





Outline

- Epidemiology
- Workup of stroke in the ED/Floor/ICU
- Imaging (which type is best)
- New time standard in catheter-based treatment
- Duel antiplatelet therapy
- Cardiac Holter monitoring

Key Points:

- Time has very limited function in determining a stroke and cerebral imaging allows for a more accurate diagnosis, identifies the mechanism of the event, and helps with early treatment and prognosis.
- Next best steps: use duel antiplatelet therapies for 21 days after stroke when ABCD2 score is ≥ 4 and NIH ≤ 3, then monotherapy with a single antiplatelet agent. Consider outpatient Holter monitoring to improve the diagnosis of atrial fibrillation that would require anticoagulation.

Case Vignette

- A 54-year-old man presents 2 hours after sudden weakness in his left.
- His symptoms lasted for 30 minutes.
- He has hypertension and hyperlipidemia, for which he takes an angiotensin-receptor blocker and a statin, and he is a smoker with a 30 packyear history.
- On examination, the blood pressure is 156/96 mm Hg.
- How should this patient be further evaluated and treated?

Amarenco P. N Engl J Med 2020;382:1933-1941





*Best cerebral imaging choices for this case:

- A. CT of the brain
- **B.** CT brain/CTA of brain and neck
- C. MRI of the brain
- D. MRI brain/MRA of brain and neck

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*Which is the best assessment scale to perform?

- A. Glasgow Coma Score
- **B. NIH Stroke Scale Score**
- C. ABCD2 score
- D. The FAST Exam (Face, Arm, Speech, Time)

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Conclusions and Recommendations

- If ipsilateral right carotid stenosis were detected on imaging of the extracranial and intracranial vasculature, I would recommend prompt carotid endarterectomy.
- I would also perform a cardiac evaluation including 3-week ECG monitoring to detect paroxysmal atrial fibrillation that would warrant long-term oral anticoagulation instead of antiplatelet therapy, particularly in the absence of severe carotid stenosis or another potential direct cause of TIA.
- I would review with the patient his increased risk of stroke and provide guidance regarding control of risk factors, including smoking cessation and lifestyle changes.

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New Definition of TIA

TIA is a brief episode of neurologic dysfunction caused by focal brain or retinal ischemia, with clinical symptoms typically lasting <u>less than one hour</u>, and <u>without evidence of acute</u> infarction

> N Engl J Med, Vol. 337, Nov 21, 2002, 1713-1717. Stroke, Vol 37, 2006, 577-617. *Stroke*. 2009;40:2276.



Working up stroke

- Neuroimaging evaluation within 24 hours of symptom onset.
 - MRI, including DWI, is the preferred brain diagnostic imaging modality.
- Noninvasive imaging of the cervicocephalic vessels should be performed routinely as part of the evaluation
- Noninvasive testing of the intracranial vasculature reliably excludes the presence of intracranial stenosis
- Patients with suspected TIA should be evaluated as soon as possible after an event
- ECG/ECHO/Holter

Stroke. 2009;40:2276



Lacunar

Helgason CM et al. Circulation. 1997;96:701-707.

CT vs MRI in acute stroke

- CT is widely available and fast
- Noncontrast CT, CT angiography and CT perfusion can be performed in under 15 minutes
- Superior to MRA in evaluating the vessels
 Less artifact and better quantification of lesions
- MRI stroke protocol takes longer
- -Conventional MRI, DWI, MRA and PWI
- -No radiation
- Can be performed without contrast
 Arterial spin labelling, time-of-flight
- The two modalities are equally useful for evaluating acute stroke
- -Equivalent depiction of the penumbra

Imaging approach to acute stroke

- Four P's
- Parenchyma
 - Assess early signs of acute stroke
 - Rule out haemorrhage
- Pipes
 - Assess extracranial circulation (carotid & vertebral) and
 - intracranial circulation for evidence of intravascular thrombus
- Perfusion
 - Assess Cerebral blood volume (CBV), Cerebral blood flow (CBF) and Mean transit time (MTT)
- Penumbra
 - Assess tissue at risk of dying if ischemia continues without recanalization of intravascular thrombus

