Everything the Intensivist Needs to Know About Stroke

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I have no conflicts of interest

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
- Intracranial HTN Treatment

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.

Stroke in the US

- 795 000 people experience a new or recurrent stroke.
  - Approximately 610 000 of these are first attacks, and 185 000 are recurrent attacks.
- 137 000 stroke deaths annually in the United States.
- Leading cause of serious, long-term disability
- Third leading cause of death in the U.S.; second leading cause worldwide
- Second-leading cause of hospital admission among older adults

Stroke. 2011;42:849-877

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 pack-year 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

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Table 1. Common Symptoms Suggestive of TIA.*

Definite TIA
Focal cerebral or retinal symptoms lasting for seconds or minutes and typically lasting <1 hr
Motor weakness in two limbs or in one limb and the face
Sensory deficit in two limbs or in one limb and the face
Visual-field defect (homonymous hemianopia) or monocular blindness
Aphasia or dysarthria
Possible TIA†
Unsteady gait
Diplopia
Vertigo, dizziness
Dysphagia
Usually not a TIA‡
Amnesia
Confusion
Incoordination of limbs
Partial sensory deficit (abnormal sensation or deficit in one limb or only in the face)
Unusual cortical visual symptoms (lone bilateral blindness and bilateral positive visual phenomena)§
Transient loss of consciousness
Headache
Phosphenes, photopsias, complex visual hallucinations, and palinopsia

* TIA denotes transient ischemic attack.
† When combined, at least two of these symptoms suggest definite TIA; when isolated, they suggest possible TIA.
‡ "Bizarre spells" or isolated atypical symptoms are nonfocal or not clearly focal transient neurologic events for which the type of onset, topography, and course of symptoms do not fulfill the criteria for definite or possible TIA or another definite or possible neurologic syndrome (e.g., epilepsy or migraine).
§ Brief positive visual phenomena affecting one or both eyes or one hemifield are often described as flashes of light, stars, colored spots, or swirls of light. Transient positive visual phenomena involving both eyes include a variety of symptoms such as distortion, tilt of images, trails of images, and formed or unformed visual hallucinations.

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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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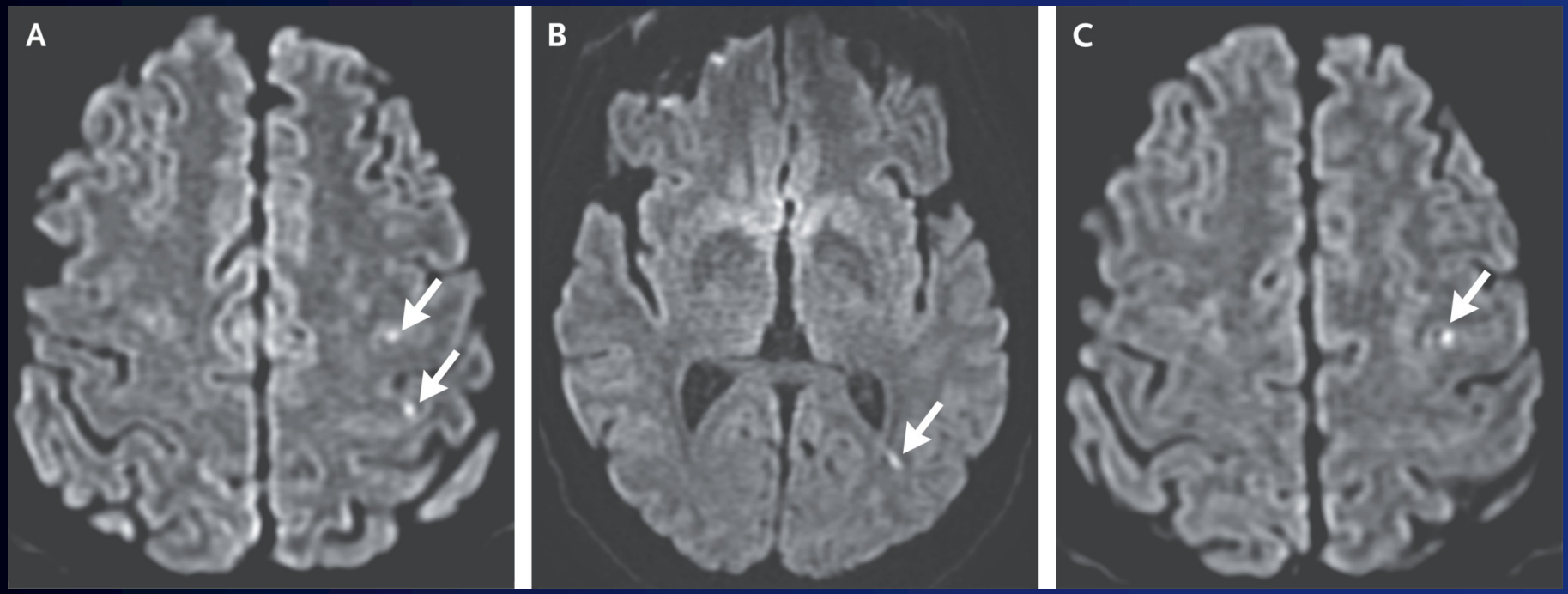
Neuroimaging Evaluation.



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Which is the best assessment scales 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

- The patient described in the vignette presented with symptoms consistent with a motor TIA.
- I would have recommended that he take 300 mg of aspirin if possible.
- Without having self-administered aspirin, I would have administered the aspirin as well as 300 mg of clopidogrel.
- In a prompt assessment of diffusion-weighted imaging on brain MRI, the finding of a bright spot in the right hemisphere would confirm ischemia.
- I would then prescribe clopidogrel at a dose of 75 mg plus aspirin at a dose of 75 mg for 21 days, followed by long-term aspirin monotherapy (75 mg).

