Acute Stroke

Rahul Mahajan, MD PhD
Instructor in Neurology, HMS
Division of Neurocritical Care, Dept. of Neurology, BWH

Disclosures

- Relevant to this talk:
  - None
- All relationships:
  - Site investigator for NINDS StrokeNet funded clinical trial in acute stroke.
  - Previous Consulting relationship with NQ Medical Inc. developing digital biomarkers in neurodegenerative disease.
  - Consulting fees from Violet Therapeutics advising on clinical applications of cell signaling measurement technology

Outline

- What is it?
- Pathophysiology
- Clinical Features
- Diagnostic Approach
- Treatment

Learning Objectives

- Understand triage, evaluation and treatment of acute stroke
- Know common acute stroke subtypes and recommended treatment for each.

Stroke

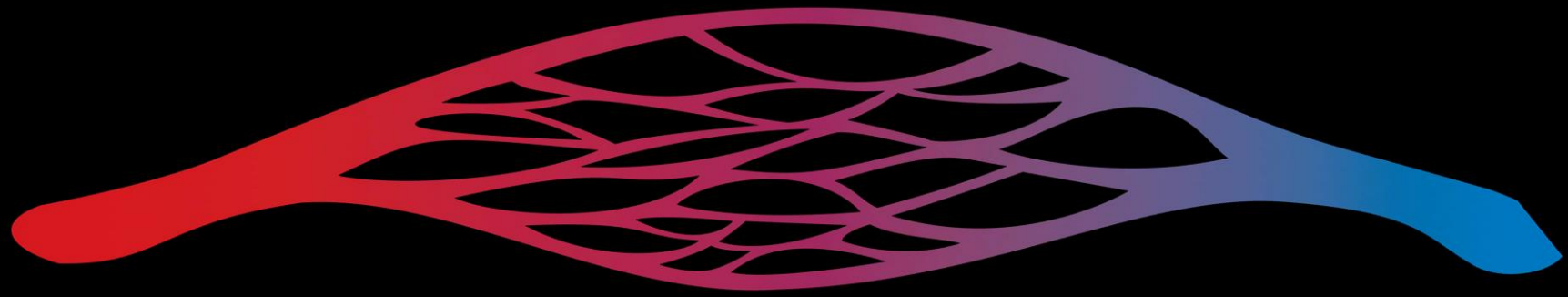
- Globally, stroke remains the second-leading cause of death and the third-leading cause of death and disability combined
- ~85% of all strokes are ischemic strokes
- ~15% Hemorrhagic strokes including
  - Intracerebral hemorrhage (parenchymal)
  - Subarachnoid hemorrhage (aneurysmal)

GBD 2019 et al. *Lancet Neurol.* 2021

CDC.gov/stroke

What causes infarction?

- Oxygen delivery < Demand for a critical period of time
  - Diminished Blood Flow (volume / time)
  - Diminished O_2 Delivery (with unchanged flow)
  - Disruption of energy metabolism



Flow: Embolism, Thrombosis, Dissection, Direct vascular injury, vasospasm, external compression, systemic hypotension

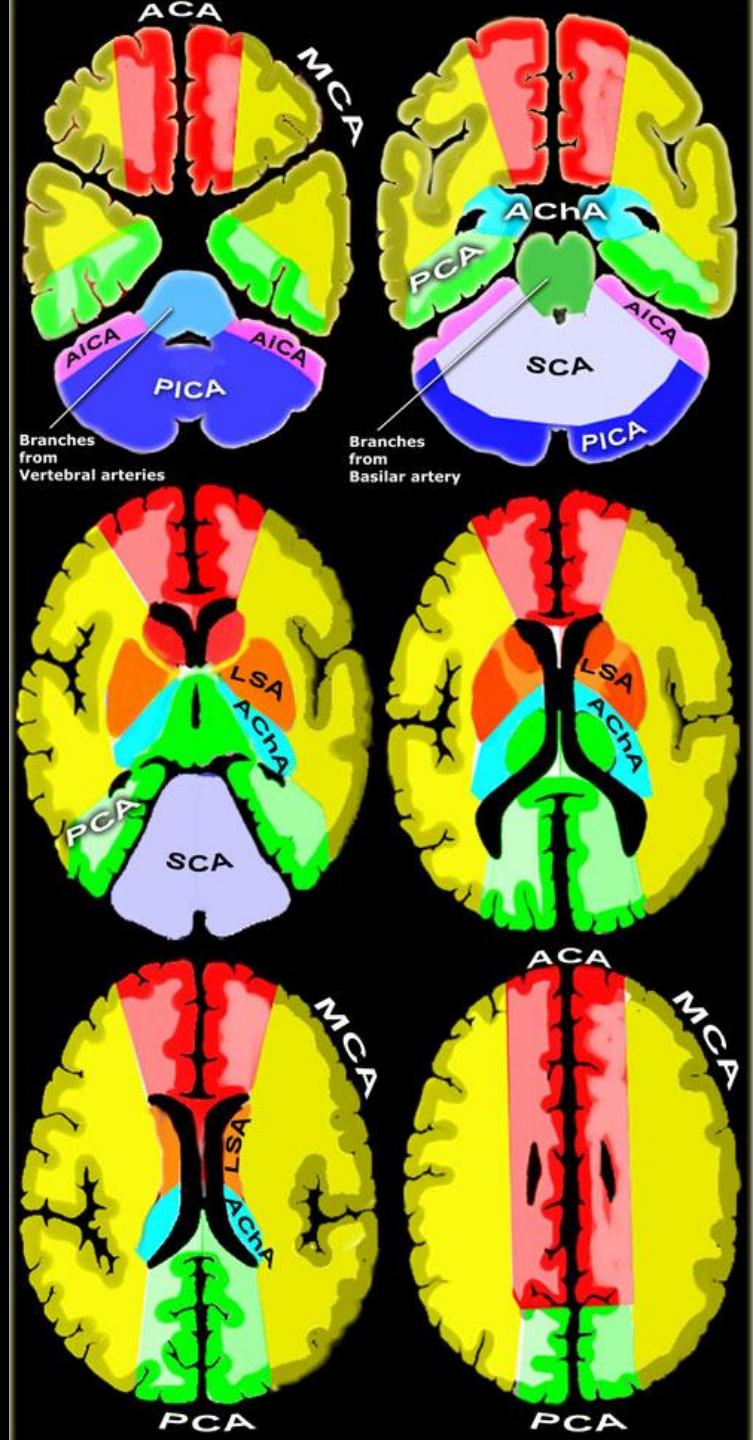
O2 Content: Hypoxemia, CO poisoning

Flow: Increased ICP
O2 Utilization: Hypoglycemia, seizures

Flow: Cerebral venous thrombosis

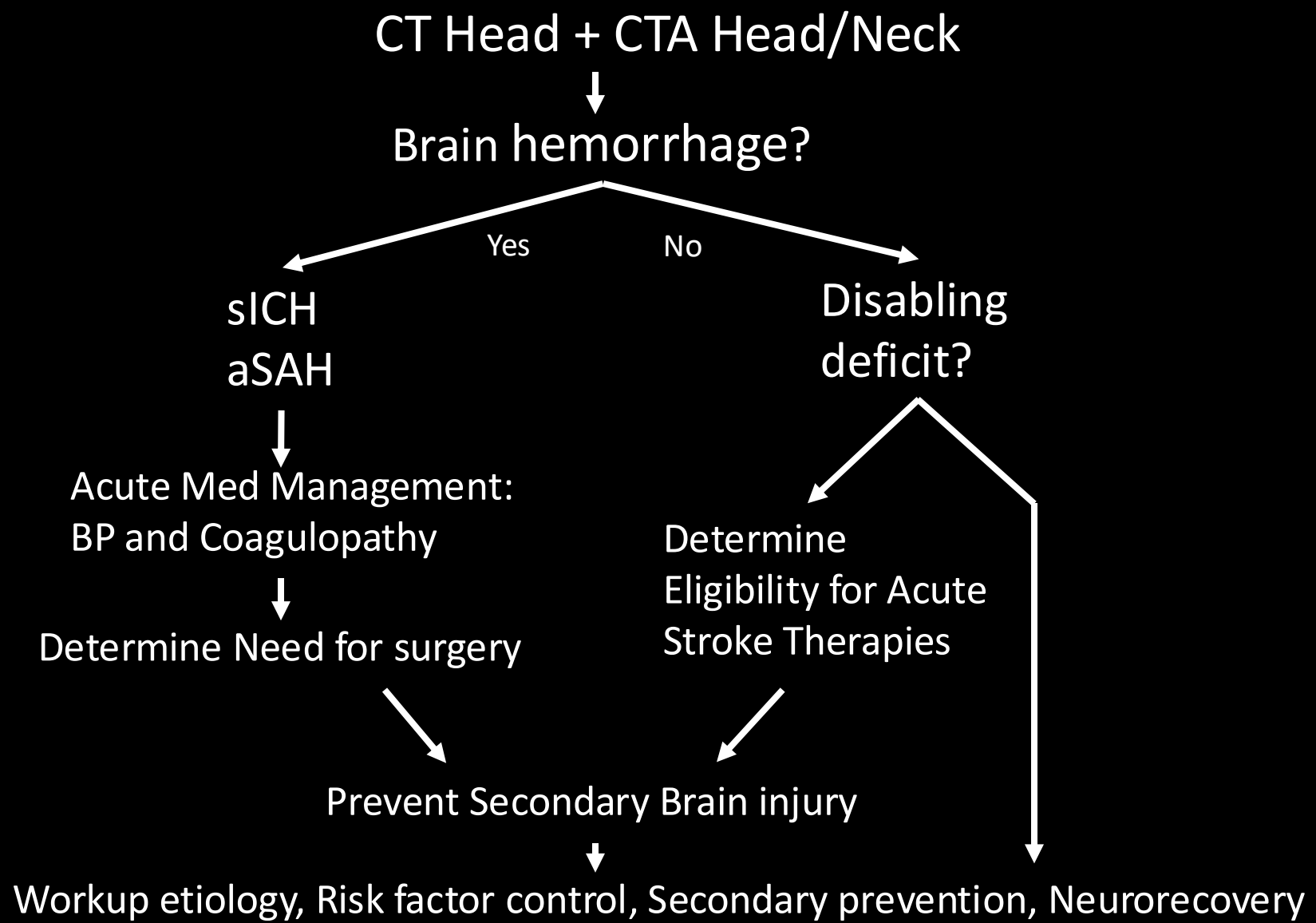
Selected Vascular Syndromes

- L MCA: **Aphasia,** L gaze preference, R side weak
- R MCA: **Neglect,** R gaze preference, L sided weak
- PCA: Binocular Visual field deficits
- Basilar/Vertebral: Decreased arousal, vertigo, ataxia, cranial nerve palsies with opposite side weakness
- Hemorrhagic strokes may not follow clear vascular syndromes.
  - Usually still unilateral deficits often with Headache



