Brigham and Women's Hospital
Founding Member, Mass General Brigham

Stroke Management in 2026

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- Clinical focus: ischemic and hemorrhagic stroke
- Research focus: Quality Improvement

DISCLOSURES

I have no relevant financial relationships with ineligible companies.

OBJECTIVES

- To review the updated 2026 American Heart Association guidelines for the management of acute ischemic stroke, as it relates to IV thrombolysis (alteplase and Tenecteplase) and endovascular therapy (EVT)

- To review the standard and then expanded evaluation for patients presenting with TIA/ischemic stroke, and how to use this work-up to determine stroke etiology and secondary stroke prevention management

- To review indications for dual antiplatelet therapy in ischemic stroke (limited indications: intracranial atherosclerosis and high-risk TIAs/minor strokes)

- To review guidelines for management of other co-morbidities that increase stroke risk, including hypertension, hyperlipidemia, diabetes, and lifestyle modifications

AHA Guidelines

AHA/ASA GUIDELINE

2026 Guideline for the Early Management of Patients With Acute Ischemic Stroke: A Guideline From the American Heart Association/American Stroke Association

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AHA/ASA GUIDELINE

2021 Guideline for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack

A Guideline 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 of Vascular and Interventional Neurology

The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists.

Dawn O. Kleindorfer, MD, FAHA, Chair; Amytis Towfighi, MD, FAHA, Vice Chair; Seemant Chaturvedi, MD, FAHA; Kevin M. Cockroft, MD, MSc, FAHA; Jose Gutierrez, MD, MPH; Debbie Lombardi-Hill, BS, FAHA; Hooman Kamel, MD; Walter N. Kernan, MD*; Steven J. Kittner, MD, MPH, FAHA; Enrique C. Leira, MD, MS, FAHA; Olive Lennon, PhD; James F. Meschia, MD, FAHA; Thanh N. Nguyen, MD, FAHA; Peter M. Pollak, MD; Pasquale Santangeli, MD, PhD; Anjail Z. Sharrief, MD, MPH, FAHA; Sidney C. Smith Jr, MD, FAHA; Tanya N. Turan, MD, MS, FAHA†; Linda S. Williams, MD, FAHA

Key Words: AHA Scientific Statements ■ ischemic attack, transient ■ secondary prevention ■ stroke

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Acute Stroke Management: Tissue Plasminogen Activator (tPA)

- Class of drugs that activate plasminogen > plasmin resulting in fibrin degradation, clot lysis, and vessel recanalization
- Offered to patients via IV within 4.5 hours last seen well with disabling deficits due to ischemic stroke without contraindications (e.g., intracranial hemorrhagic, coagulopathy)
- Alteplase is has been tPA standard of care since FDA-approval for ischemic stroke in 1996
- Tenecteplase “TNK” is a modified version of alteplase with amino acid substitutions at 3 sites that offer several advantages
  - Longer half-life, given as single bolus
  - Higher fibrin specificity
  - Less effect on in vivo markers of coagulopathy
  - Lower cost

Acute Stroke Management: TNK

- Now several clinical trials that have shown TNK to be as safe and effective (non-inferior) to alteplase
- Studies have shown superiority for recanalization of large vessel occlusions
- Real world studies have shown
  - Similar or lower rates of ICH
  - Faster door-to-needle times given easier preparation and single bolus
  - Decreased health care costs
- TNK is now FDA approved for ischemic stroke (March 2025) and endorsed by AHA guidelines (0.25 mg/kg, max 25 mg)
  - Many centers are switching to TNK with good success given these benefits
  - AHA continues to endorse both alteplase or Tenecteplase

Extended window TNK beyond 4.5H from LSW

- Longstanding recommendations: adults with AIS with disabling deficits within 4.5 hours of LNW => Intravenous thrombolysis after CT head