Evaluation of Tissue Status: Noncontrast Head CT

<u>Advantages</u>

- Almost universally available
- Rapid
- High sensitivity for detection of hemorrhage (100% ICH, 90% SAH)

Disadvantages

•Often normal in hyperacute phase

 Insensitive to lacunar and posterior fossa strokes

Evaluation of Tissue Status: Multimodal MRI (including DWI)

Advantages

- More sensitive to acute ischemia
- More sensitive to posterior fossa lesions
- More sensitive to small vessel, lacunar lesions

- Disadvantages
- Not universally available
- -Longer scanning time
- Patient contraindications (e.g. pacemaker)



Evaluation of Vessel Status

- 1. CT Angiography
- 2. MR Angiography
- 3. Ultrasound Techniques
- 4. Catheter Angiography

Role of neck vessel imaging

- Why do we get neck imaging?
- -We don't want to miss a carotid stenosis
- Which patients should be referred vascular surgery for consideration for CEA or stenting?
- Patients with <u>></u> 70% stenosis
- When should this referral/evaluation happen?
- -CEA/stenting should occur within 2 weeks of stroke/TIA
- Should this ever happen in the index hospitalization? When?
- -Yes, at the time of diagnosis

CT Angiography

 Requires injection of intravenous contrast agent

•New generation helical scanners allow rapid evaluation of aortic arch, neck, and intracranial vessels with 1 injection

•80-100% accuracy compared with catheter angiography

•Disadvantages: iodinated contrast agent, radiation exposure

CTA: Carotid Stenosis



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MR Angiography

Noninvasive means to evaluate neck and intracranial vessels

•Time of flight technique may overestimate stenoses

•Not reliable in identifying distal or branch intracranial occlusions

•Sensitivity and specificity 70-100% compared to catheter angiography

 Power-injector, contrast-enhanced techniques – increased sensitivity

Subject to limitations of standard MRI

MR Angiography



Neck MRA: Right Carotid Stenosis



Intracranial MRA: Left ICA Occlusion

Evidence-based guideline: The role of diffusion and perfusion MRI for the diagnosis of acute ischemic stroke

- DWI should be considered superior to noncontrast CT scan for the diagnosis of acute ischemic stroke in patients presenting within 12 hours of symptom onset (Level A).
- There is insufficient evidence to support or refute the value of PWI in diagnosing acute ischemic stroke (Level U).
- Baseline DWI volume should be considered useful in predicting baseline clinical stroke severity and final lesion volume in anterior-circulation stroke syndromes (Level B).

NEUROLOGY 2010;75:177-185



Which scan to order?

- In ED/Floor/ICU and symptomatic CT/CTA
- In ICU and asymptomatic MRI/MRA
- When there is a consideration of thrombolysis
 IV/IA Either

CT is minimum

• IV TPA < 4.5 hours

Acute Ischemic Stroke: ASA/AAN/ACCP Guidelines

Pharmacotherapies

- tPA (tissue plasminogen activator) within 4.5 hours of stroke onset
- Aspirin for acute stroke (within 48 hours of symptom onset) (Grade 1A) to reduce stroke mortality and decrease morbidity; ONLY if no contraindications or if patient will not be given rtPA¹
- Heparin and low molecular weight heparin (LMWH): not indicated and may increase bleeding complications
- LMWH and heparinoids may be considered for DVT prophylaxis in at-risk patients¹
- Early consultation by neurologist or stroke team critical²

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1. Coull BM et al. Stroke. 2002;33:1934-1942.
2. Adams HP et al. Stroke. 2003;34:1056-1083.
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Eligibility for IV treatment with rt-PA

- Age 18 or older
- Clinical diagnosis of ischemic stroke causing a measurable neurological deficit
- Time of symptom onset well established to be less than 180 minutes before treatment would begin

Exclusion Criteria

Stroke or head trauma in 3 mos
Major surgery within 14 days
Any history of intracranial hemorrhage
SBP > 185 mm Hg
DBP > 110 mm Hg
Rapidly improving or minor symptoms
Symptoms suggestive of subarachnoid hemorrhage
Glucose < 50 or > 400 mg/dl
Gl hemorrhage within 21 days
Urinary tract hemorrhage within 21 days