radiologyassistant.nl

Algorithm: Acute Neurological Deficit



Ischemic Stroke: Goals of Acute Therapy

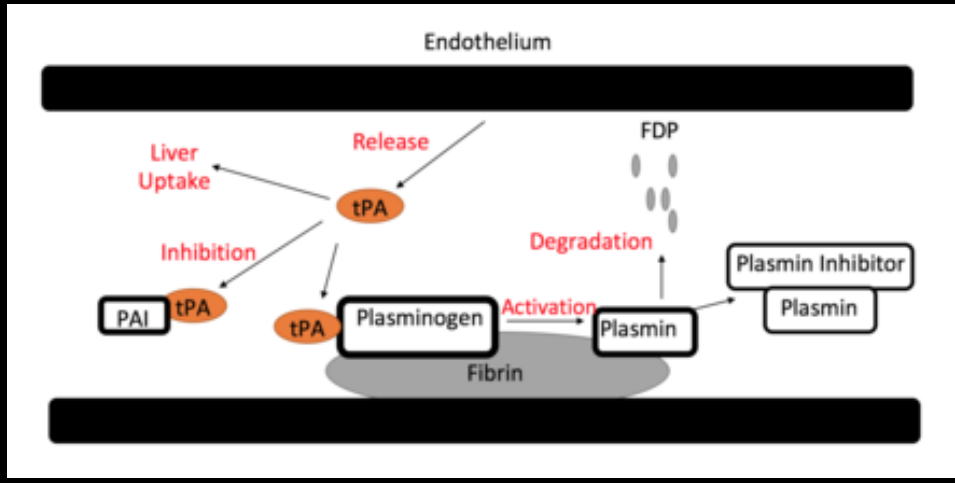
- **<u>Identify patients who are having ISCHEMIA and prevent INFARCTION</u>**

- Rapidly triage and identify patients who are candidates for
  - 1) Systemic IV thrombolysis
  - 2) Mechanical thrombectomy

- After the above:
  - Prevent secondary brain injury (Cerebral edema, mass effect etc)
  - What caused the stroke?
  - Prevent another stroke

Acute Therapies: IV Thrombolysis

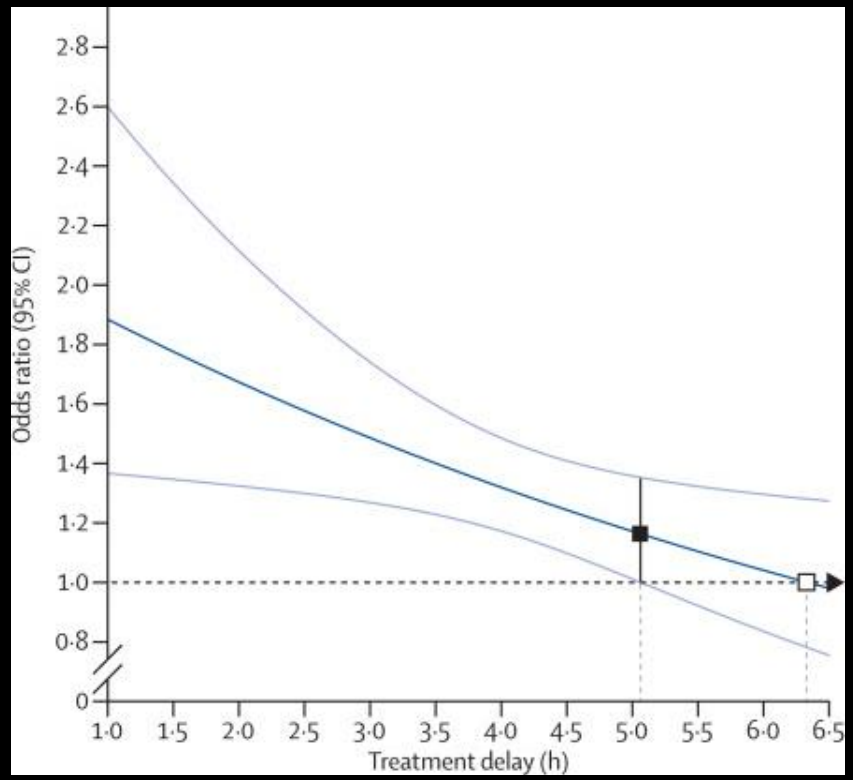
- tPA is FDA approved < 3 hrs from last known well
- Recommendations to give < 4.5 hrs from last known well
- Treat: Disabling deficits, no recent hemorrhage, no large established infarct
  - Need to treat BP <185/110 before administration
- Meta-analysis of eminent tPA trials:
  - At 3 months, for pts treated within 3 hours:
    - Placebo: 31% alive independent,
    - tpA 40% (OR 1.4)
    - Placebo 1.2% symptomatic ICH
    - tPA 8%



Wikipedia

Wardlaw et al. *Lancet* 2012.

Why < 4.5 hours?



Emberson et al. *Lancet*. 2014

Tenecteplase (TNK)

- Genetically modified variant of alteplase
  - increased fibrin specificity
  - longer plasma half-life given as bolus rather than infusion
  - possibly increased efficacy (suggestion of better rates of early neurological improvement, reperfusion rates, 90-day outcomes)
- Logistically simplified administration
  - Single IV bolus over few seconds 0.25mg/kg
- Demonstrated Non-inferiority to IV tPA
- Now standard of care at BWH and MGH

Intravenous tenecteplase compared with alteplase for acute ischaemic stroke in Canada (AcT): a pragmatic, multicentre, open-label, registry-linked, randomised, controlled, non-inferiority trial

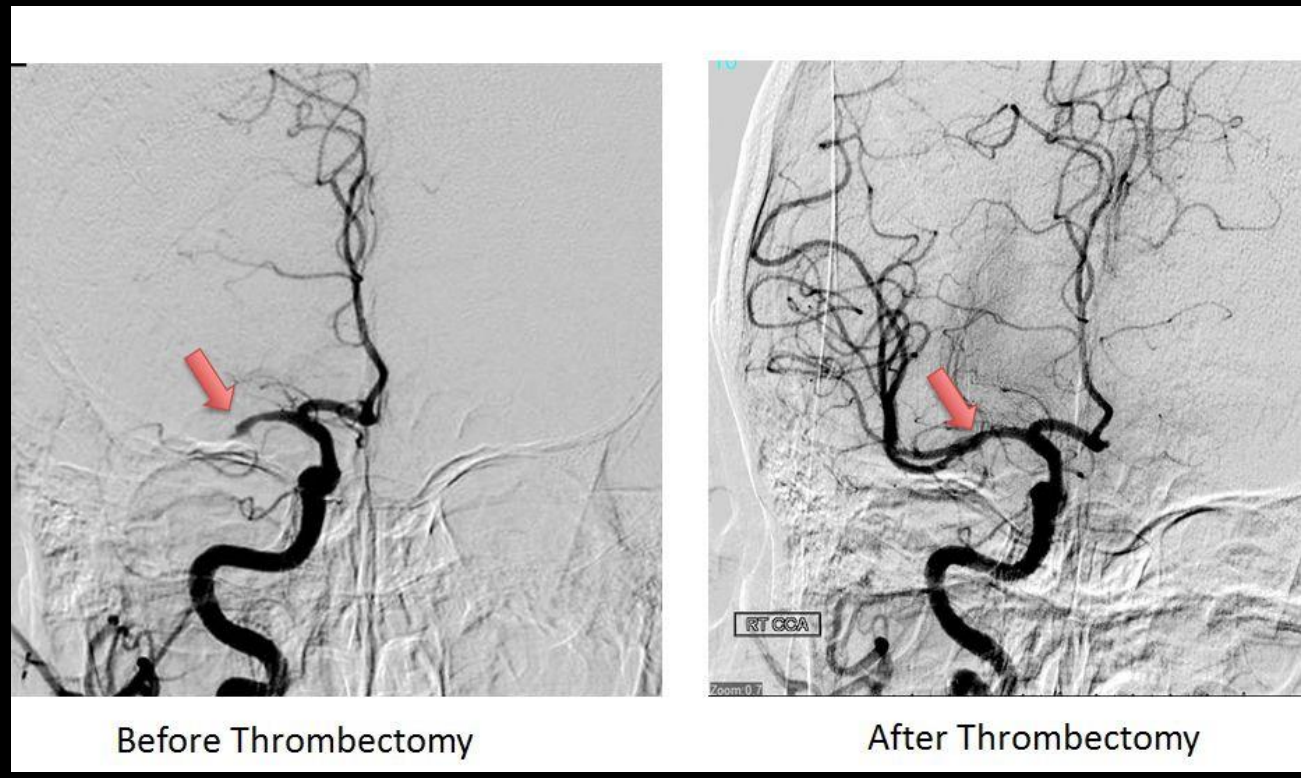
Bijoy K Menon, Brian H Buck, Nishita Singh, Yan Deschaintre, Mohammed A Almekhlafi, Shelagh B Coutts, Sibi Thirunavukkarasu, Houman Khosravani, Ramana Appireddy, Francois Moreau, Gord Gubitz, Aleksander Tkach, Luciana Catanese, Dar Dowlatshahi, George Medvedev, Jennifer Mandzia, Aleksandra Pikula, Jai Shankar, Heather Williams, Thalia S Field, Alejandro Manosalva, Muzaffar Siddiqui, Atif Zafar, Oje Imoukhuede, Gary Hunter, Andrew M Demchuk, Sachin Mishra, Laura C Gioia, Shirin Jalini, Caroline Cayer, Stephen Phillips, Elsadig Elamin, Ashkan Shoamanesh, Suresh Subramaniam, Mahesh Kate, Gregory Jacquin, Marie-Christine Camden, Faysal Benali, Ibrahim Alhabli, Fouzi Bala, MacKenzie Horn, Grant Stotts, Michael D Hill, David J Gladstone, Alexandre Poppe, Arshia Sehgal, Qiao Zhang, Brendan Cord Lethebe, Craig Doram, Ayoola Ademola, Michel Shamy, Carol Kenney, Tolulope T Sajobi, Richard H Swartz, for the AcT Trial Investigators