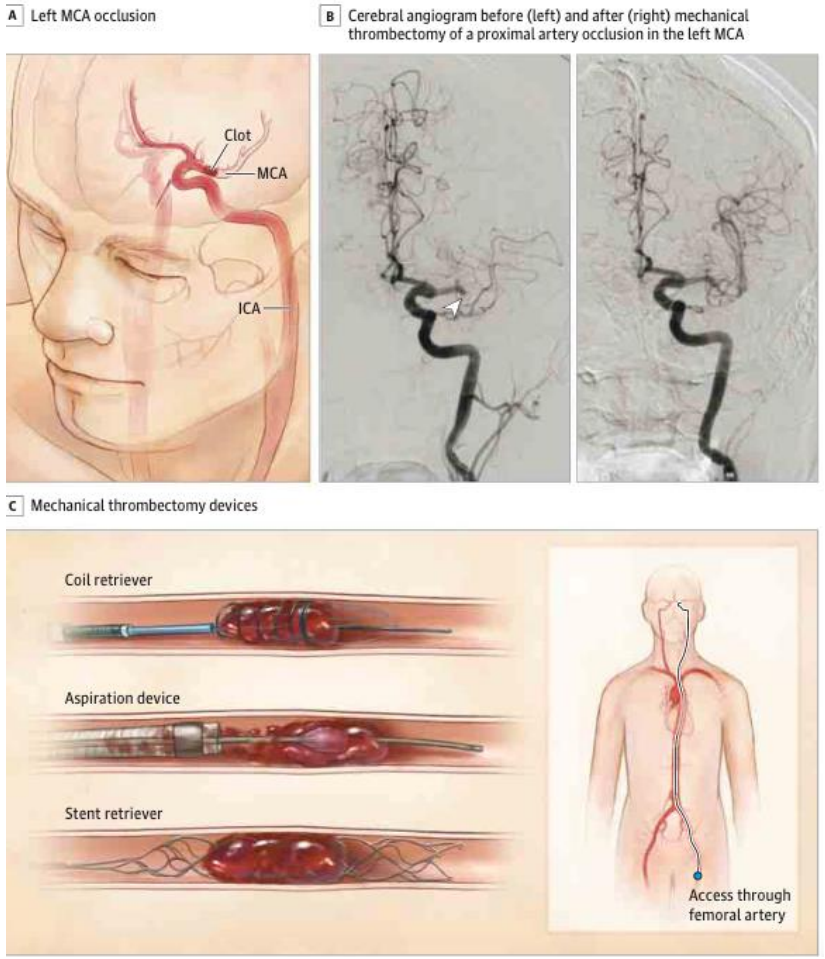
- **2026 guideline updates**

  - Unknown LNW but within 4.5 hours from symptoms recognition, DWI-MRI <1/3 MCA territory and no changes on FLAIR => can offer intravenous thrombolysis (MRI can ”be used as time marker”)

  - Awake with stroke symptoms within 9H from midpoint of sleep or 4.5-9H from LNW, perfusion imaging shows salvageable ischemic penumbra => can offer intravenous thrombolysis

Acute Stroke Management: Mechanical Thrombectomy for Large Vessel occlusions (LVO)

- LVO: occlusion of the intracranial internal carotid artery and/or the proximal middle cerebral artery (anterior circulation)
- Early 2010s, three RCT failed to show benefit of mechanical thrombectomy (clot retrieval) for AIS/LVO
  - Patient selection, endovascular techniques
- By 2015, five RCT showed benefit of of MT for AIS/LVO within ”early window” (majority of patients within 6H LSW) and small established stroke
- By 2018, two RCT that used advanced imaging (MRI, CTP) to select patients with small established stroke and large penumbra (area at risk) in “late window” (up to 24H LSW) and showed benefit of MT



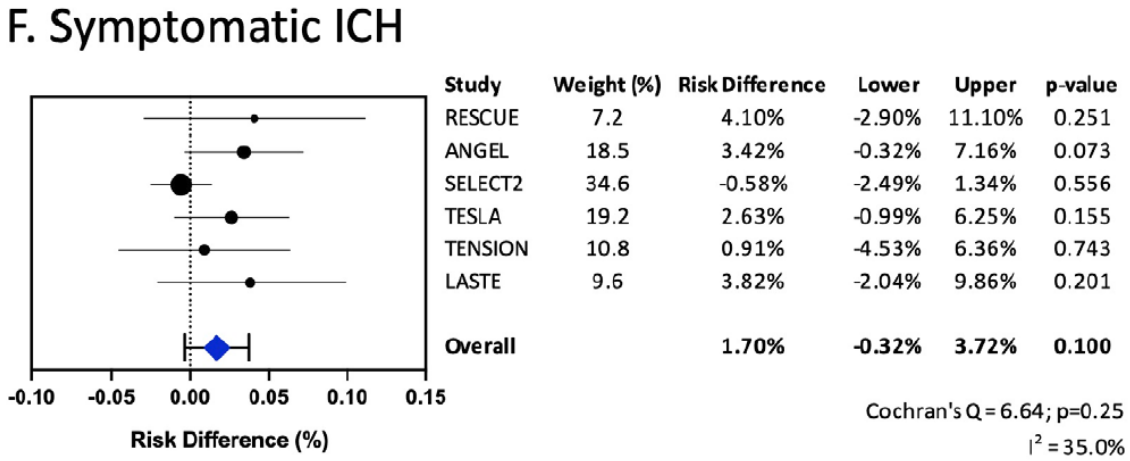
Acute Stroke Management: Mechanical Thrombectomy for Large Vessel occlusions (LVO) with Large Established Strokes