Exclusion Criteria

Arterial puncture at non-compressible site past 7 days
Seizures at the onset of stroke
Patients taking oral anticoagulants
Heparin within 48 hours AND an elevated PTT
PT >15 / INR >1.4
Platelet count <100 X 10/L

35-40% of Ischemic Strokes are Considered "Large Vessel"

- This subset of ischemic stroke comprises blockages in the:
 - Internal Carotid Artery (ICA)
 - Middle Cerebral Artery (MCA)
 - Vertebral / Basilar Artery
- Patient prognosis with these types of stroke is poor

9% ¹
7% ²
9-90% ³
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CORRESPONDENCE

COVID-19 CASES

To rapidly communicate information on the global clinical effort against Covid-19, the Journal has initiated a series of case reports that offer important teaching points or novel findings. The case reports should be viewed as observations rather than as recommendations for evaluation or treatment. In the interest of timeliness, these reports are evaluated by in-house editors, with peer review reserved for key points as needed.

Large-Vessel Stroke as a Presenting Feature of Covid-19 in the Young

sented to our health system in New York City. years of age presented with new-onset symptoms Severe acute respiratory syndrome coronavirus 2 of large-vessel ischemic stroke. All five patients (SARS-CoV-2) infection was diagnosed in all five tested positive for Covid-19. By comparison, every

We report five cases of large-vessel stroke in 2020, a total of five patients (including the afore-patients younger than 50 years of age who pre-mentioned patient) who were younger than 50 2 weeks over the previous 12 months, our ser

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., Monica Millan, M.D., Elad I. Levy, M.D., Peter Mitchell, M.D., Michael Chen, M.D., Joey D. English, M.D., Qaisar A. Shah, M.D., Frank L. Silver, M.D., Vitor M. Pereira, M.D., Brijesh P. Mehta, M.D., Blaise W. Baxter, M.D., Michael G. Abraham, M.D., Pedro Cardona, M.D., Erol Veznedaroglu, M.D., Frank R. Hellinger, M.D., Lei Feng, M.D., Jawad F. Kirmani, M.D., Demetrius K. Lopes, M.D., Brian T. Jankowitz, M.D., Michael R. Frankel, M.D., Vincent Costalat, M.D., Nirav A. Vora, M.D., Albert J. Yoo, M.D., Ph.D., Amer M. Malik, M.D., Anthony J. Furlan, M.D., Marta Rubiera, M.D., Amin Aghaebrahim, M.D., Jean-Marc Olivot, M.D., Wondwossen G. Tekle, M.D., Ryan Shields, M.Sc., Todd Graves, Ph.D., Roger J. Lewis, M.D., Ph.D., Wade S. Smith, M.D., Ph.D., David S. Liebeskind, M.D., Jeffrey L. Saver, M.D., Tudor G. Jovin, M.D., for the DAWN Trial Investigators

> N Engl J Med Volume 378(1):11-21 January 4, 2018



Thrombectomy: bottom lines

- Consider transferring for thrombectomy or observation if there is a persistent disabling neurologic deficit associated with a vascular cut-off
- How can I figure out which patients might benefit?
- -CT angiography or MR angiography
- What is the time window of potential benefit of thrombectomy for appropriate patients?
- -Proven benefit within 24 hours

Telestroke

- AAN and ASA are supporters of bipartisan legislation which was recently introduced in Congress, the Furthering Access to Stroke Telemedicine (FAST) Act (H.R. 2799).
- This bipartisan bill expands access to stroke telemedicine (also called "telestroke") treatment in Medicare. Similar legislation (S.1465) has been introduced in the Senate.



ASA Treatment Guidelines: Ischemic Stroke Not Eligible for Thrombolytic Therapy

BP Level (mm Hg)	Treatment
SBP <220 OR DBP <120	No treatment unless end-organ involvement
SBP > 220 OR DBP < 121-140	Nicardipine or labetalol to 10% -15% ↓ in BP
DBP > 140	Nitroprusside to 10% -15% ↓ in BP

ASA = American Stroke Association; IS = ischemic stroke; SBP = systolic blood pressure; DBP = diastolic blood pressure. Adams HP, et al. *Stroke*. 2007;38:1655-1711.