Menon et al. *Lancet* 2022.

Acute Therapies: The Thrombectomy Revolution

- Treatment for large vessel occlusion (LVO) stroke subtype.

- Advantages vs tPA:
  - Highly effective
  - No bleeding-risk exclusions
  - Select patients can be treated up to 24 hours from LKW.

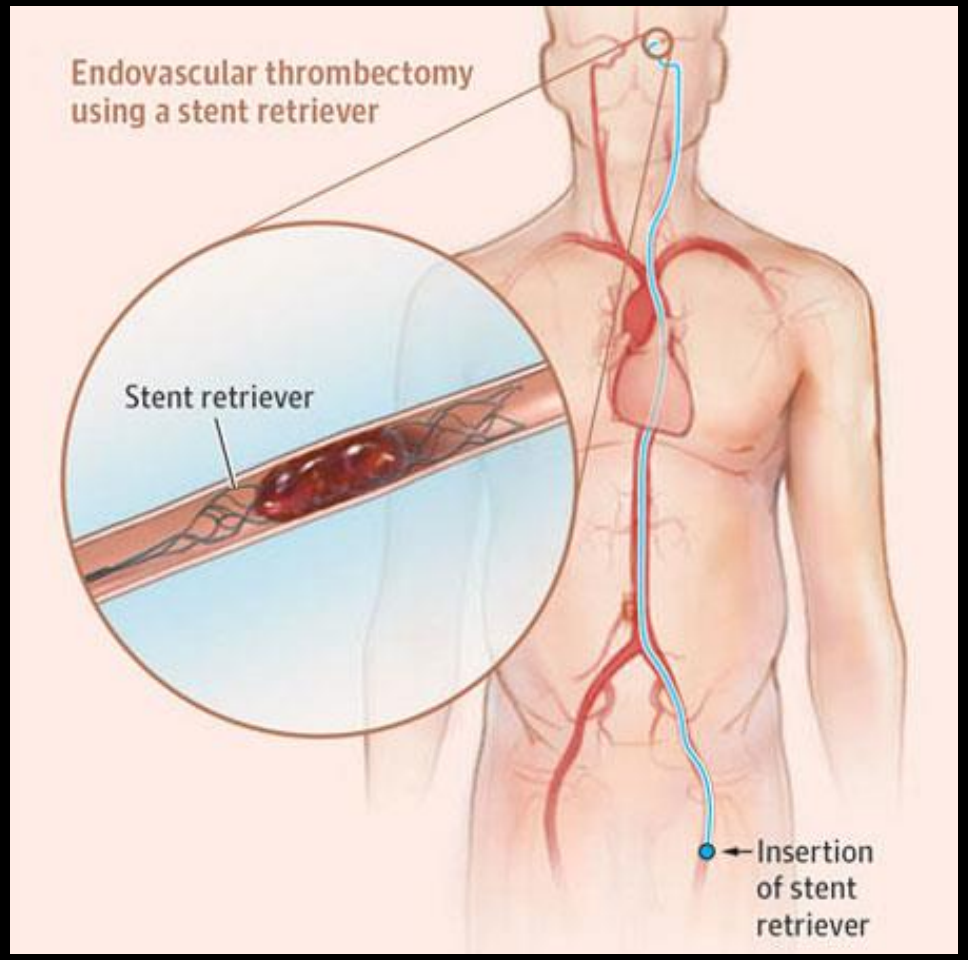


Before Thrombectomy

After Thrombectomy

https://newsroom.ucla.edu/

Mechanical Thrombectomy



https://edhub.ama-assn.org/

Mechanical Thrombectomy

- Outcomes at 3 months for acute (< 6 hours) trials:
  - Standard of care: 27% independent
  - Thrombectomy: 46% independent

  - NNT (reduced disability): 2.6
  - NNT (functional independence): 5

ORIGINAL ARTICLE

Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection

Bruce C.V. Campbell, M.D., Peter J. Mitchell, M.D., Timothy J. Kleinig, M.D., Helen M. Dewey, M.D., Leonid Churilov, Ph.D., Nawaf Yassi, M.D., Bernard Yan, M.D., Richard J. Dowling, M.D., Mark W. Parsons, M.D., Thomas J. Oxley, M.D., Teddy Y. Wu, M.D., Mark Brooks, M.D., et al., for the EXTEND-IA Investigators*

ORIGINAL ARTICLE

A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke

Olvert A. Berkhemer, M.D., Puck S.S. Fransen, M.D., Debbie Beumer, M.D., Lucie A. van den Berg, M.D., Hester F. Lingsma, Ph.D., Albert J. Yoo, M.D., Wouter J. Schonewille, M.D., Jan Albert Vos, M.D., Ph.D., Paul J. Nederkoorn, M.D., Ph.D., Marieke J.H. Wermer, M.D., Ph.D., Marianne A.A. van Walderveen, M.D., Ph.D., Julie Staals, M.D., Ph.D., et al., for the MR CLEAN Investigators*

ORIGINAL ARTICLE

Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke

Mayank Goyal, M.D., Andrew M. Demchuk, M.D., Bijoy K. Menon, M.D., Muneer Eesa, M.D., Jeremy L. Rempel, M.D., John Thornton, M.D., Daniel Roy, M.D., Tudor G. Jovin, M.D., Robert A. Willinsky, M.D., Biggya L. Sapkota, M.B., B.S., Dar Dowlatshahi, M.D., Ph.D., Donald F. Frei, M.D., et al., for the ESCAPE Trial Investigators*

ORIGINAL ARTICLE

Stent-Retriever Thrombectomy after Intravenous t-PA vs. t-PA Alone in Stroke

Jeffrey L. Saver, M.D., Mayank Goyal, M.D., Alain Bonafe, M.D., Hans-Christoph Diener, M.D., Ph.D., Elad I. Levy, M.D., Vitor M. Pereira, M.D., Gregory W. Albers, M.D., Christophe Cognard, M.D., David J. Cohen, M.D., Werner Hacke, M.D., Ph.D., Olav Jansen, M.D., Ph.D., Tudor G. Jovin, M.D., et al., for the SWIFT PRIME Investigators*

ORIGINAL ARTICLE

Thrombectomy within 8 Hours after Symptom Onset in Ischemic Stroke

Tudor G. Jovin, M.D., Angel Chamorro, M.D., Erik Cobo, Ph.D., María A. de Miquel, M.D., Carlos A. Molina, M.D., Alex Rovira, M.D., Luis San Román, M.D., Joaquín Serena, M.D., Sonia Abilleira, M.D., Ph.D., Marc Ribó, M.D., Mònica Millán, M.D., Xabier Urra, M.D., et al., for the REVASCAT Trial Investigators*

ORIGINAL ARTICLE

Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging

Gregory W. Albers, M.D., Michael P. Marks, M.D., Stephanie Kemp, B.S., Soren Christensen, Ph.D., Jenny P. Tsai, M.D., Santiago Ortega-Gutierrez, M.D., Ryan A. McTaggart, M.D., Michel T. Torbey, M.D., May Kim-Tenser, M.D., Thabele Leslie-Mazwi, M.D., Amrou Sarraj, M.D., Scott E. Kasner, M.D., et al., for the DEFUSE 3 Investigators*

ORIGINAL ARTICLE

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

Raul G. Nogueira, M.D., Ashutosh P. Jadhav, M.D., Ph.D., Diogo C. Haussen, M.D., Alain Bonafe, M.D., Ronald F. Budzik, M.D., Parita Bhuva, M.D., Dileep R. Yavagal, M.D., Marc Ribo, M.D., Christophe Cognard, M.D., Ricardo A. Hanel, M.D., Cathy A. Sila, M.D., Ameer E. Hassan, D.O., et al., for the DAWN Trial Investigators*

Algorithm: Acute Neurological Deficit

Is deficit disabling?

Algorithm: Acute Neurological Deficit

Is deficit disabling?