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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

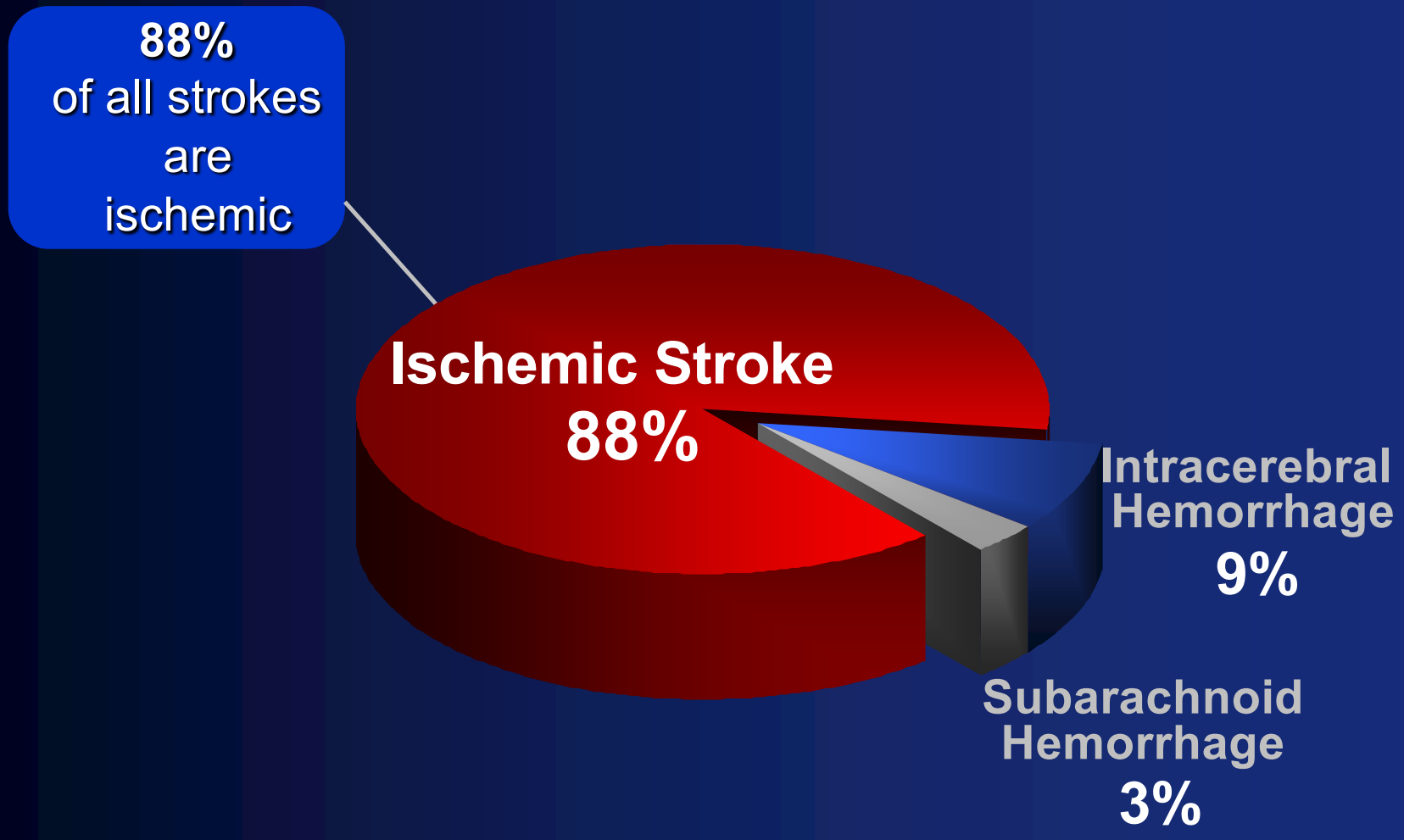
TIA is a brief episode of neurologic dysfunction caused by focal brain or retinal ischemia, with clinical symptoms typically lasting *less than one hour*, and *without evidence of acute infarction*

N Engl J Med, Vol. 337, Nov 21, 2002, 1713-1717.

Stroke, Vol 37, 2006, 577-617.

Stroke. 2009;40:2276.

Prevalence of Ischemic Stroke



American Heart Association. *Heart Disease and Stroke Statistics—2005 Update*. 2005.

ABCD^2 of TIA

- **Patients with TIA score points for each of the following factors:**
  - Age 60 years (1 point)
  - Blood pressure 140/90 mm Hg on first evaluation (1 point)
  - Clinical symptoms of focal weakness with the spell (2 points) or speech impairment without weakness (1point)
  - Duration 60 minutes (2 points) or 10 to 59 minutes (1 point)
  - Diabetes (1 point).
  - 2-day risk of stroke:
    - 0% for scores of 0 -1
    - 1.3% for 2 -3
    - 3, 4.1% for 4-5
    - 8.1% for 6-7

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

Common Causes – Not a single disease

- Atherothrombosis
  - Large-vessel
    - Extracranial
      - Aortic
      - Cervical ICA
      - Cervical CCA
    - Intracranial
      - ICA
      - MCA
      - Vertebral artery
      - Basilar artery
  - Small vessel
    - Lacunar
- Cardiac source
  - Atrial fibrillation
  - Dilated cardiomyopathy
- Nonatherosclerotic arteriopathies, eg:
  - Vasculitis
  - Migraine
- Prothrombotic disorders

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 artefacts 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

