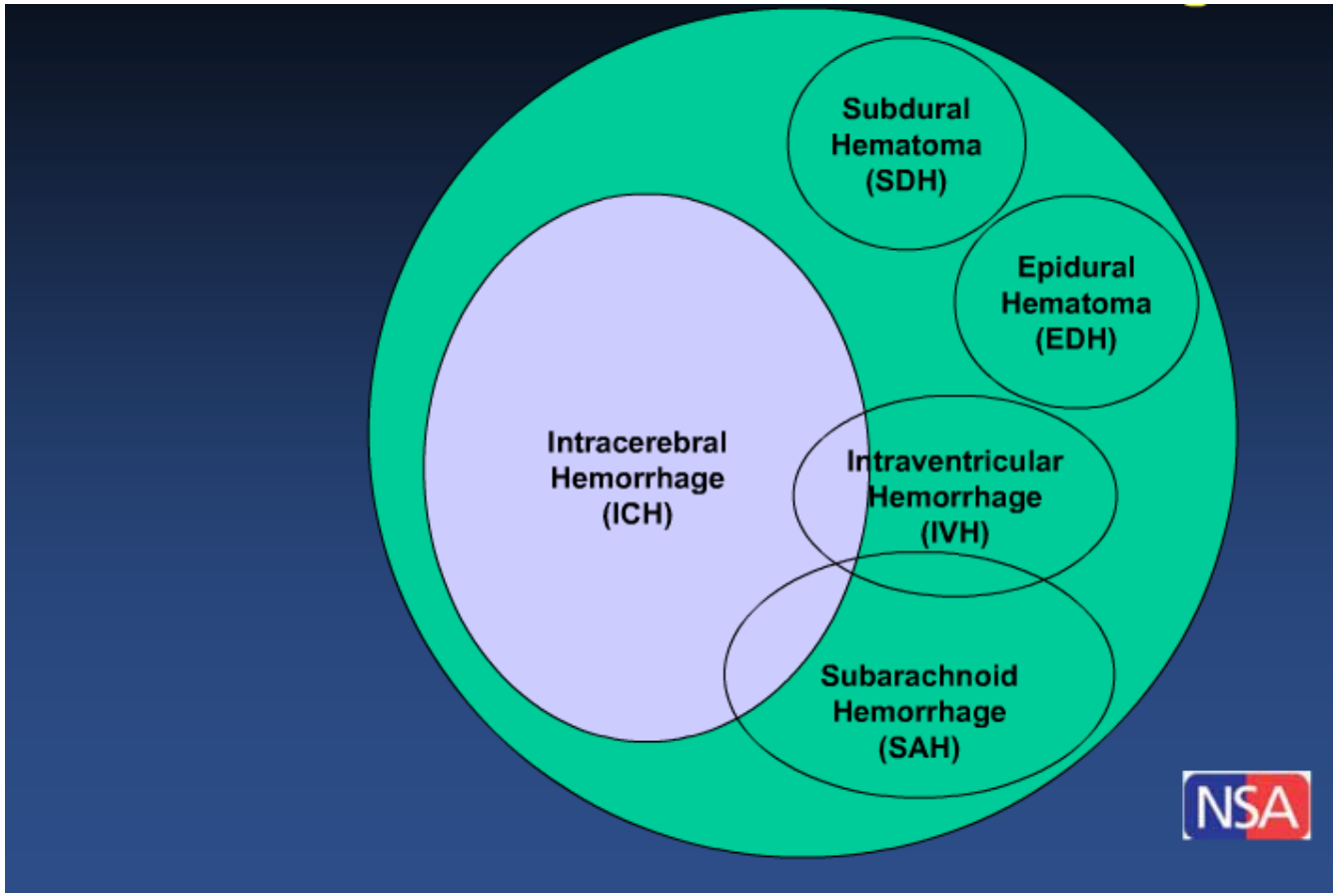


Figure courtesy of National Stroke Association

Goals

- Rapid decision making
- Recognition of time limits
- Detection of hemorrhage
- ? thrombolytic administration
- Recognition of large vessel occlusion (LVO)
- Blood pressure control

Sudden Onset Signs and Symptoms of Acute Stroke

- Unilateral body weakness
- Aphasia
- Facial weakness
- Dysarthria
- Sudden loss of vision
- Numbness
- Tingling
- Ataxia
- Worst headache of life

Critical Information Needed

- Time of last known well
- Current blood glucose
- Current complete vital signs (T, HR, BP, O2 sat, RR)
- Patient's baseline level of function: modified Rankin Scale (mRS)
- Relevant medical history
- Anything to suggest a seizure or history of seizures

- *Use the above information to determine whether there is an alternative explanation for the patient's neurological symptoms*