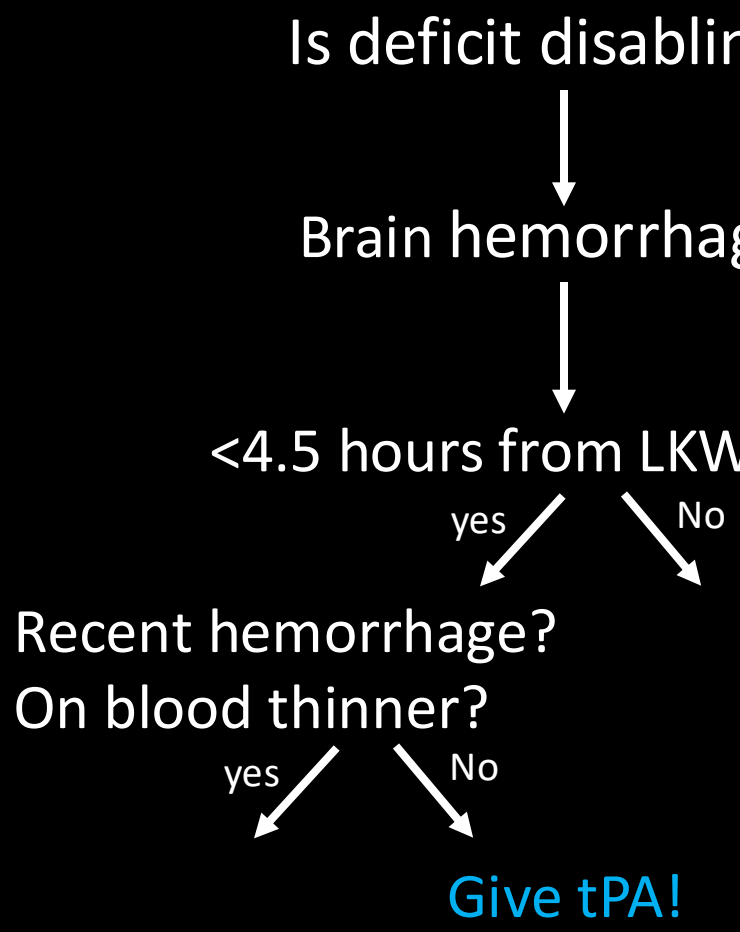
↓

Brain hemorrhage?