- 6 RCT since 2022 that together show benefit of MT for patients with moderate to large MCA ischemic strokes compared to medical therapy (benefit overall less than those with small strokes on presentation)

Table 2 Number needed to treat for favorable clinical outcomes

90-Day outcome	Number needed to treat	95% CI
Better functional status (mRS score shift)	4.7	3.7 to 6.6
Independent walking (mRS score 0–3)	7.1	5.6 to 9.6
Functional independence (mRS score 0–2)	10.6	8.2 to 14.8

mRS, modified Rankin Scale.



Acute Stroke Management: Mechanical Thrombectomy for Basilar Artery Occlusions

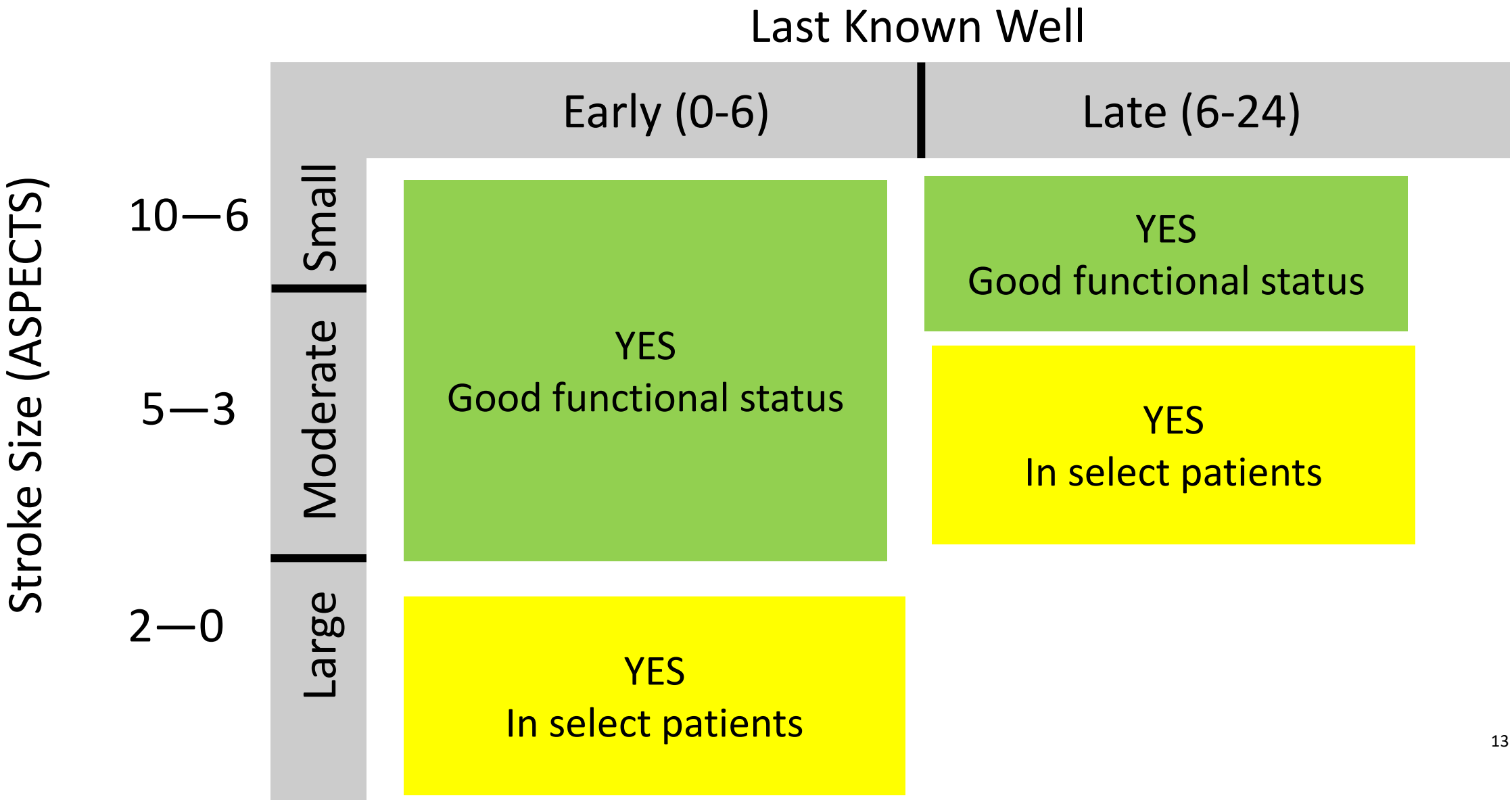
- Basilar artery occlusions
  - Hard to diagnosis (mimics non-stroke conditions) leading to delay in care
  - Very high mortality with or without treatment → fatalistic approach