Advantages

- 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

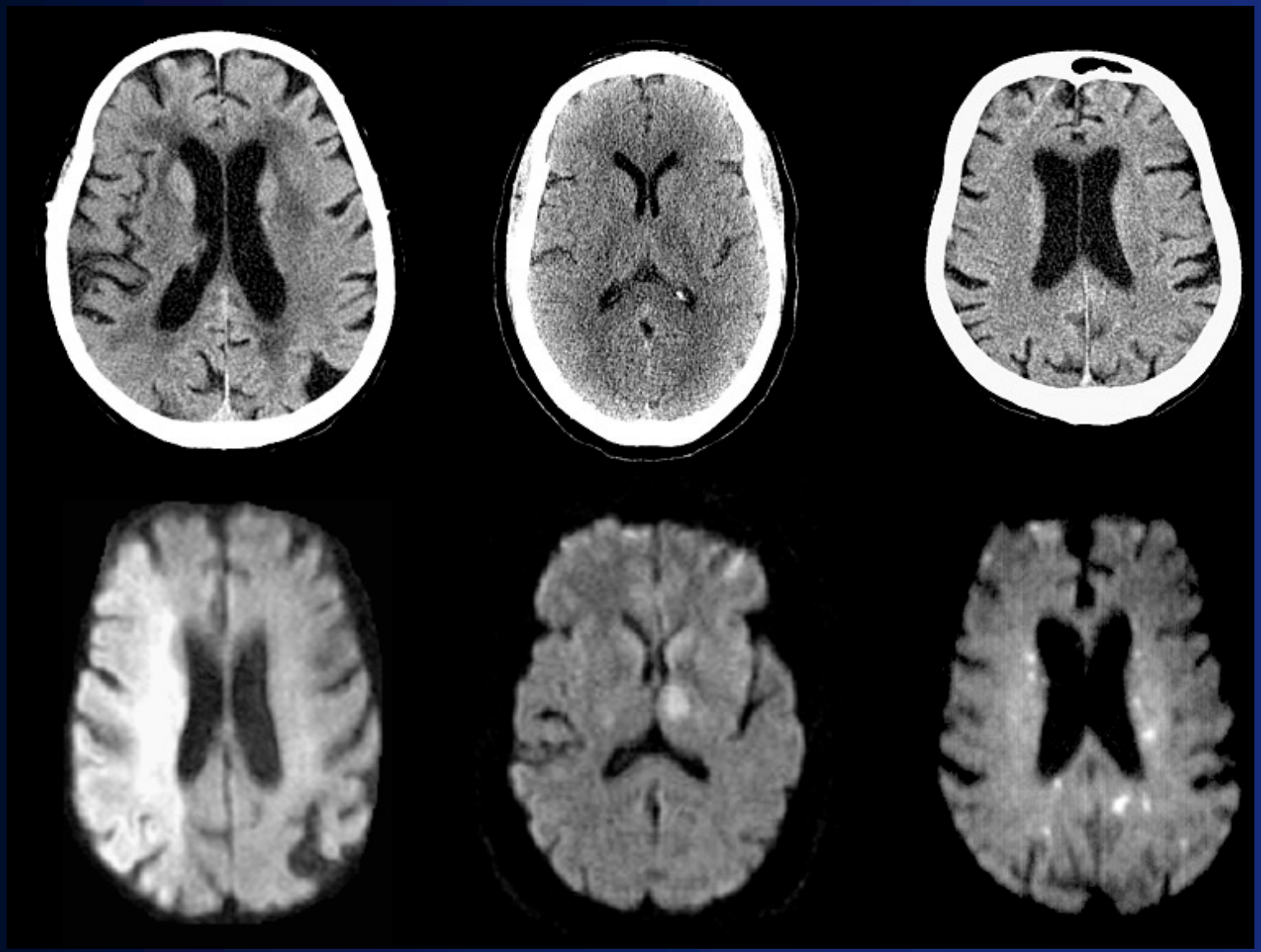
- More sensitive to acute ischemia
- More sensitive to posterior fossa lesions
- More sensitive to small vessel, lacunar lesions

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

MRI - Tissue Status: Ischemia

CT

DWI



Evaluation of Vessel Status

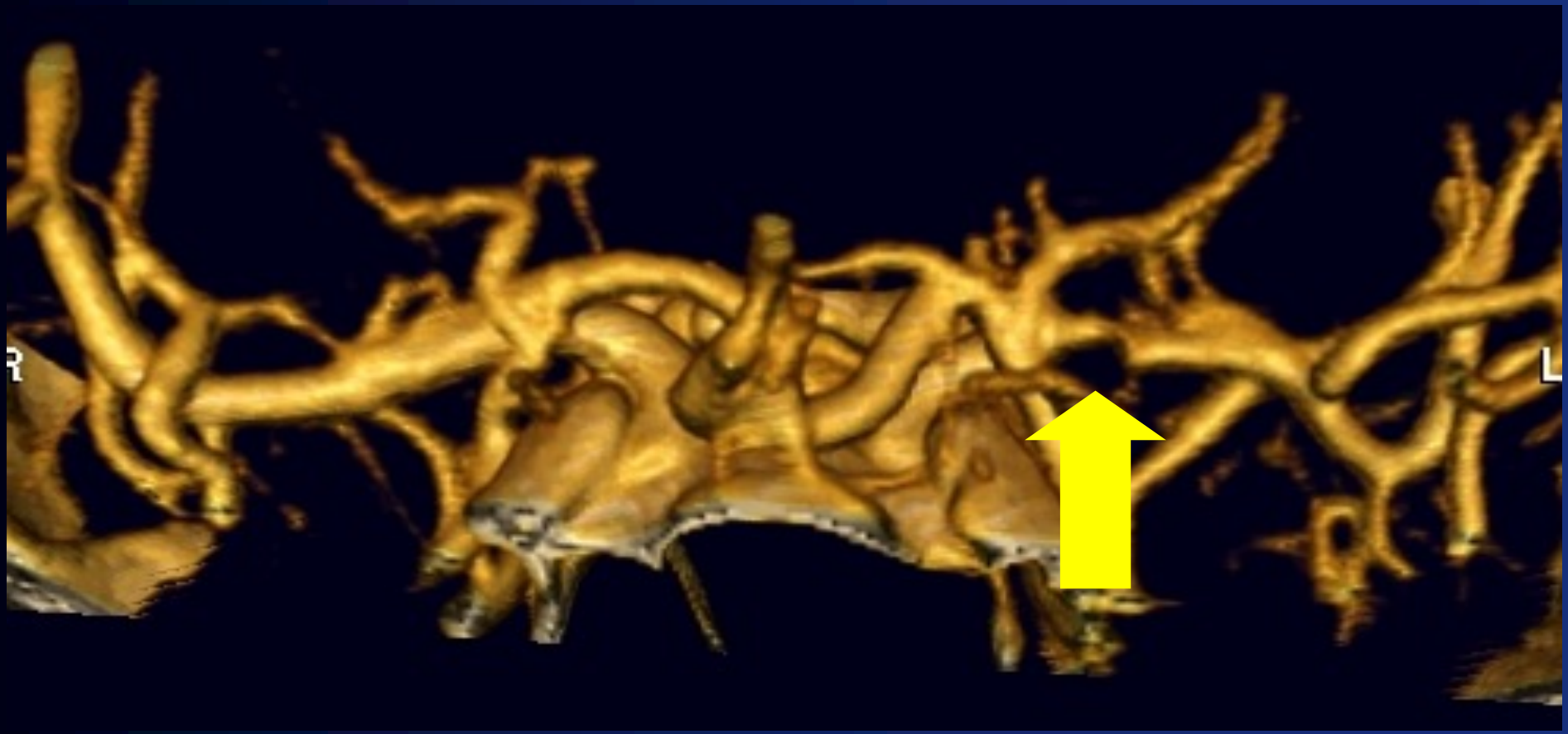
1. CT Angiography
2. MR Angiography
3. Ultrasound Techniques
4. Catheter Angiography