Non-contrast CT Brain

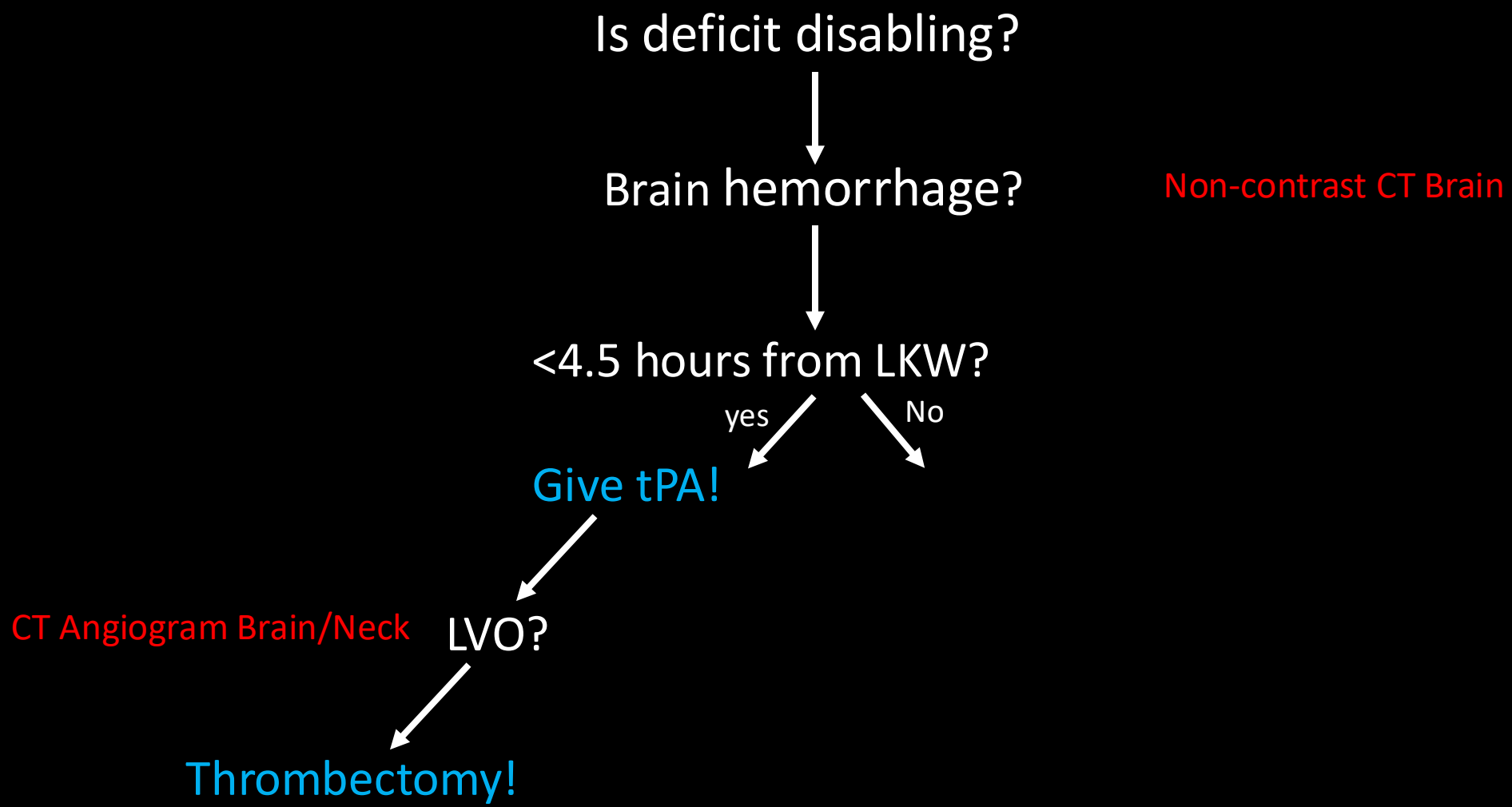
↓

Algorithm: Acute Neurological Deficit

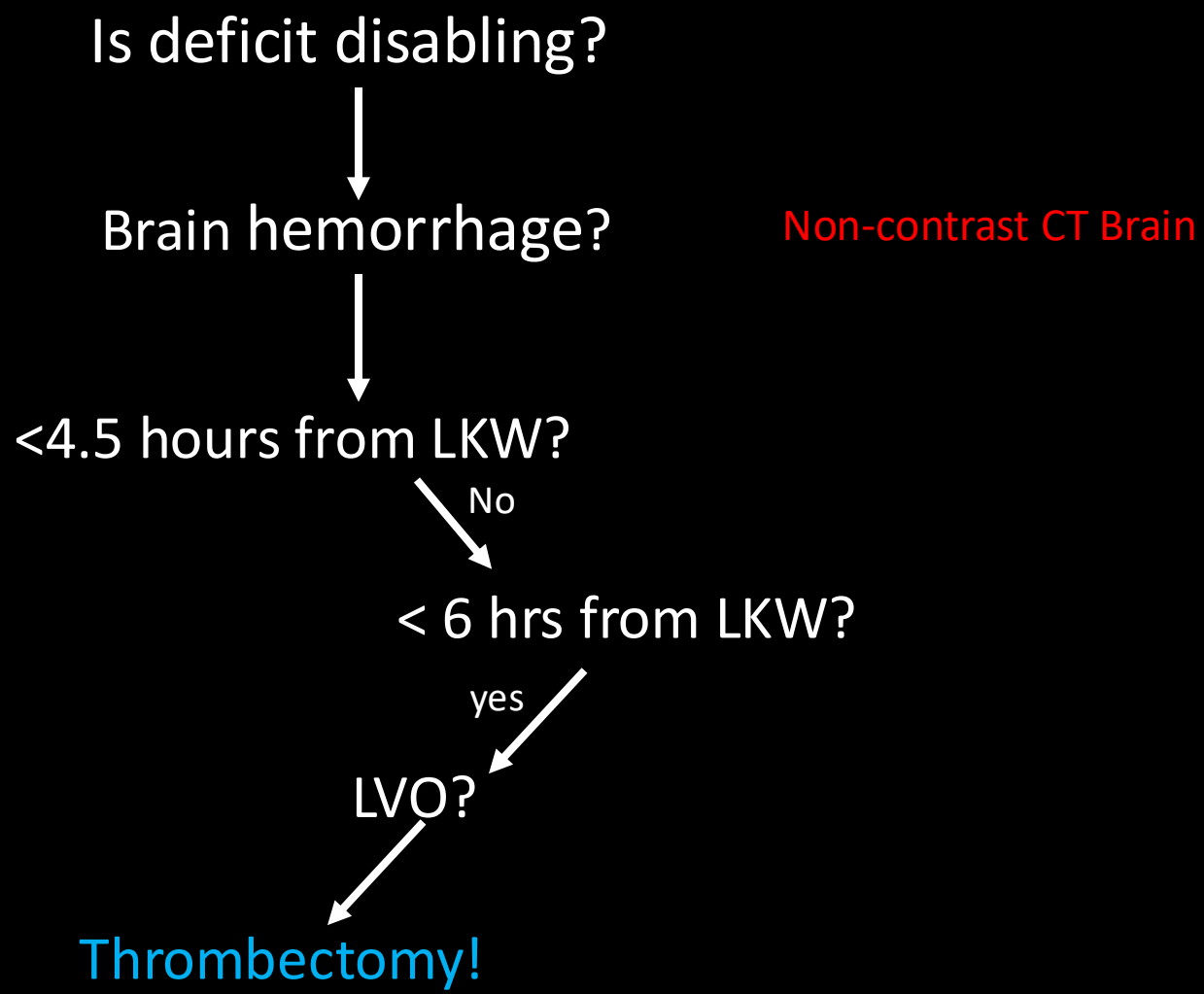


Non-contrast CT Brain

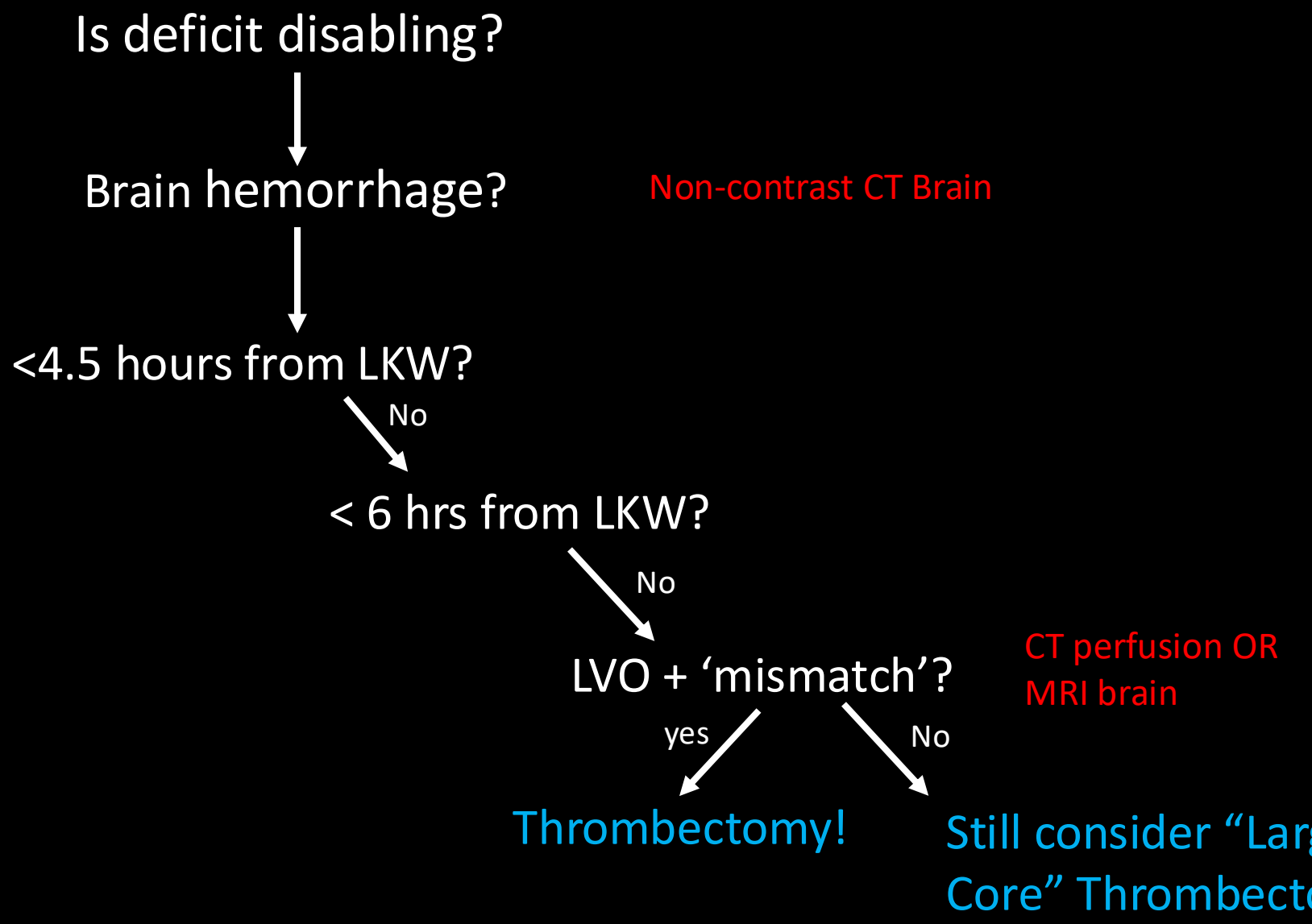
Algorithm: Acute Neurological Deficit



Algorithm: Acute Neurological Deficit



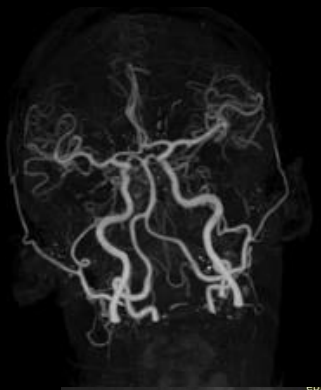
Algorithm: Acute Neurological Deficit



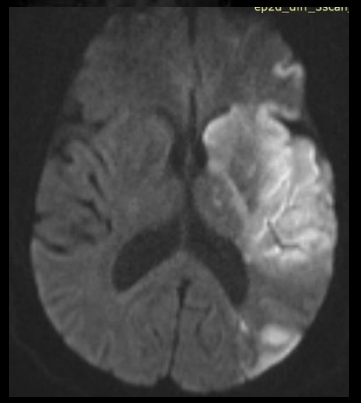
Diagnostic Neuro-Imaging

- **RULE OUT BLEED:** CT Head
  - Very fast
  - Sensitive for ICH
  - Insensitive for acute stroke

- **IDENTIFY LVO:** CT-Angiogram Head/Neck
  - Very fast
  - Sensitive for LVO
  - Nephrotoxic(?) contrast agent

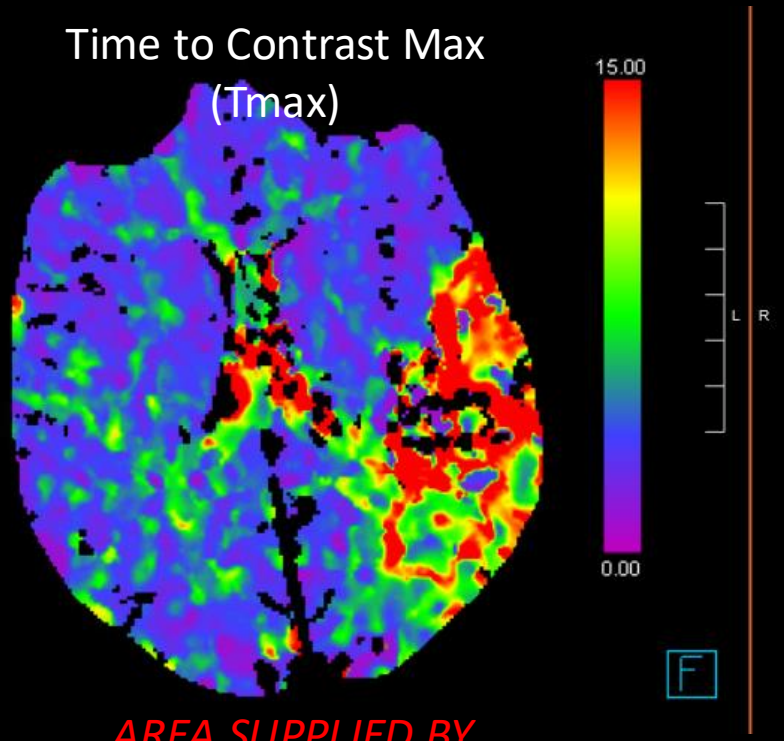


- **DIAGNOSE STROKE:** MRI brain
  - Very slow
  - Very sensitive for acute stroke
  - Patients must be cooperative and have no internal metal



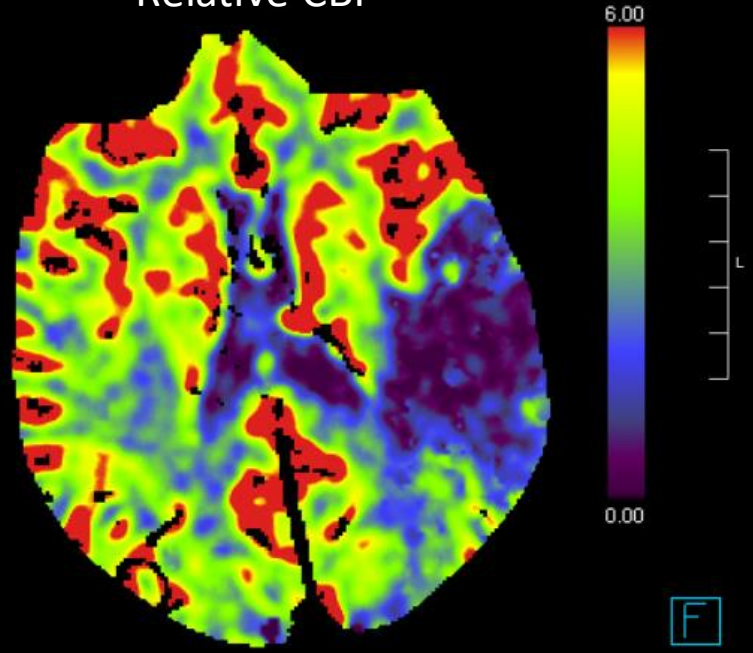
CT Perfusion

Time to Contrast Max (Tmax)