- Two negative RCT for MT versus medical therapy
  - High cross over rates
  - Terminated early

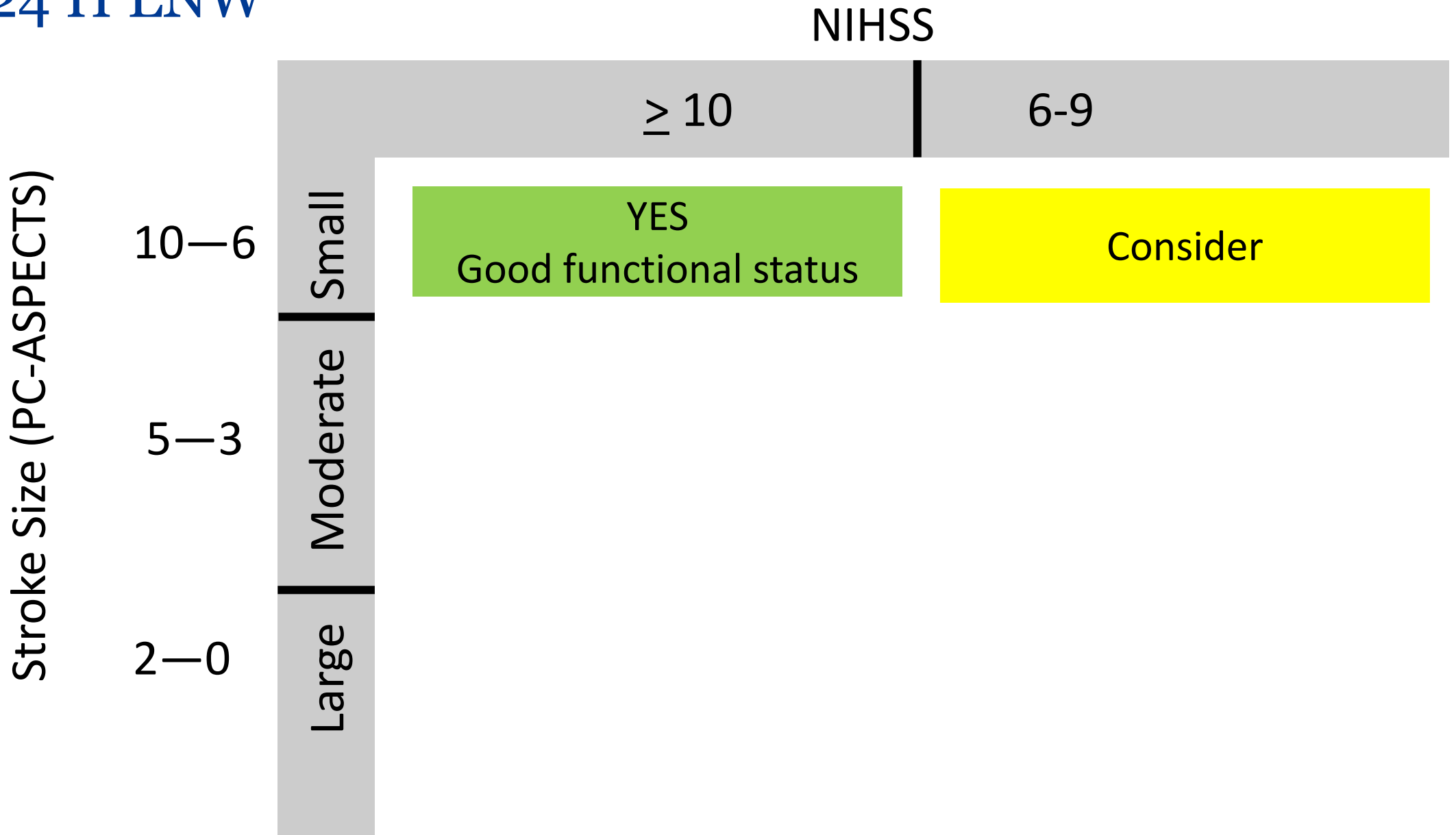
- In 2022, two positive RCT that showed MT had better functional outcomes but more ICH