Modified Rankin Scale

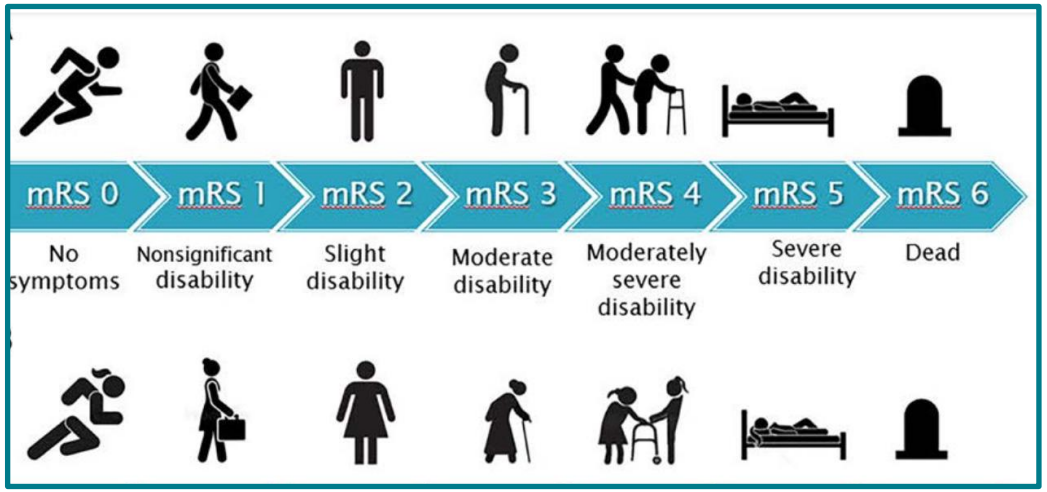
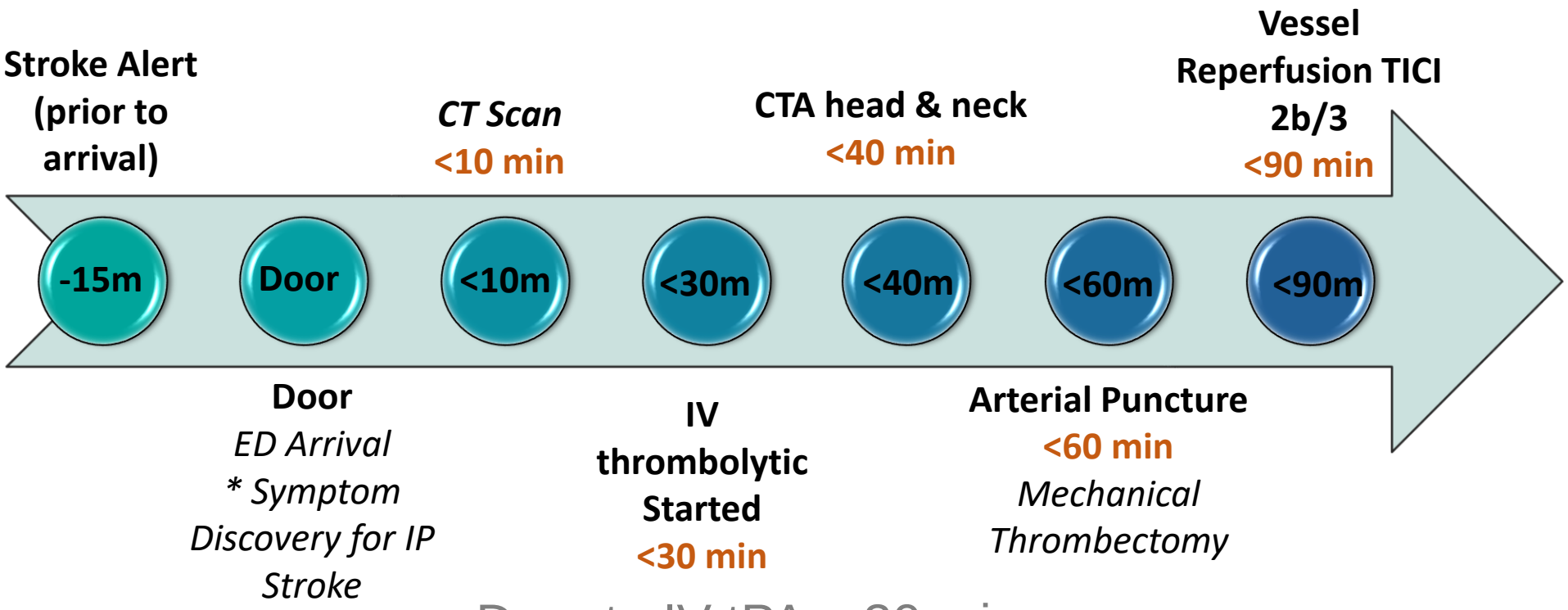


Figure courtesy of American Stroke Association

Stroke Alert Process



Door to IV tPA < 30 min

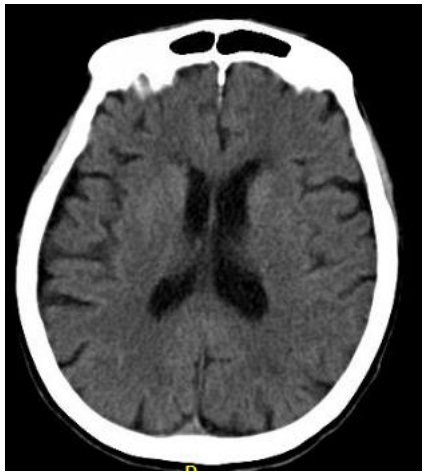
Door to Arterial Puncture < 60 min

Door to TICI 2b/3 <90 min

Non-contrast Head CT in Acute Stroke

- Helps differentiate between ischemic and hemorrhagic stroke
- Hemorrhagic stroke only 15% of all strokes
- Non-contrast head CT is unrevealing in acute ischemic stroke which supports the decision to potentially administer IV thrombolytic
  - Use physical exam to localize the ischemic stroke then focus on that part of CT