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

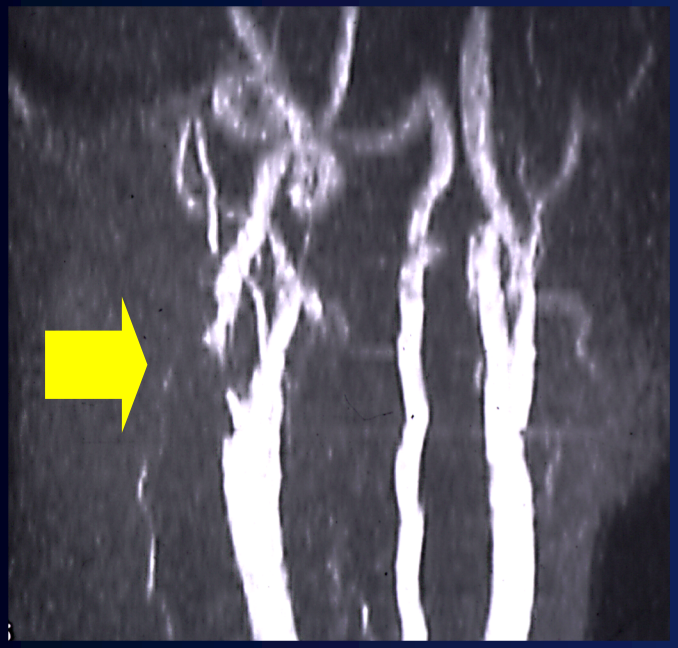
CTA: MCA Stenosis



MR Angiography

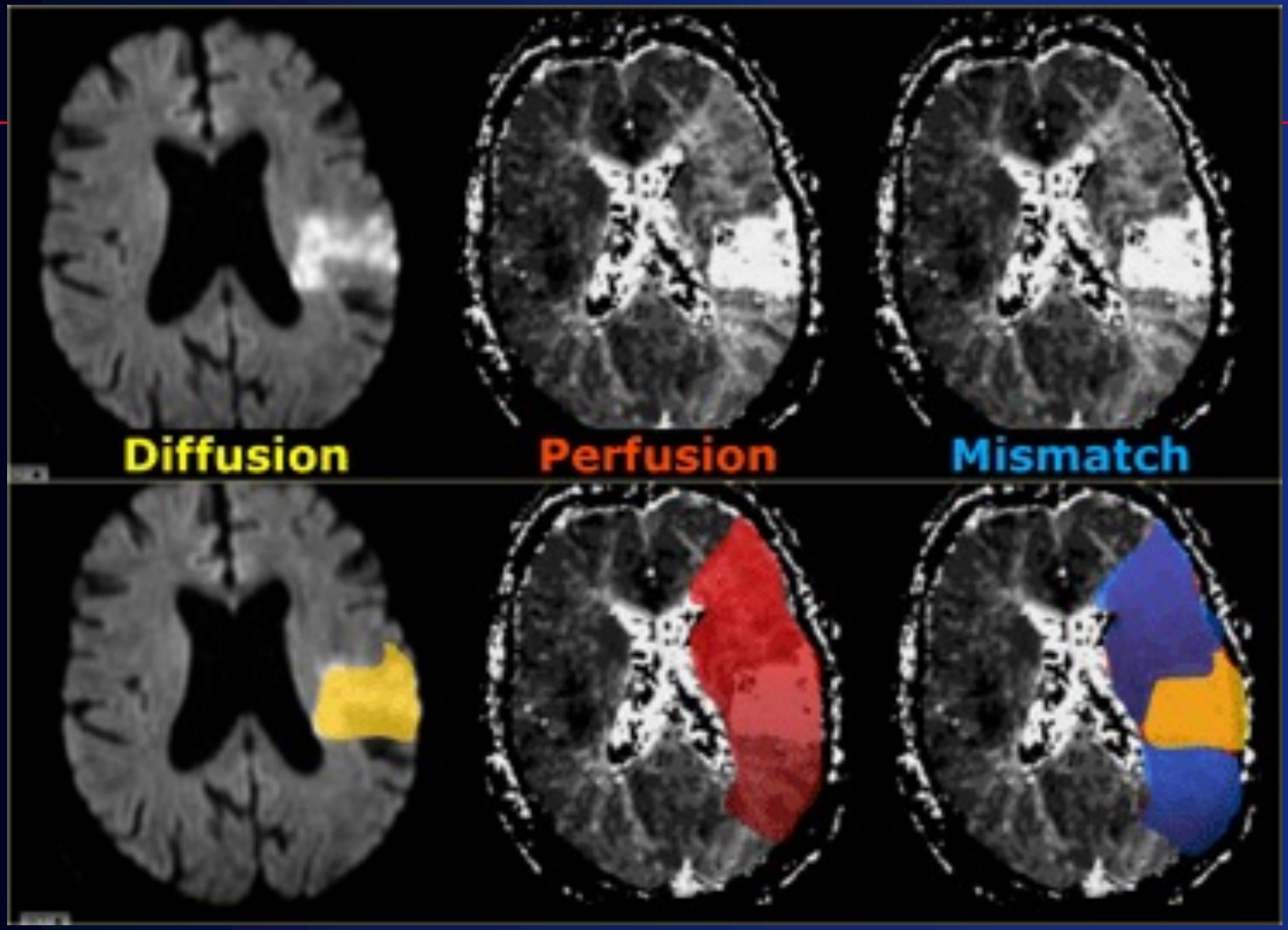
- Noninvasive means to evaluate neck and intracranial vessels
- Time of flight technique may overestimate stenoses
- Not reliable in identifying distal or branch intracranial occlusions
- Sensitivity and specificity 70-100% compared to catheter angiography
- Power-injector, contrast-enhanced techniques – increased sensitivity
- Subject to limitations of standard MRI

MR Angiography



Neck MRA: Right Carotid Stenosis

Intracranial MRA: Left ICA Occlusion


Diffusion
Perfusion
Mismatch

Whics scan to order?

- In ICU and symptomatic — CT/CTA
- In ICU and asymptomatic — MRI/MRA

- When there is a consideration of thrombolysis IV/IA — Either

- IV TPA < 4.5 hours — CT is min.