- Provides more confidence to offer MT for basilar artery occlusions in select patient population

Current 2026 AHA EVT Indications For Anterior Circulation ICA/Proximal MCA and Severe Stroke Syndrome (NIHSS ≥6)



Current 2026 AHA EVT Indications For Basilar Artery within 24 H LNW



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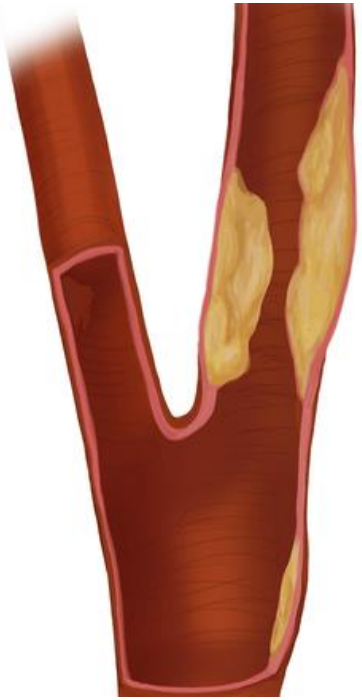
Standard Ischemic Stroke Evaluation

- Brain parenchymal imaging to confirm stroke (CT or MRI)
- Vessel imaging (CTA, MRA, carotid ultrasound)
  - Carotid ultrasound gives poor views of posterior circulation and only evaluates extra-cranial arteries
- Transthoracic echocardiogram (TTE)
- EKG, external cardiac monitor
  - American Heart Association Guidelines do not provide specific recommendations on length of monitoring
- Serum labs: CBC, troponin, PT, PTT, HgbA1c, Lipid profile
- Timing: testing ideally is performed within 48-hours of symptom onset

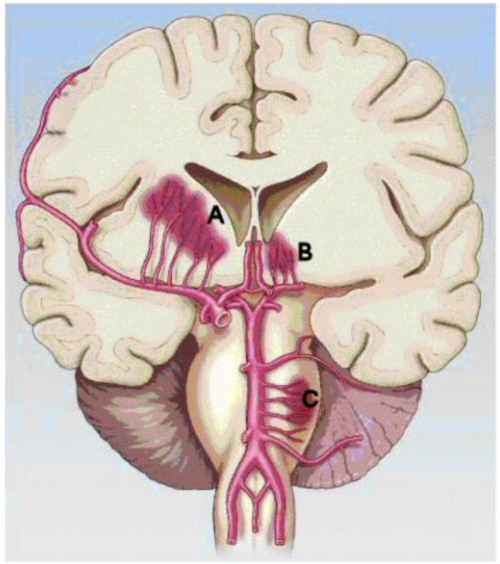
Stroke Etiologies (TOAST CRITERIA)

Large Artery Atherosclerosis



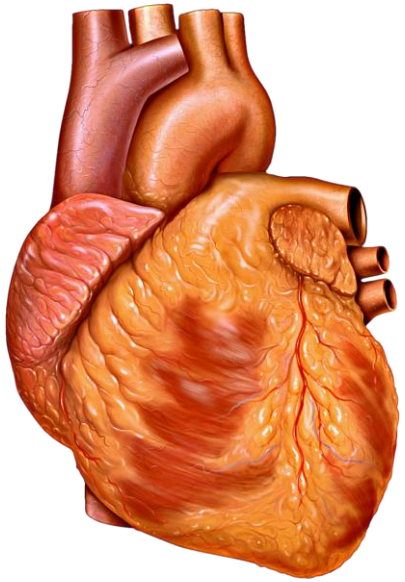
>50% stenosis/occlusion

Small-Artery Occlusion (Lacune)



< 1.5 cm diameter
Usually due to small vessel disease

Cardioembolic



> 1 vascular territory supports diagnosis

Most common: AF

Patent Foramen Ovale

Other

Dissections | Hypercoag

Unknown (cryptogenic)

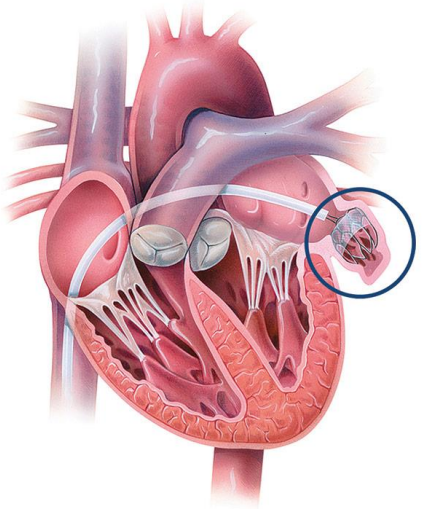
Embolic Stroke of Undetermined Source (ESUS)/non-lacunar

??