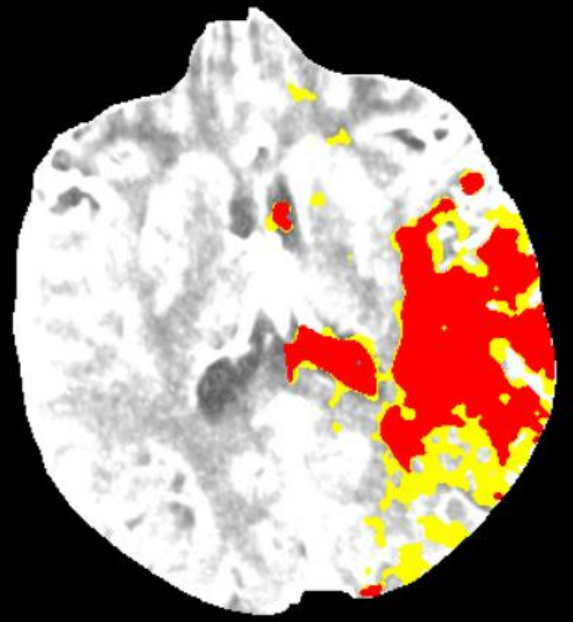
AREA SUPPLIED BY BLOCKED VESSEL

Relative CBF



Estimated INFARCT CORE
If image >6h from onset

PENUMBRA

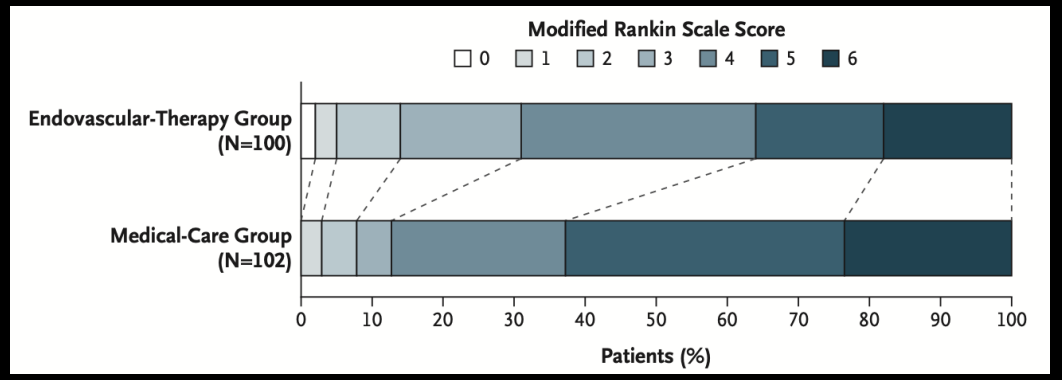


YELLOW = MISMATCH

Parameter cutoffs depend on Perfusion software. Commonly Tmax >6s, rCBF<30% or 20%

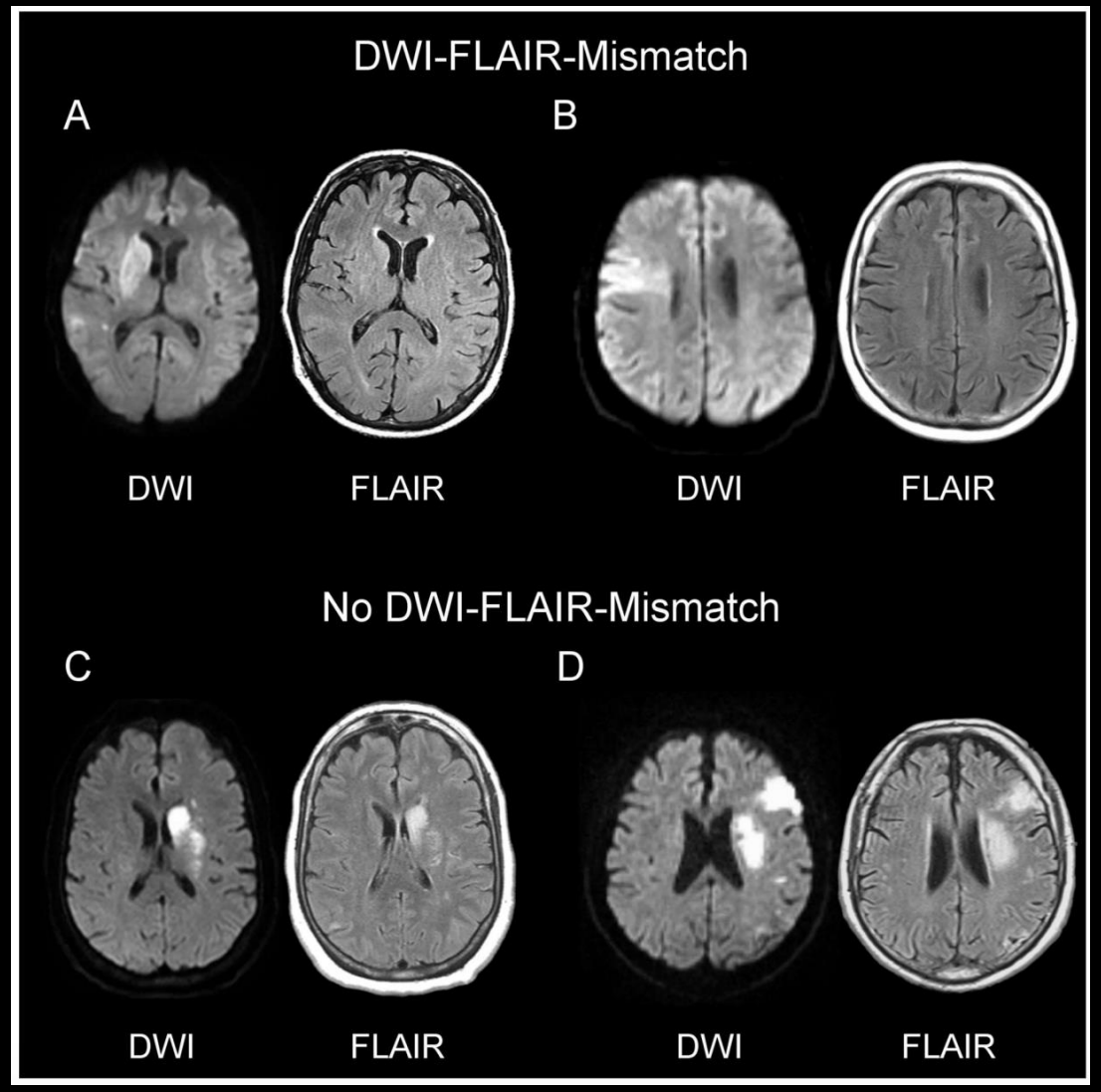
Thrombectomy indications are expanding

- Established Benefit:
  - 6-24 hours from symptom onset or LKW:
    - Mismatch between infarct core and at-risk tissue
    - Mismatch between infarct core and clinical symptoms
- Expanding inclusion:
  - 12 hours from symptom onset and *large* infarction core
    - Likely benefit, with higher NNT
    - Excluded poor baseline status, distal clots
  - Selection of patients without advanced perfusion imaging
    - Core by non-contrast CT alone



Bendszus, et al. Lancet. 2023
Yoshimura et al. N Engl J Med. 2022
Albers GW, et al. N Engl J Med. 2018
Nogueira RG, et al. N Engl J Med. 2018

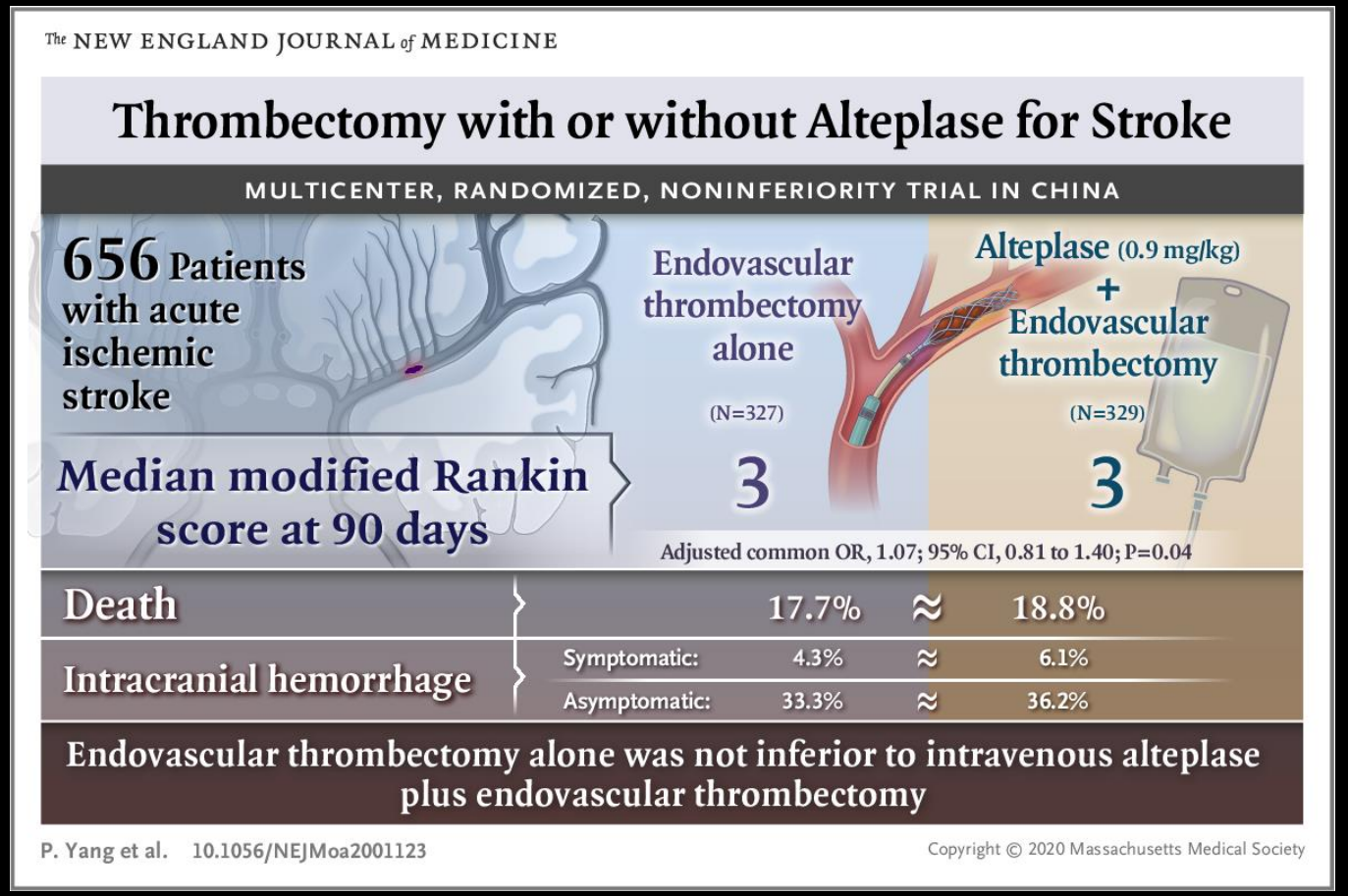
Late-window tPA?