IV tPA, the "Gold Standard"

- Systemic "Clot Buster"
- FDA Approved for the treatment of AIS in 1996
- Only 8% of ischemic stroke patients are eligible for IV tPA
  - Narrow time window
  - Risk of cerebral and systemic hemorrhage
  - Achieves early reperfusion in only 13-50% of large vessel occlusions

National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med. 1995;333:1581-1587. Kleindorfer DO, Broderick JP, et al. Emergency department arrival times after acute ischemic stroke during the 1990s. Neurocrit Care. 2007;7(1):31-5. del Zoppo GJ, Poeck K, Pessin MS, et al. Recombinant tissue plasminogen activator in acute thrombotic and embolic stroke. Ann Neurol 1992;32:78-86. **6.** Bhatia R, Hill MD, Shobha N, et al. Low rates of acute recanalization with intravenous recombinant tissue plasminogen activator in ischemic stroke: realworld experience and a call for action. Stroke 2010;41:2254-8.

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

Vessel	Mortality Rate
ICA	53%[1]
MCA	27%[2]
Basilar Artery	89-90%[3]

1. Jansen O, et al.
2. Furlan A et al. PROACT II Trial
3. Brückmann H et al.

Turning Point

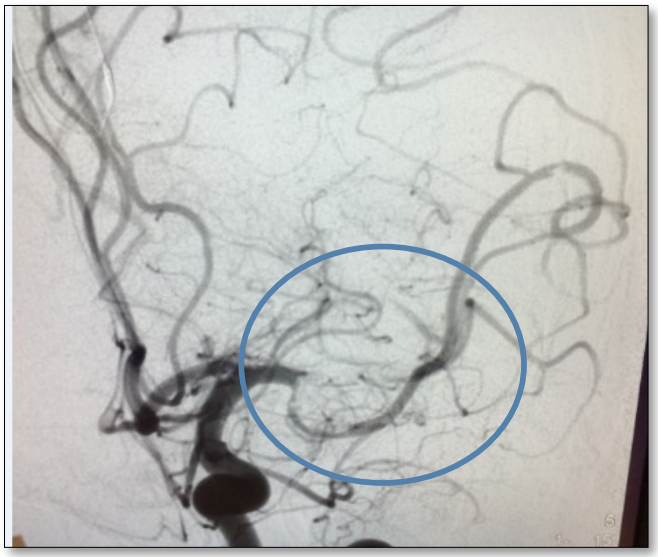
The Era of Stent-Retrievers

Technological advances

- Stent-retriever technology for safe, reliable performance

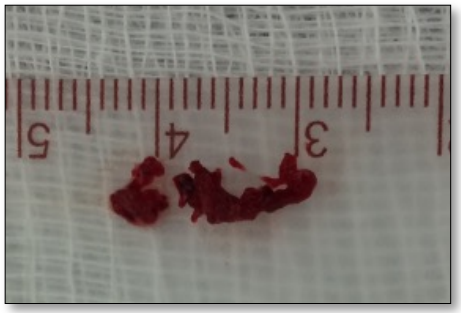
- Significant improvement in revascularization and patient outcomes vs older technology, proven in randomized clinical trials*

Goal of Ischemic Stroke Treatment



Before Intervention

After Successful Intervention



Published April 29, 2020, NEJM

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CORRESPONDENCE

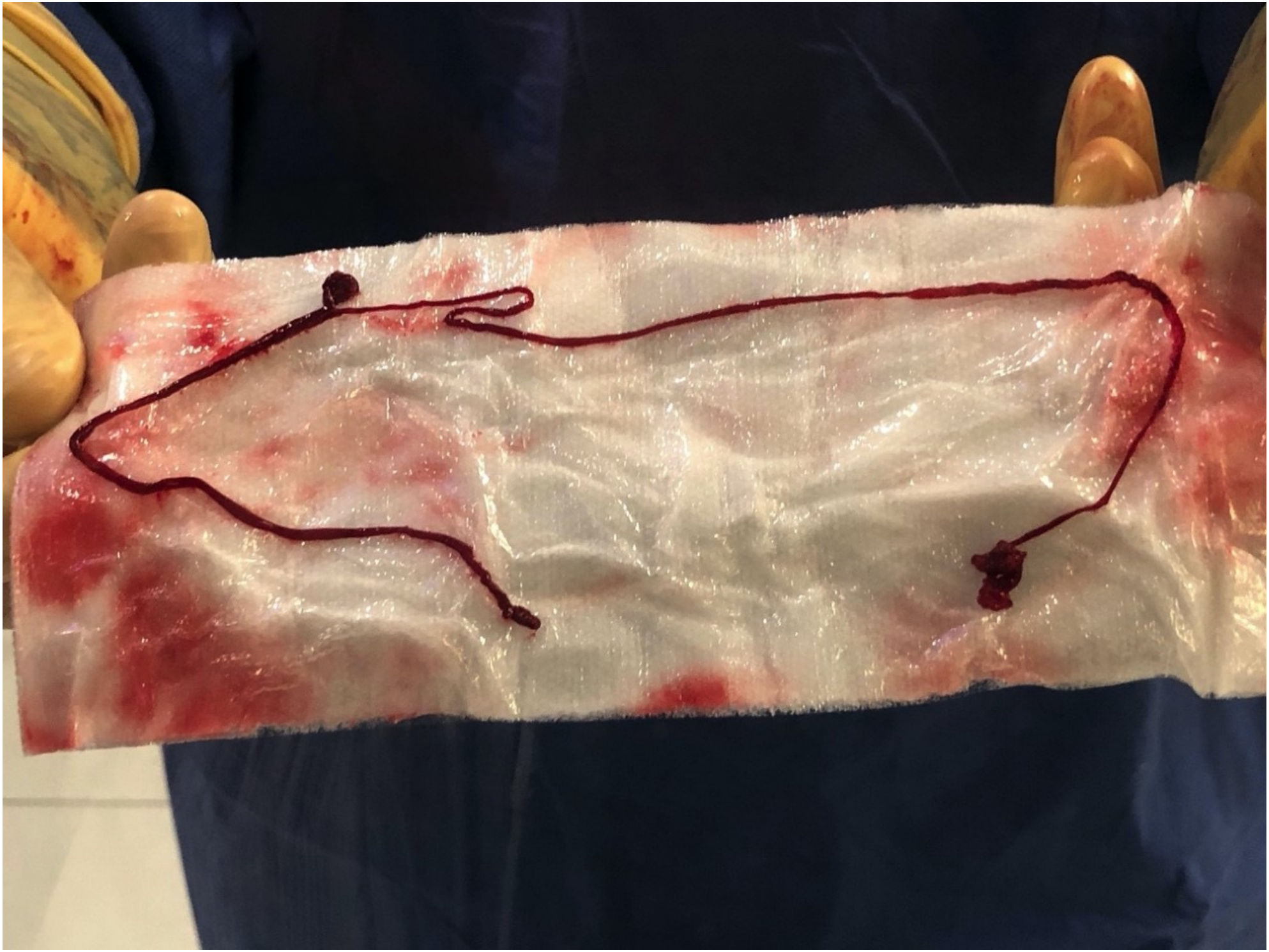
COVID-19 CASES

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

We report five cases of large-vessel stroke in patients younger than 50 years of age who presented to our health system in New York City. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was diagnosed in all five patients.