Minimum work-up includes arterial imaging, TTE, extended rhythm monitoring, basic serum studies

Atrial Fibrillation

- Once patient has had stroke, CHADS-VASc warrants treatment
- AF pattern can be paroxysmal, persistent, or permanent



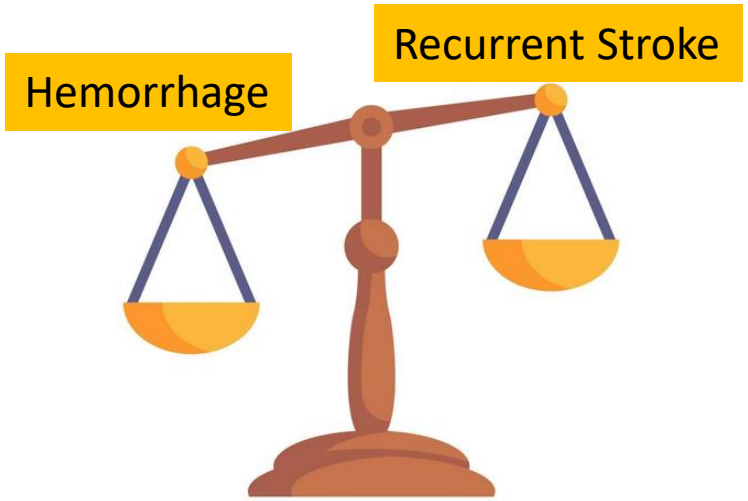
Anticoagulation

- ASA no longer recommended
- Nonvalvular AF: DOAC > Warfarin
- Valvular AF (moderate to severe mitral stenosis or mechanical heart valve): Warfarin

Left Atrial Appendage Closure

- >90% of non-valvular AF thrombi form in the LAA
- Now FDA approved percutaneous device that can occlude the LAA and prevents need for life-long AC
- Approved for those who cannot tolerate long-term AC
- PROTECT-AF (2014)[3], PREVAIL (2014)[4], PRAGUE 17 (2021)[5]

When to restart anticoagulation after ischemic stroke for patients with AF?



American Heart Association Guidelines[7]

In patients who are **high risk** for hemorrhagic transformation [large infarcts], reasonable to delay AC beyond **14-days** after index event to reduce risk of ICH

- Defining high risk: NIHSS >15, full territory, early signs of hemorrhage, uncontrolled HTN, bleeding diathesis

In patients with **low risk** for HT [moderate to small infarcts], may be reasonable to initiate AC **2-14 days** after index event to reduce risk of ICH

- Those w/ TIAs can start immediately

When to restart anticoagulation after ischemic stroke for patients with AF?

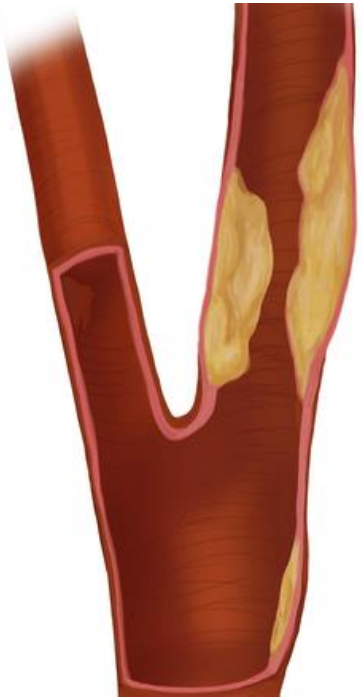
- New RCT data that support SAFETY of starting AC sooner after ischemic stroke (no increased rates of ICH), but this is not clearly superior (no decreased rates of systemic embolism)

- ELAN (2023): started anticoagulation within 6-7 days after major stroke (versus 12-14 days) with lower numerical rates of recurrent ischemic stroke (*NS) and similar rates of symptomatic intracranial hemorrhage

- OPTIMAS (2024): compared early DOAC initiation (within 4 days of stroke onset) with delayed initiation (7-14 days from stroke) non-inferiority was met for composite outcome (recurrent ischemic stroke and ICH) but superiority was not identified

Stroke Etiologies (TOAST CRITERIA)