Patient with right hemiparesis, left gaze deviation, and aphasia with last known well 2 hours ago, focus on left MCA distribution



Normal Head CT

Indications and Contraindications for IV Thrombolytics

- **Indications**
  - Diagnosis of acute ischemic stroke
  - Symptom onset less than 4.5 hours ago
  - Age greater than 18 (consent needed for less than 18 as it is off label)

*6% historical chance of hemorrhagic complication based on 1995 NINDS trial
*Modern day risk is 1% in most registries
*10X risk of being sued for not giving IV thrombolytic than giving it with a complication

30-50% improved functional neurological outcome at 90 days with IV tPA

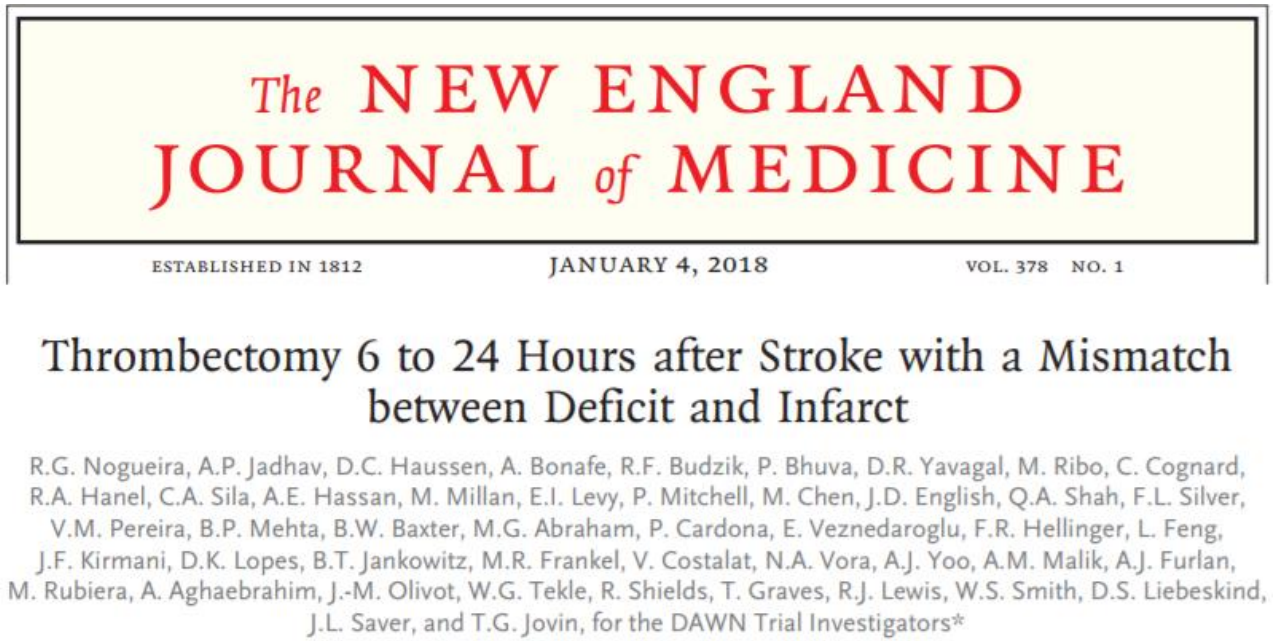
- **Contraindications**
  - Do not suspect an acute ischemic stroke
  - Presence of hemorrhage on head CT
  - Acute ischemic stroke or severe head injury in last 3 months
  - On anticoagulation or known coagulation defect (INR, platelet count, PTT, etc.)
  - SBP > 185 or DBP >110 (needs to be lowered before treatment)
  - Suspected aortic arch dissection or infective endocarditis

BP Control

- Hemorrhage rate tied to control of hypertension
  - Violations of guideline
  - Hypertension post recanalization (re-perfusion injury)
- Best managed initially by short acting agents
  - Clevidipine
  - Nicardipine
- Labetalol best if near target and likely to need one dose
  - BP tends to fall somewhat over time

DAWN Trial

- Established need for urgent evaluation of ischemic stroke patients at 6-24 hours from last known well for possible mechanical thrombectomy



The NEW ENGLAND JOURNAL of MEDICINE

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Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct

R.G. Nogueira, A.P. Jadhav, D.C. Haussen, A. Bonafe, R.F. Budzik, P. Bhuva, D.R. Yavagal, M. Ribo, C. Cognard, R.A. Hanel, C.A. Sila, A.E. Hassan, M. Millan, E.I. Levy, P. Mitchell, M. Chen, J.D. English, Q.A. Shah, F.L. Silver, V.M. Pereira, B.P. Mehta, B.W. Baxter, M.G. Abraham, P. Cardona, E. Veznedaroglu, F.R. Hellinger, L. Feng, J.F. Kirmani, D.K. Lopes, B.T. Jankowitz, M.R. Frankel, V. Costalat, N.A. Vora, A.J. Yoo, A.M. Malik, A.J. Furlan, M. Rubiera, A. Aghaebrahim, J.-M. Olivot, W.G. Tekle, R. Shields, T. Graves, R.J. Lewis, W.S. Smith, D.S. Liebeskind, J.L. Saver, and T.G. Jovin, for the DAWN Trial Investigators*