Thomalla G, et al NEJM. 2018

Mechanical thrombectomy with or without thrombolysis?

- **Both** is current standard of care
- However, 2 of 3 recent trials showed non-inferiority of mechanical thrombectomy alone



Yang et al. *NEJM.* 2020.
Suzuki et al. *JAMA.* 2021.
Zi et al. *JAMA.* 2021.

Care after Acute ischemic stroke therapy

- **IV Thrombolysis (tPA or TNK)**
  - BP goal strictly <180/105
  - Frequent Neurologic assessments to monitor for decline due to ICH
  - Avoid unnecessary invasive procedures
  - Repeat CT 24h after dose
- Mechanical Thrombectomy
  - SBP goal generally <180
  - Monitoring arteriotomy access site and extremity distal perfusion
- No acute therapy given
  - Allow BP to autoregulate as high as SBP 220/120 for 24h

September 5, 2023

Intensive vs Conventional Blood Pressure Lowering After Endovascular Thrombectomy in Acute Ischemic Stroke

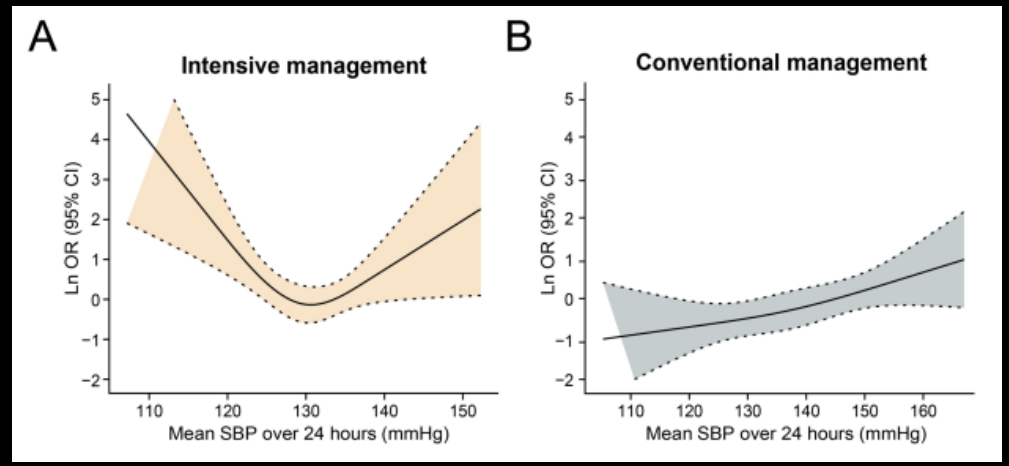
The OPTIMAL-BP Randomized Clinical Trial

Hyo Suk Nam, MD, PhD[1]; Young Dae Kim, MD, PhD[1]; JoonNyung Heo, MD[1]; et al

Author Affiliations | Article Information

JAMA. 2023;330(9):832-842. doi:10.1001/jama.2023.14590

Correlation between BP and Poor outcome



Nam et al. *JAMA* 2023.

Secondary prevention: What caused the stroke?

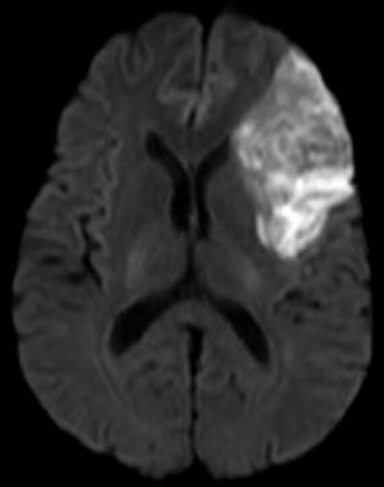
- **Proximal embolic source**
  - Central embolism
    - Atrial fibrillation*
    - Paradoxic embolism via PFO shunt
    - Aortic Arch athero-embolism
  - Large Cervical artery atherosclerosis
    - Carotid artery stenosis*
    - Embolism or flow limitation
  - Large intracranial atherosclerosis

- **Intracranial (small-vessel) atherosclerotic disease**
  - “Lacunar”

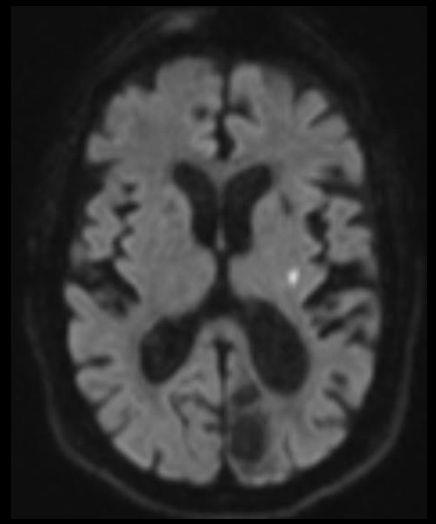
For secondary prevention: How to Figure out what happened?

- Need history and more information
  - (1) Appearance of intra- and extra-cranial vessels
  - (2) Pattern of infarction on CT/MRI

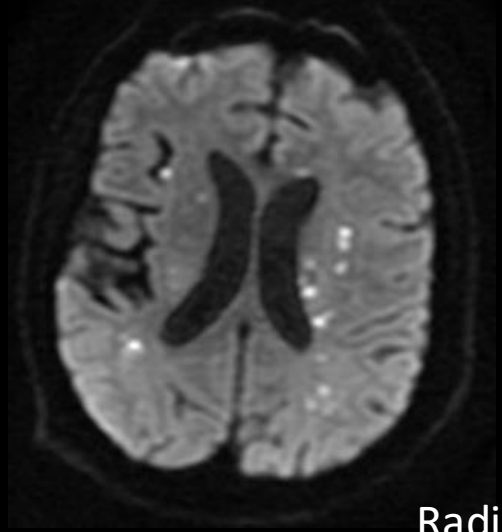
Single “wedge”: proximal embolism or large vessel atherosclerosis