ASA Treatment Guidelines: Ischemic Stroke Eligible for Thrombolytic Therapy

BP Level (mm Hg)	Treatment
Pretreatment SBP >185 or DBP >110	Labetalol (may repeat once), nitropaste, or nicardipine If BP not reduced and maintained, do not administer rt-PA
During and after rt-PA	
SBP 180-230 OR DBP 105-120	Labetalol
SBP > 230 OR	Nicardipine or labetalol If BP not controlled, consider nitroprusside

Blood Pressure and Stroke What to Conclude

- All studies support detection and aggressive treatment of blood pressure for both primary and secondary prevention
- Reduction of stroke by 35%-40% possible¹
- Thiazide-type diuretic recommended as first therapeutic agent¹
- ACEI and ARBs are more effective in reducing progression of renal disease and are recommended as first-choice medications for patients with diabetes

 Chobanian AV et al, and the National High Blood Pressure Education Program Coordinating Committee. JAMA. 2003;289:2560-2572.
 Stroke, Vol 37, 2006, 577-617.
 Schrader J. Stroke. 2003;34:1199-1703.



In patients with a history of <u>noncardioembolic</u> ischemic stroke or TIA, we recommend long-term treatment with:

- Aspirin (75-100 mg once daily)
- Clopidogrel (75 mg once daily)
- Aspirin/extended-release dipyridamole (25 mg/200 mg bid)
- Cilostazol (100 mg bid)

<u>Over</u>

- No antiplatelet therapy (Grade 1A)
- Oral anticoagulants (Grade 1B)
- Combination of clopidogrel plus aspirin (Grade 1B)
- Triflusal (Grade 2B)

CHEST. 2012;141(2_suppl):1S-1S. doi: 10.1378/chest.1412S1

BMJ 2018;364k1508

-Meta analysis and systemic review involving 10K patients, dual antiplatelet therapy with clopidogrel and aspirin given within 24 hours after high risk TIA or minor stroke reduces subsequent stroke (20 in 1000). Benefit after 21 days is unlikely.

ACC/AHA Guidelines for the Treatment of Blood Cholesterol in Primary Prevention

- Recommendations based on the 10 year risk for cardiovascular disease
- Shifts away from specific cholesterol goals
- Estimated risk dictates intensity of statin Rx: high risk mandates high intensity statin Rx
- Atorvastatin 10 mg is moderate intensity statin Rx and 40 to 80 mg is high intensity
- 10-year risk calculator







Benefits of Certification

- Builds the structure required for a systematic approach to clinical care
- Reduces variability and improves the quality of patient care
- Pushes you to look at yourself more closely
- Creates a loyal, cohesive clinical team
- Provides an objective assessment of clinical excellence
- Differentiates clinical care in the marketplace
- Promotes achievement to referral sources

Work-up of TIA and Ischemic Stroke

All Patients

- Brain Imaging
- Neurovascular
- imaging
- Blood glucose
- Serum electrolytes
- CBC w/ Platelets
- •PT/PTT/INR
- •12 lead EKG/ROMI
- Holter monitoring
- •TTE/TEE
- Supplemental O₂
- Fever reduction

Lipids

Selected Patients

- -Hepatic functions
- -Toxicology
- -Blood alcohol level
- -Pregnancy
- -Hypercoagulable w/u
- -EEG
- -LP

Original Article Atrial Fibrillation in Patients with Cryptogenic Stroke David J. Gladstone, M.D., Ph.D., Melanie Spring, M.D., Paul Dorian, M.D., Val Panzov, M.D., Kevin E. Thorpe, M.Math., Judith Hall, M.Sc., Haris Vaid, B.Sc., Martin O'Donnell, M.B., Ph.D., Andreas Laupacis, M.D., Robert Côté, M.D., Mukul Sharma, M.D., John A. Blakely, M.D., Ashfaq Shuaib, M.D., Vladimir Hachinski, M.D., D.Sc., Shelagh B. Coutts, M.B., Ch.B., M.D., Demetrios J. Sahlas, M.D., Phil Teal, M.D., Samuel Yip, M.D., J. David Spence, M.D., Brian Buck, M.D., Steve Verreault, M.D., Leanne K. Casaubon, M.D., Andrew Penn, M.D., Daniel Selchen, M.D., Albert Jin, M.D., David Howse, M.D., Manu Mehdiratta, M.D., Karl Boyle, M.B., B.Ch., Richard Aviv, M.B., Ch.B., Moira K. Kapral, M.D., Muhammad Mandani, Pharm.D., M.P.H., for the EMBRACE Investigators and Coordinators