DAWN Trial

Table 2. Efficacy Outcomes.*

Outcome	Thrombectomy Group (N=107)	Control Group (N=99)	Absolute Difference (95% CI)†	Adjusted Difference (95% Credible Interval)‡	Posterior Probability of Superiority
Primary end points					
Score on utility-weighted modified Rankin scale at 90 days§	5.5±3.8	3.4±3.1	2.1 (1.2–3.1)	2.0 (1.1–3.0)	>0.999
Functional independence at 90 days — no. (%)¶	52 (49)	13 (13)	36 (24–47)	33 (21–44)	>0.999
				Risk Ratio (95% CI)	P Value
Secondary end points					
Early response — no. (%)‖	51 (48)	19 (19)	29 (16–41)	3 (2–4)	<0.001**
Recanalization at 24 hr — no. (%)††	82 (77)	39 (39)	40 (27–52)	2 (2–4)	<0.001**
Change from baseline in infarct volume at 24 hr — ml††					0.003‡‡
Median	1	13			
Interquartile range	0–28	0–42			
Infarct volume at 24 hour — ml††					<0.001‡‡
Median	8	22			
Interquartile range	0–48	8–68			
Grade of 2b or 3 on mTICI scale — no. (%)§§	90 (84)	NA			

* Plus–minus values are means ±SD. CI denotes confidence interval, and NA not applicable.
† Absolute differences are reported in percentage points, except for the absolute difference in the score on the utility-weighted modified Rankin scale, which is reported in points.
‡ Adjusted differences were estimated with the use of a Bayesian general linear model with adjustment for infarct volume at baseline.
§ The utility-weighted modified Rankin scale ranges from 0 (death) to 10 (no symptoms or disability).
¶ Functional independence was defined as a score of 0, 1, or 2 on the modified Rankin scale, which ranges from 0 to 6, with higher scores indicating more severe disability.
‖ Early response was defined as a decrease in the NIHSS score of 10 points or more from baseline or an NIHSS score of 0 or 1 on day 5, 6, or 7 of hospitalization or at discharge if it occurred before day 5.
** The P value was calculated with the use of Fisher's exact test.
†† For details on the assessment of this end point, see Section S2 in the Supplementary Appendix.
‡‡ The P value was calculated with the use of the nonparametric Wilcoxon test.
§§ The modified Thrombolysis in Cerebral Infarction (mTICI) scale ranges from 0 to 3, with a grade of 2b or 3 indicating reperfusion of more than 50% of the affected territory.

DAWN Trial

- Resulted in change in Stroke Guidelines

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

AHA/ASA Guideline

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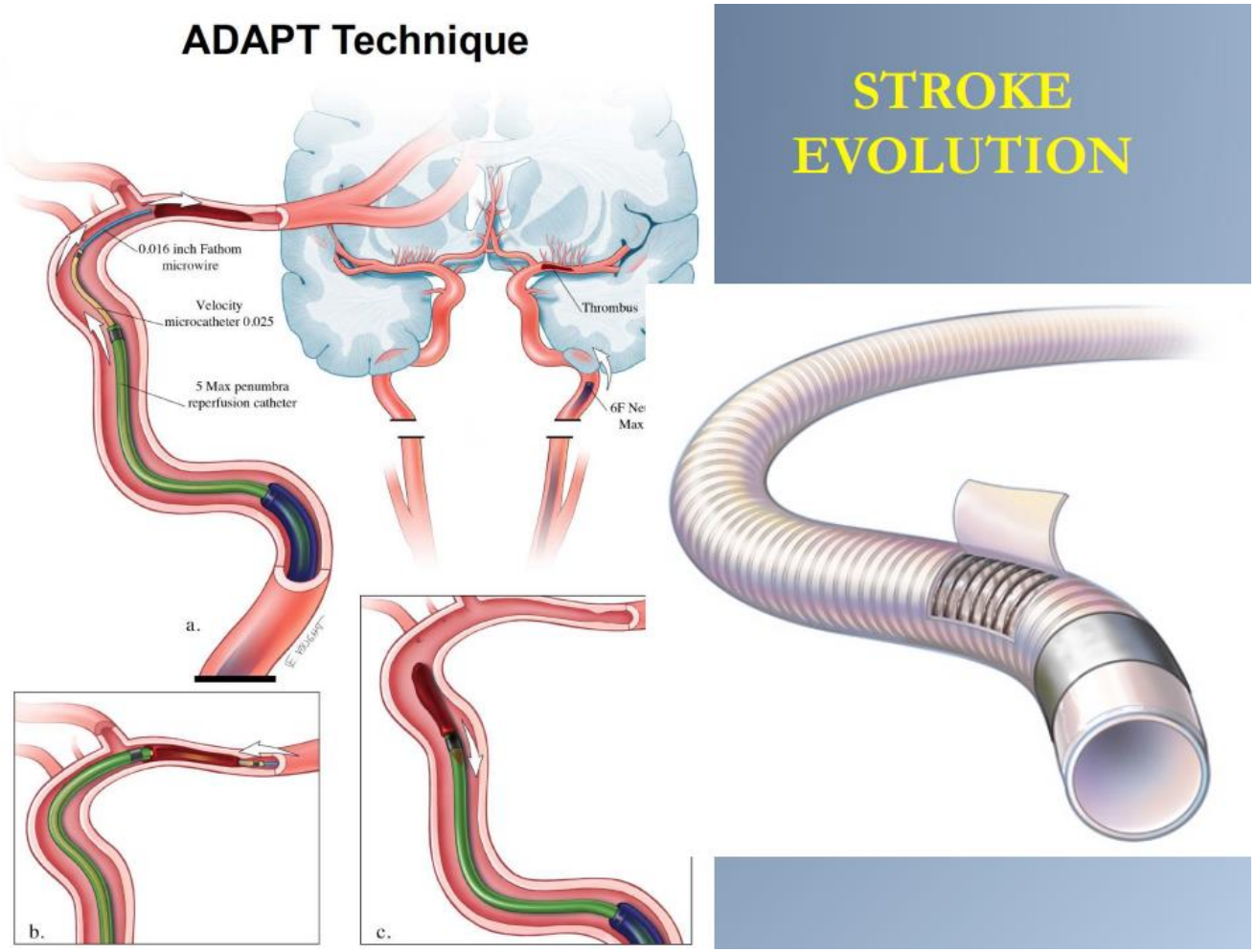
Indications for Mechanical Thrombectomy (our local practice)