Single small *deep* “lacune”: Likely 2/2 hypertensive small vessel disease

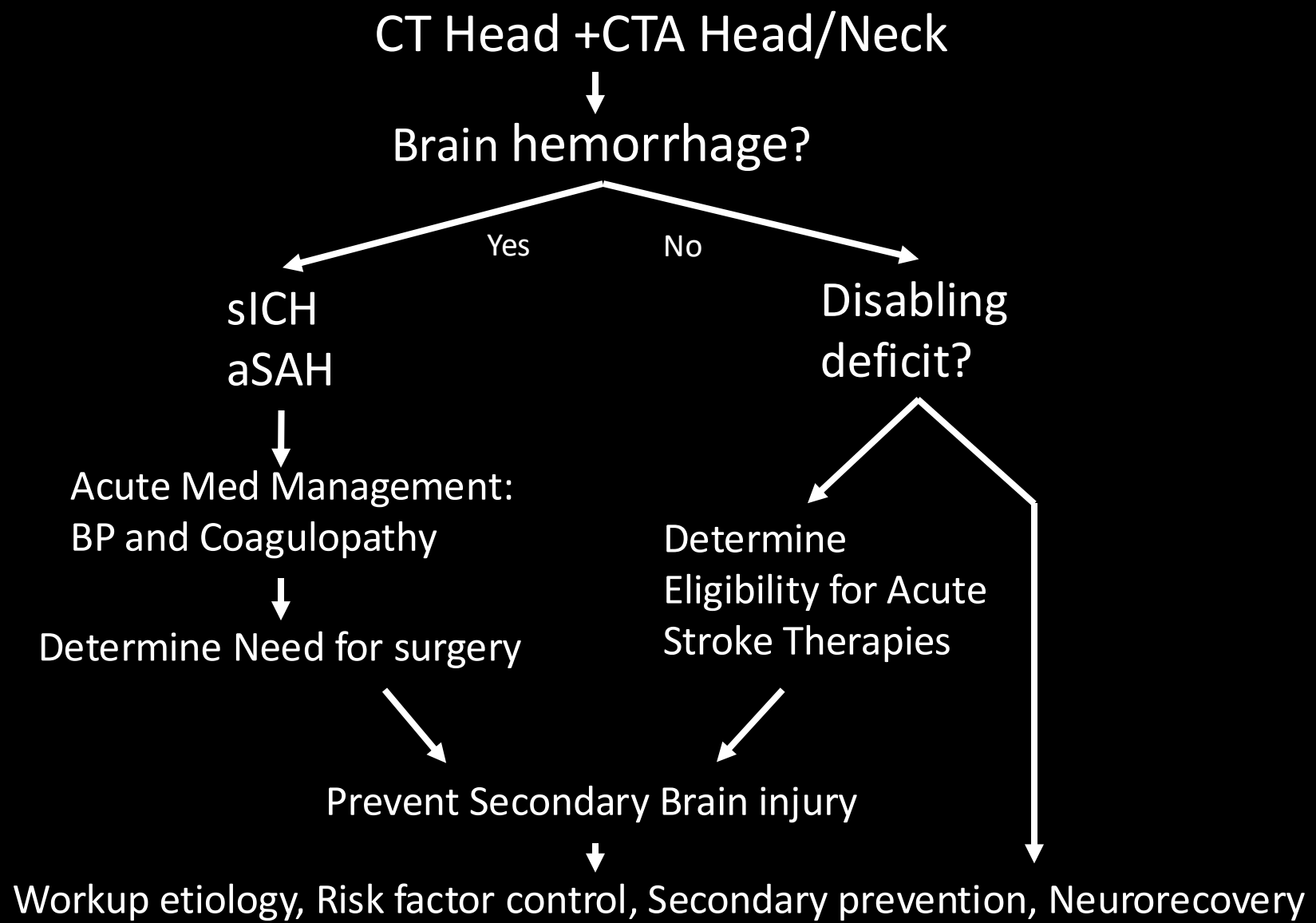


Multiple small:
? Embolic ?
hypotension



Radiopaedia.org

Algorithm: Acute Neurological Deficit



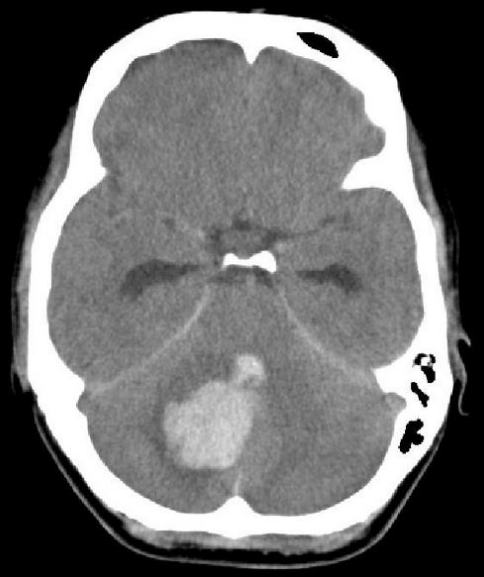
Acute Stroke: Spontaneous ICH

- ICH: Intracerebral Hemorrhage (intraparenchymal)
  - Deep: usually due to HTN
  - Lobar: Anticoagulation, tumor, CAA, endocarditis, HTN
- Acute Management: Goal prevent hematoma expansion
  - Lower SBP to target goal 130-150
    - Aggressive lowering <130 may be harmful (AKI)
    - Gtt for smooth and continuous control is preferred, avoid fluctuation
  - Correct coagulopathy
    - PLT, INR, Fibrinogen
    - Reverse anticoagulation
      - Consider individualized thrombotic risk
      - Antiplatelet reversal with platelet transfusion may be harmful for non-surgical sICH
  - Other
    - Repeat CT 4-6hr to determine hematoma stability
    - CTA if not already done to look for underlying vascular lesion/malformation
    - Anti-seizure medications only if seizure clinically suspected
    - Frequent GCS and Neurologic assessments
    - Treat blood sugars >180, avoid hypoglycemia
    - Treat Fever, target normothermia
    - NPO until swallow screen completed

Radiopaedia.org

Acute Stroke: sICH

- Emergent Surgery:
  - Cerebellar hemorrhage >15cc or associated with neurologic decline, brainstem compression hydrocephalus
  - Life saving craniotomy for evacuation or decompressive craniectomy considered usually in patients presenting with decreased level of consciousness due to hematoma
  - Emerging: improved functional outcomes with Early minimally invasive hemorrhage evacuation in select patients
    - Early <24h, stable on repeat imaging,
    - Lobar sICH without underlying vascular malformation
    - Hematoma Volume 30-80cc
    - GCS 5-14



Radiopaedia.org

Pradilla et al. *NEJM* 2024.

ICH: Subarachnoid Hemorrhage

- Aneurysmal : usually seen in cisterns near brainstem
- Cortical: various causes traumatic, anticoagulation, endocarditis, RCVS
- aSAH Acute Management:
  - Avoid SBP>180, but target is individualized
    - Preserve cerebral perfusion pressure
    - Gtt for smooth and continuous control is preferred, avoid fluctuation
  - Correct coagulopathy
    - Reverse anticoagulation – strongly indicated
  - Other
    - CTA is needed to help identify ruptured aneurysm
    - Anti-seizure medications often prophylactically given
    - Frequent GCS and Neurologic assessments
    - Treat blood sugars >180, avoid hypoglycemia
    - Treat Fever, target normothermia
    - NPO until swallow screen completed
    - Prolonged ICU admission to monitor/mitigate delayed cerebral ischemia/vasospasm

Radiopaedia.org

ICH: aSAH

- Emergent Neurosurgical consultation is required
  - Secure aneurysm via endovascular treatment versus craniotomy
  - CSF diversion (EVD or lumbar drain) for treatment of obstructive or communicating hydrocephalus is often needed
    - Acutely poor neurologic exam (comatose, “blown” pupils) will often improve after CSF diversion, if completed rapidly
- Emerging: Early lumbar drainage for clearance of subarachnoid blood to prevent delayed cerebral ischemia


June 18, 2023

Effectiveness of Lumbar Cerebrospinal Fluid Drain Among Patients With Aneurysmal Subarachnoid Hemorrhage

A Randomized Clinical Trial

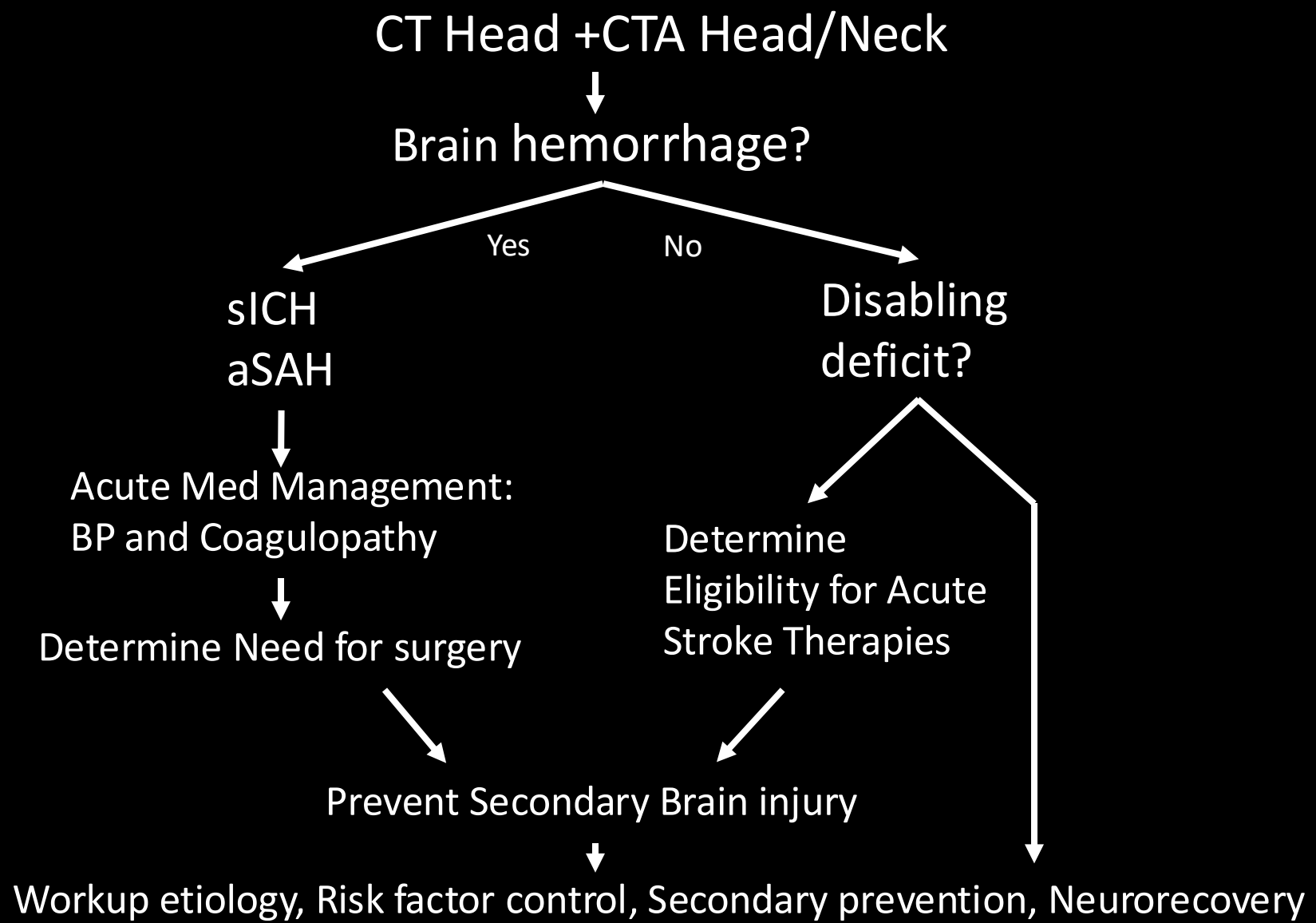
Stefan Wolf, MD[1]; Dorothee Mielke, MD[2]; Christoph Barner, MD[3]; et al

» Author Affiliations | Article Information

JAMA Neurol. 2023;80(8):833-842. doi:10.1001/jamaneurol.2023.1792

Wolf et al. *JAMA Neurol* 2023.

Algorithm: Acute Neurological Deficit



Thank you