2020, a total of five patients (including the aforementioned patient) who were younger than 50 years of age presented with new-onset symptoms of large-vessel ischemic stroke. All five patients tested positive for Covid-19. By comparison, every 2 weeks over the previous 12 months, our ser-



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 DBP **121-140**	**Nicardipine** or **labetalol** If BP not controlled, consider nitroprusside

rt-PA = recombinant tissue plasminogen activator.

Adams HP, et al. *Stroke*. 2007;38:1655-1711.

In patients with a history of noncardioembolic 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)

Over

- 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

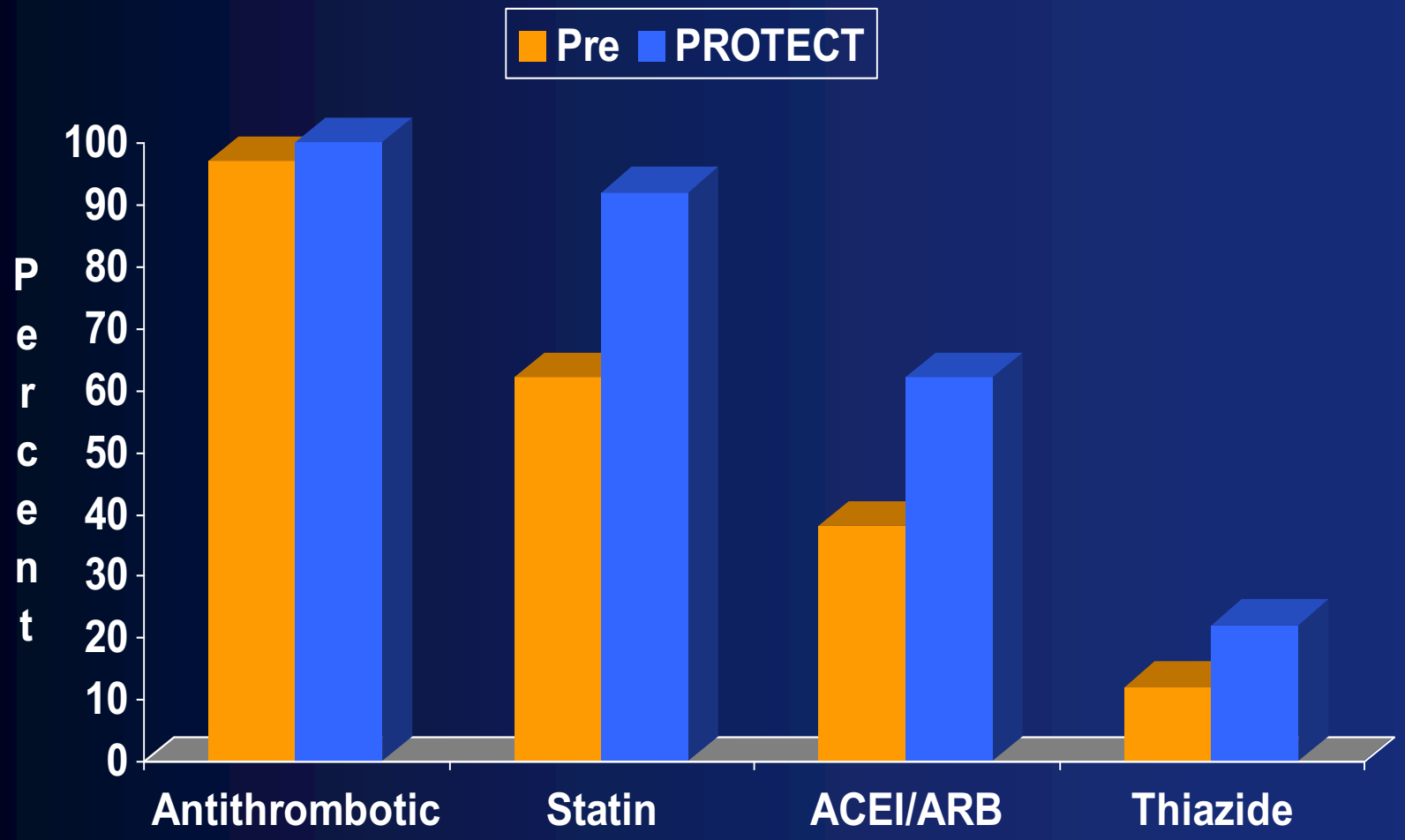
BMJ 2018;364k1508

- 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 t0 80 mg is high intensity
- 10 year Risk calculator