Table 5. Indications for Mechanical Thrombectomy
Indications
NIHSS ≥ 6 or disabling neurological deficit
Large vessel occlusion on vascular imaging corresponding to neurological deficit
ASPECTS score > 3
CT Perfusion imaging suggestive of viable penumbra of at least 1/3 affected territory or eloquent region of brain
Favorable collateral score on CT angiogram
Pre-morbid mRS ≤ 3
**Note: Other cases not defined in the indications list will be evaluated for treatment based on collaborative decision-making between the Neuroendovascular and Neurology provider.*

Mechanical Thrombectomy



From: https://www.tmh.org/-/media/files/neurosciences/symposiumpresentations/stroke-intervention.pdf?la=en, accessed 8/25/20

Mechanical Thrombectomy

Table 3 Proposed revised Thrombolysis In Cerebral Infarction scale (TICI) scale including a 2C designation

Score	Revised TICI
0	No perfusion or anterograde flow beyond site of occlusion
1	Penetration but not perfusion. Contrast penetration exists past the initial obstruction but with minimal filling of the normal territory
2	Incomplete perfusion wherein the contrast passes the occlusion and opacifies the distal arterial bed but rate of entry or clearance from the bed is slower or incomplete when compared with non-involved territories
2A	Some perfusion with distal branch filling of <50% of territory visualized
2B	Substantial perfusion with distal branch filling of ≥50% of territory visualized
2C	Near-complete perfusion except for slow flow in a few distal cortical vessels or presence of small distal cortical emboli
3	Complete perfusion with normal filling of all distal branches

From: https://www.tmh.org/-/media/files/neurosciences/symposiumpresentations/stroke-intervention.pdf?la=en, accessed 8/25/20

Implications of TICI Grade

- TICI 0: No perfusion (flow) past the blockage
  - Therefore, want a very high blood pressure (up to 220 mm Hg) to allow the maximal chance for flow past the blockage
- TICI 1: Contrast makes it through the blockage
  - “Poked a hole in the blockage”
  - Therefore, want a very high blood pressure (up to 220 mm Hg) to allow the maximal chance for flow past the blockage

Implications of TICI Grade

- TICI 2A or 2B: Some perfusion past the blockage (less than 50% or greater than 50%, respectively)
  - Usually ends up with a “custom blood pressure”
    - Less than 160 mm Hg
    - Less than 140 mm Hg
- TICI 2C: Near complete perfusion past the blockage with only minimal distal clots
  - Less than 130 mm Hg
- TICI 3: Complete perfusion
  - Less than 130 mm Hg

Following tPA

- Less than 185/110 mm Hg
- Prevent reperfusion injury
- Prevent systemic bleeding