Large Artery Athero



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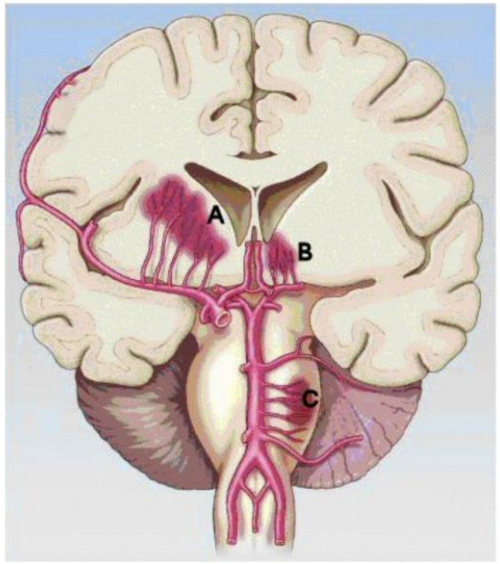

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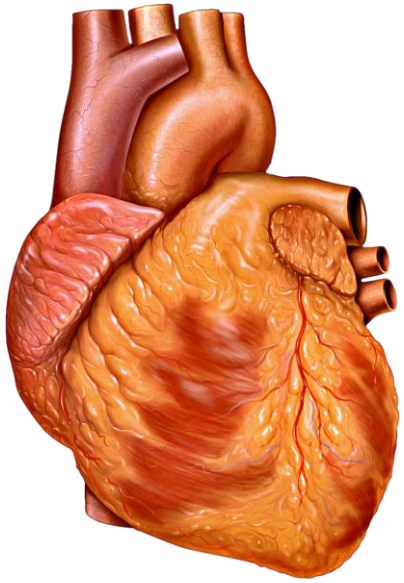

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“Cryptogenic” Etiologies

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- The extent of workup is the most important factor in establishing a diagnosis of cryptogenic stroke
- As the number of diagnostic investigations performed increases, the number of patients with cryptogenic stroke decreases

Implantable Loop Recorder (ILR)

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- Subclinical AF may contribute up to 25% of cryptogenic stroke in older adults
- External monitors can range from 24-hours to 30 days
  - Most providers will monitor anywhere from 7-30 days
- ILR implanted under the skin and can monitor up to 3-5 years
- ILRs yield much higher rates of AF detection than external monitors
  - 15% with 12-months of ILR versus 4.7% with 30-day external monitor
  - On-going research how device detected AF modifies stroke risk
- American Heart Association Guidelines do not specify which cryptogenic stroke patients should get ILRs
  - Many neurologist refer patients with risk factor for AF (CHF, older age, etc.)
- Smart Watches actively being studied for this patient population

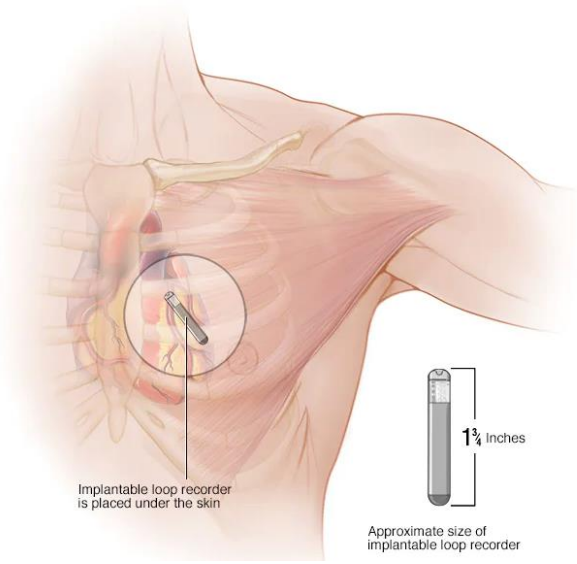


Image: https://www.mayoclinic.org/tests-procedures/implantable-loop-recorder/pyc-20384986#dialogId30001384

TCD with Bubble to Evaluate for PFOs

- PFOs allow for right to left shunt such that venous embolism can cause strokes (paradoxical embolism)

- Present in 25% of population
  - Challenge to establish causality between PFO and stroke