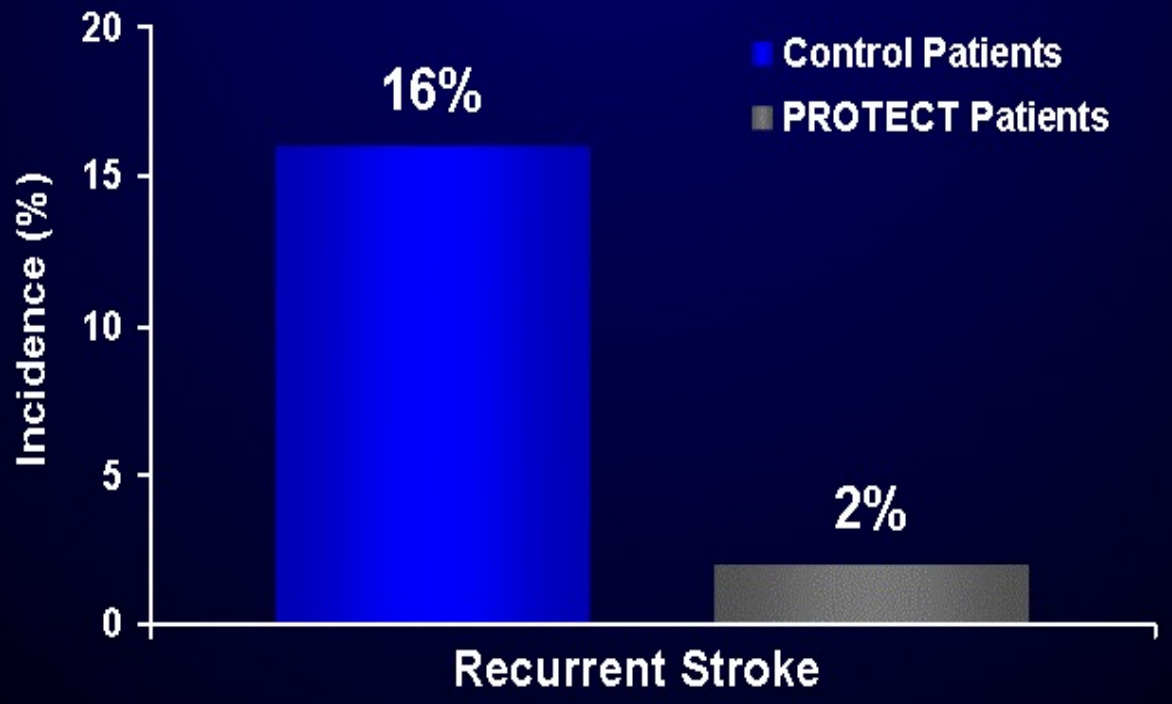
Impact of PROTECT pilot phase on Treatment Rates at Discharge



--Ovbiagele et al, Stroke 2003

PROTECT: Incidence of Recurrent Stroke

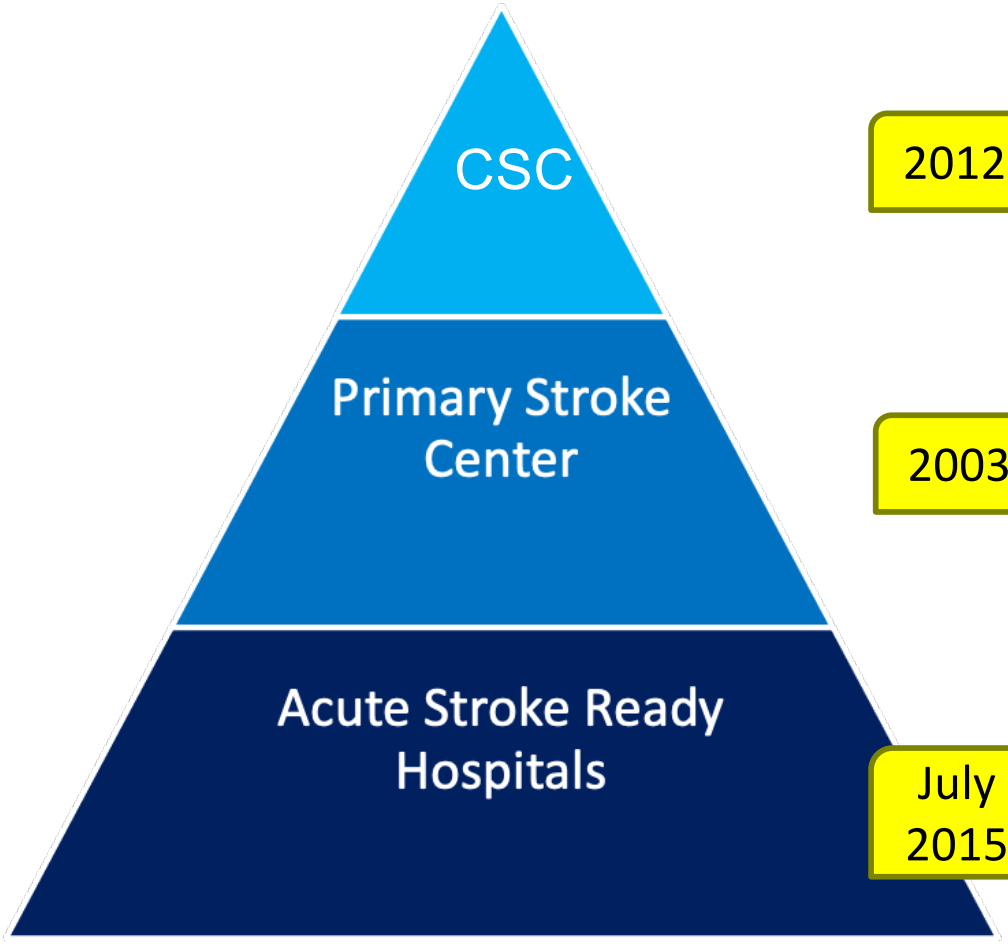
A significant difference was observed at 90 days with regard to the incidence of recurrent strokes



P=0.045.

Rahiman A et al. *Stroke*. 2005;36:429. Abstract 58.