Without tPA

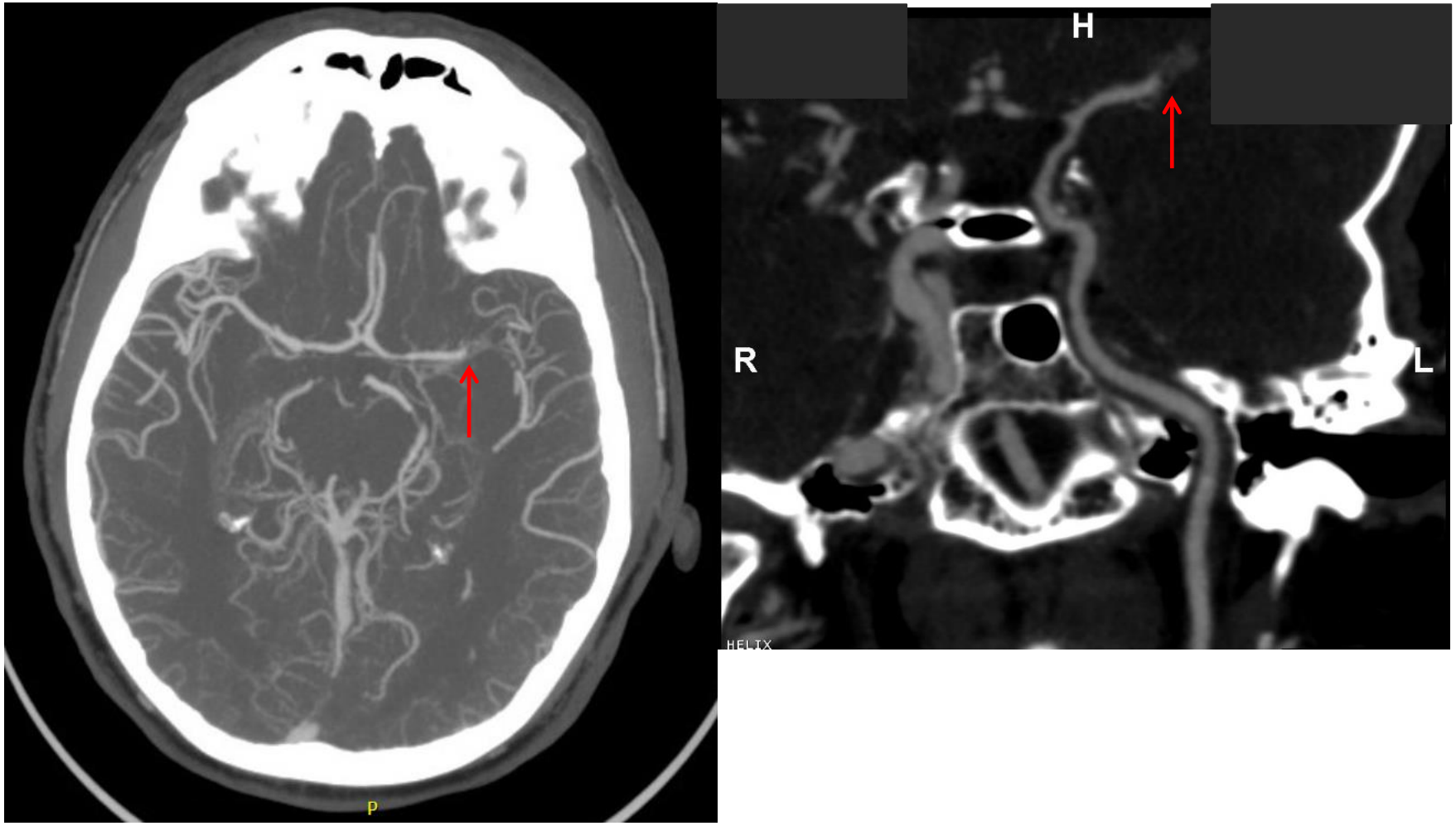
- Ensure cerebral perfusion past the blockage
- Less than 220/120 mm Hg

Case

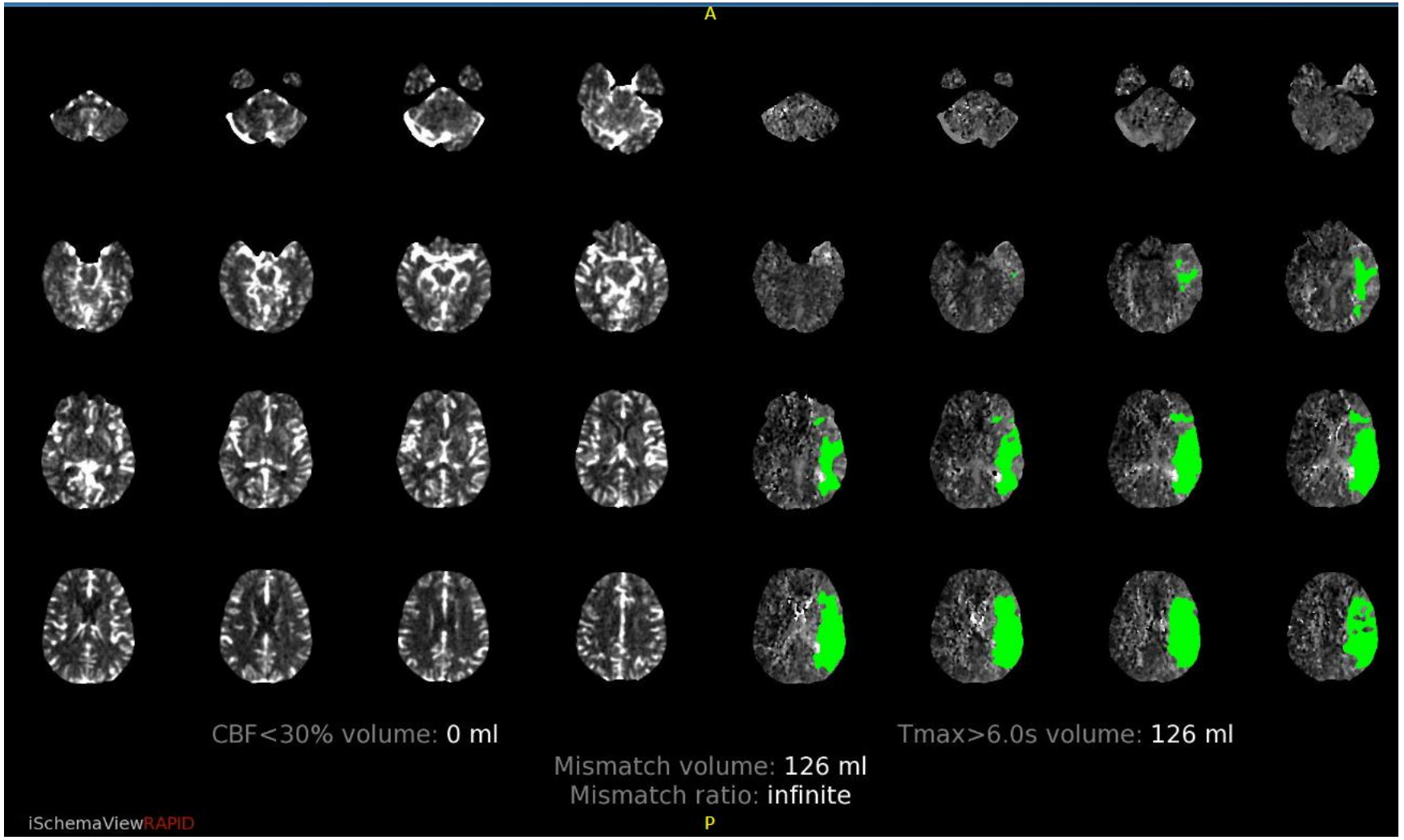
- 52 year-old right-handed male with PMH of HTN presented with complaint of aphasia and right hemiparesis, last known well 3.5 hours ago
- Normal vitals and glucose, patient not on anticoagulation
- Initial CT demonstrates left M1 thrombosis but otherwise, normal