N Engl J Med Volume 370(26):2467-2477 June 26, 2014



Study Overview

 In this study, patients with cryptogenic stroke who were randomly assigned to undergo intensive ECG monitoring for 30 days had a higher incidence of detected atrial fibrillation (16%) than those assigned to receive standard 24-hour monitoring (3%).

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Conclusions

- Among patients with a recent cryptogenic stroke or TIA who were 55 years of age or older, paroxysmal atrial fibrillation was common.
- Noninvasive ambulatory ECG monitoring for a target of 30 days significantly improved the detection of atrial fibrillation by a factor of more than five and nearly doubled the rate of anticoagulant treatment, as compared with the standard practice of short-duration ECG monitoring.

Key Points:

- Time has very limited function in determining a stroke and cerebral imaging allows for a more accurate diagnosis, determine mechanism of the event and helps with early treatment and prognosis.
- Next best steps: Utilize duel antiplatelet therapies for 21 days after stroke when ABCD2 score is \geq 4 and NIH \leq 3 then monotherapy with antiplatelets and consider longer Holter monitoring as outpatients to improve the diagnosis of A Fib that would require anticoagulation.

Summary

- Workup of stroke in the ED/Floor/ICU
- Imaging (which type is best)
- New time standard in catheter-based treatment
- Duel antiplatelet therapy
- Cardiac Holter monitoring



- Mr. Jones has 3 hours of sudden onset dysarthria and arm/hand weakness and then symptoms completely resolve.
- Is this a:
- A. Stroke
- B. TIA
- C. RIND
- **D.** Complicated migraine

- Then answer is A.
- The definition of TIA is < 1 hour and negative imaging
- Reversible ischemic neurologic deficit is no longer a valid term
- Migraine symptoms are not sudden

What is the most practical cerebral imaging study within 3 hours of stroke signs and symptoms?

- A. CT of brain
- B. CT of brain/CT angiogram of head and neck
- C. MRI of brain
- D. MRI of brain/MRA of head and neck

- The answer is B.
- CT/CTA scans seem to to be the most practical cerebral imaging study in the EDs, ICUs, and for other inpatients.

- Mr. Jones 83 years old right-handed male has a NIHSS of 12, had a witnessed onset of his stroke and is within 2 hours with a negative CT
- A. Too old to consider to give TPA
- **B.** Give ASA only
- C. If there are no protocol exclusions, give TPA
- **D.** Give Clopidogrel only

- The answer is C.
- In giving IV TPA within 3 hours, there is no age cutoff.
- ASA or Clopedigril should be given ASAP only if the patient <u>is not</u> a TPA candidate

Which is the most appropriate antiplatelet therapy for noncardioembolic stroke?

- A. Aspirin
- **B.** Clopidogrel
- C. ASA/dyp combination
- D. ASA/Clopidogrel
- E. Any listed above

- The answer is E.
- Ischemic stroke is a very heterogeneous disease and the treatment regimen depends on the etiology of the patient's ischemic event.

How do I workup the patient with the diagnosis of TIA?

- A. Cardiac Echo
- **B.** EKG/Holter
- **C.** Brain imaging (CT or MRI)
- **D.** Vascular imaging (CTA or MRA)
- E. All of the above

- The answer is E.
- Echo to r/o PFO and to evaluate ejection fraction.
- EKG and Holter to r/o Afib.
- We always need brain imaging and neurovascular imaging

Reference:

- 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
 - Stroke. 2018;49:e46–e99. DOI: 10.1161/STR.000000000000158.)