Models of Stroke Care



2012

Academic medical center, tertiary care facility

2003

Wide range of hospitals; standard stroke care; stroke unit; uses tPA

July 2015

Rural hospitals; basic care; drip and ship; use tele-technologies

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 O_2
- 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 Mamdani, 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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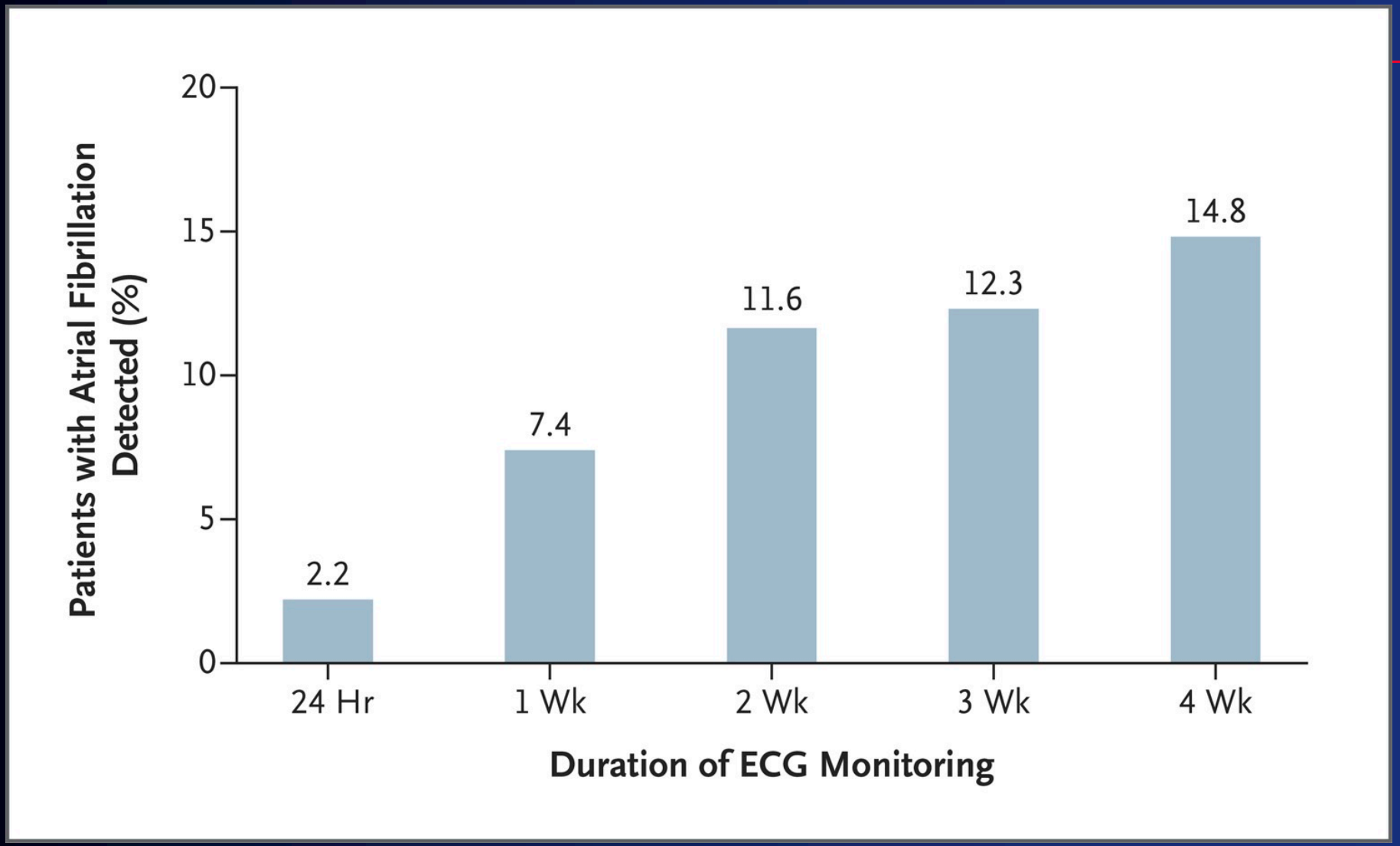
Incremental Yield of Prolonged ECG Monitoring for the Detection of Atrial Fibrillation in Patients with Cryptogenic Stroke or TIA.



Gladstone DJ et al. N Engl J Med 2014;370:2467-2477

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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.

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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.

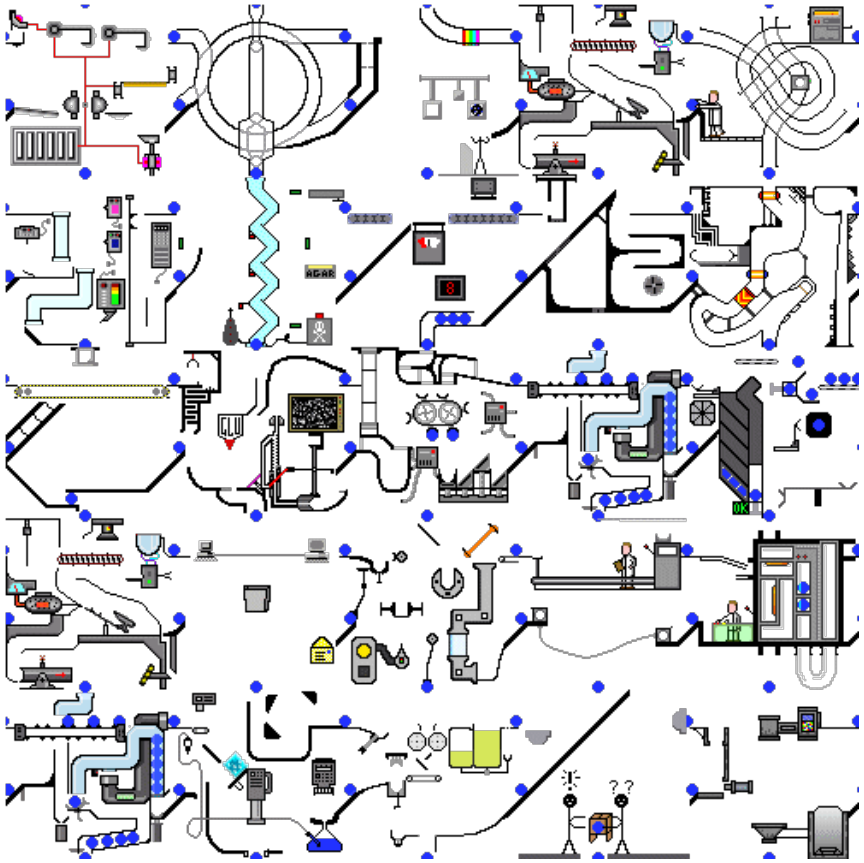
- Next best steps: Utilize duel antiplatelet therapies for 21 days after stroke when ABCD2 score is $\geq$ 4 and NIH $\leq$ 3 then monotherapy with antiplatelets and consider longer Holter monitoring as outpatients to improve the diagnosis of A Fib that would require anticoagulation.

Summary

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
- Treatment of Intracranial HTN

Thank you for your Attention



Question 1

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

Answer to Question 1

- 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

Question 2

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

Answer to Question 2

- 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.

Question 3

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 neg. 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

Answer to Question 3

- 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 is not a TPA candidate

Question 4

Which is the most appropriate antiplatelet therapy for noncardioembolic stroke?

A. Aspririn
B. Clopidogrel
C. Asp/dyp combination
D. Asp/Clopidogrel
E. Any listed above

Answer to Question 4

- 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.

Question 5

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 these above

Answer to Question 5

- 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.0000000000000158.)