Patient given IV alteplase and sent for CTA Head and neck with perfusion

CTA Head



CT Perfusion



Patient then sent for mechanical thrombectomy, had TICI 3 result

Final Head CT 2 weeks later (post thrombectomy)

Thrombolytic Practice Change at some Centers

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Tenecteplase versus Alteplase before Thrombectomy for Ischemic Stroke

B.C.V. Campbell, P.J. Mitchell, L. Churilov, N. Yassi, T.J. Kleinig, R.J. Dowling, B. Yan, S.J. Bush, H.M. Dewey, V. Thijs, R. Scroop, M. Simpson, M. Brooks, H. Asadi, T.Y. Wu, D.G. Shah, T. Wijeratne, T. Ang, F. Miteff, C.R. Levi, E. Rodrigues, H. Zhao, P. Salvaris, C. Garcia-Esperon, P. Bailey, H. Rice, L. de Villiers, H. Brown, K. Redmond, D. Leggett, J.N. Fink, W. Collecutt, A.A. Wong, C. Muller, A. Coulthard, K. Mitchell, J. Clouston, K. Mahady, D. Field, H. Ma, T.G. Phan, W. Chong, R.V. Chandra, L.-A. Slater, M. Krause, T.J. Harrington, K.C. Faulder, B.S. Steinfort, C.F. Bladin, G. Sharma, P.M. Desmond, M.W. Parsons, G.A. Donnan, and S.M. Davis, for the EXTEND-IA TNK Investigators*

METHODS

We randomly assigned patients with ischemic stroke who had occlusion of the internal carotid, basilar, or middle cerebral artery and who were eligible to undergo thrombectomy to receive tenecteplase (at a dose of 0.25 mg per kilogram of body weight; maximum dose, 25 mg) or alteplase (at a dose of 0.9 mg per kilogram; maximum dose, 90 mg) within 4.5 hours after symptom onset. The primary outcome was reperfusion of greater than 50% of the involved ischemic territory or an absence of retrievable thrombus at the time of the initial angiographic assessment. Noninferiority of tenecteplase was tested, followed by superiority. Secondary outcomes included the modified Rankin scale score (on a scale from 0 [no neurologic deficit] to 6 [death]) at 90 days. Safety outcomes were death and symptomatic intracerebral hemorrhage.

RESULTS

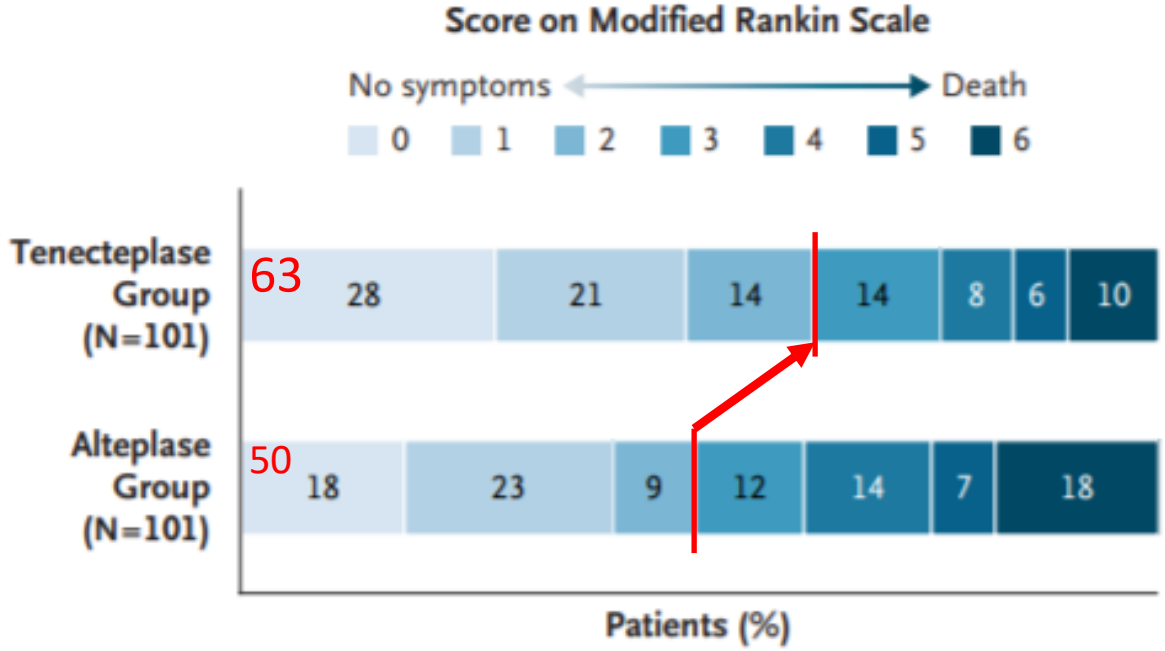
Of 202 patients enrolled, 101 were assigned to receive tenecteplase and 101 to receive alteplase. The primary outcome occurred in 22% of the patients treated with tenecteplase versus 10% of those treated with alteplase (incidence difference, 12 percentage points; 95% confidence interval [CI], 2 to 21; incidence ratio, 2.2; 95% CI, 1.1 to 4.4; P=0.002 for noninferiority; P=0.03 for superiority). Tenecteplase resulted in a better 90-day functional outcome than alteplase (median modified Rankin scale score, 2 vs. 3; common odds ratio, 1.7; 95% CI, 1.0 to 2.8; P=0.04). Symptomatic intracerebral hemorrhage occurred in 1% of the patients in each group.

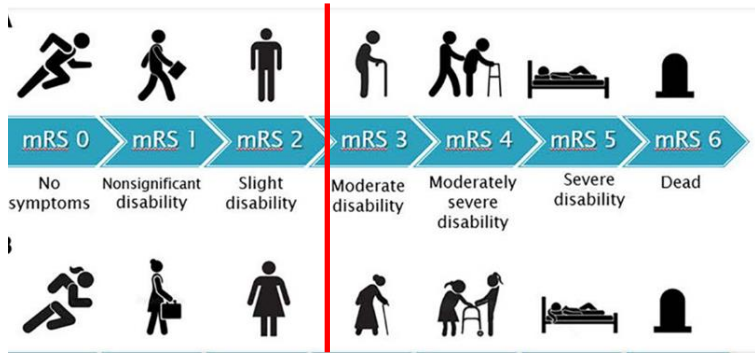
CONCLUSIONS

Tenecteplase before thrombectomy was associated with a higher incidence of reperfusion and better functional outcome than alteplase among patients with ischemic stroke treated within 4.5 hours after symptom onset. (Funded by the National Health and Medical Research Council of Australia and others; EXTEND-IA TNK ClinicalTrials.gov number, NCT02388061.)

Tenecteplase

- Larger percentage with excellent outcome (mRS 0-2)
- Fewer deaths (though not statistically significant)
- One patient in each group had symptomatic intracranial hemorrhage





Tenecteplase Properties

- One push dose administration (7 minutes less prep time, given over 5 seconds)
  - Easier than alteplase which requires a bolus and hour-long infusion
  - Guaranteed drug administration as opposed to alteplase which some drug can stay in the IV tubing
  - Does not require critical care EMS transport for management of the infusion
  - More rapid transfer of patients to thrombectomy centers from smaller hospitals

Tenecteplase Properties

- Longer acting (120 minutes vs. 10 minutes with alteplase) thus more effective with large vessel occlusions
  - Only 25% probability with alteplase alone that complete recanalization will occur
- Limited inactivation by Plasminogen Activator Inhibitor-1 compared to alteplase
- More fibrin-specific lysis which theoretically reduces the risk of bleeding

Tenecteplase Administration

- 0.25 mg/kg dose (max 25 mg)
- Post-administration monitoring parameters are the same as alteplase

- More trials ongoing. Some centers have chosen to stay with alteplase.

Summary

- Quick history (rule in or rule out thrombolytics)
- Quick exam (do you think it’s a stroke? vitals and glucose)
- Non-contrast head CT
- Give thrombolytic if no contraindication (may need to rapidly lower blood pressure to less than 185/110 with 10-20 mg IV labetalol or nicardipine infusion)
- Get CT angiogram head and neck with perfusion to evaluate for large vessel occlusion (LVO) and to determine if patient is a good candidate for reperfusion
- If LVO noted, call Neuroendovascular team
- Monitor exam and BP until patient taken for angiography
- Dispo: Admit to Neuro ICU

Thank you

Questions?

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