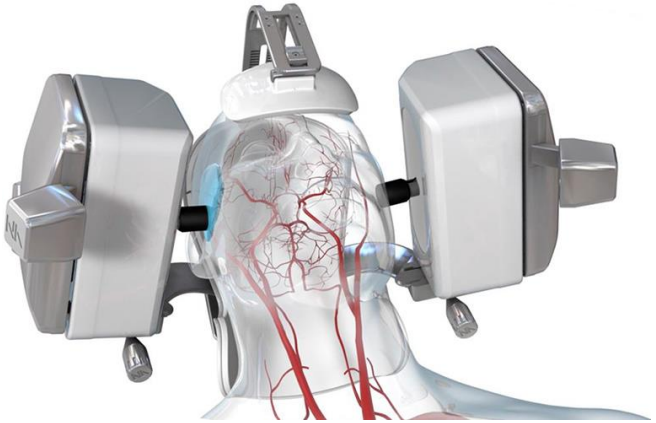
- PFO more likely to be causal in patients
  - <60 years old without traditional risk factors
  - Increased risk for venous clotting

- TTE with agitated saline is the most used “screening test” but has poor sensitivity (~45%)

- TEE is gold standard but invasive and Valsalva can be limited in sedated patient

- TCDs sensitivity 96% and specificity 92%

- Increasing interest in robotic assist TCD devices that recently shown to detect RLS 3x more likely than TTE, including large PFOs missed by TTE



Cryptogenic/ESUS Stroke Management

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- Cryptogenic (unknown cause): mono-antiplatelet and risk factor modification

- Several randomized trials for cryptogenic stroke/ESUS that caution against AC use:
  - WARSS: no benefit of warfarin over ASA in cryptogenic stroke
  - NAVIGATE ESUS: no benefit of Rivaroxaban over ASA in ESUS, significant increased risk for major bleeding
  - RE-SPECT ESUS:no benefit of dabigatran over ASA in ESUS
  - ATTICUS and ARCADIA: no benefit of Apixaban over ASA in subset of ESUS with risk of AF or evidence of atrial cardiopathy

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Dual Antiplatelet Use in Ischemic Stroke

- Non-cardioembolic high risk TIA/minor stroke
- Severe intracranial atherosclerosis defined as > 50% of major intracranial artery that supplies area of ischemia

Short-Term DAPT use for high-risk TIA/minor stroke to reduce short-term stroke risk

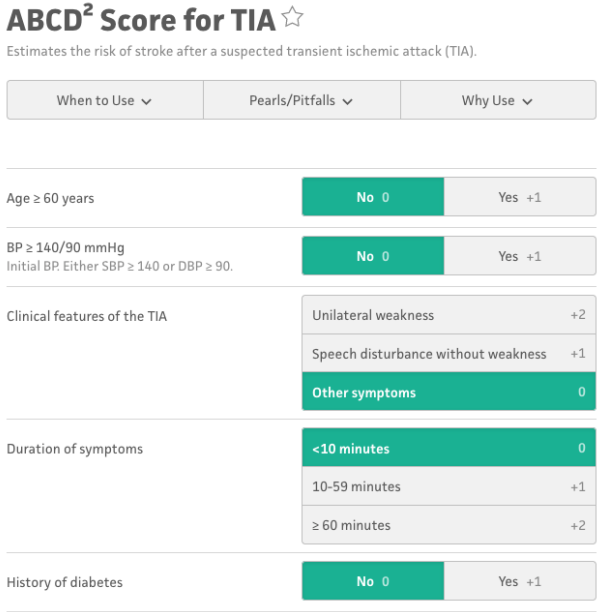
- Transient ischemic attack (TIAs): brief episode of neurological dysfunction caused by focal brain or retinal ischemic (symptoms typically last less than one hour) and there is no evidence of acute infarct on imaging (MRI)
  - With advancement in MRI, many things previously called “TIAs” were minor strokes
- TIAs can have high risk of stroke (4-10%) within the first 48H
- Lots of efforts to try and reduce this risk—most benefit seen with DAPT in high risk patients

JAMA. 2000;284(22):2901-2906

Short-Term DAPT use for high-risk TIA/minor stroke to reduce short-term stroke risk (AHA Guidelines)[7]

- Applied to non-cardioembolic High Risk TIA and Minor Non-Disabling Minor Stroke
  - High Risk TIA is defined by the ABCD^2 ≥4-5
  - Minor Stroke NIHSS ≤ 3-5

  - Validated risk-stratification calculators exist
    - ABCD^2 is commonly used
    - Limitations to calculators (e.g., carotid stenosis, crescendo TIAs, posterior circulation symptoms)
    - Needs to use calculators + comprehensive evaluation



Antiplatelet Choice for TIA (Noncardioembolic)

TIA

Low Risk:
$ABCD^2 < 4$

Single Antiplatelet:

- ASA 81-325 mg qD

OR

- Clopidogrel 75 mg qD

High Risk:
$ABCD^2 \geq 4$

Dual Antiplatelet:

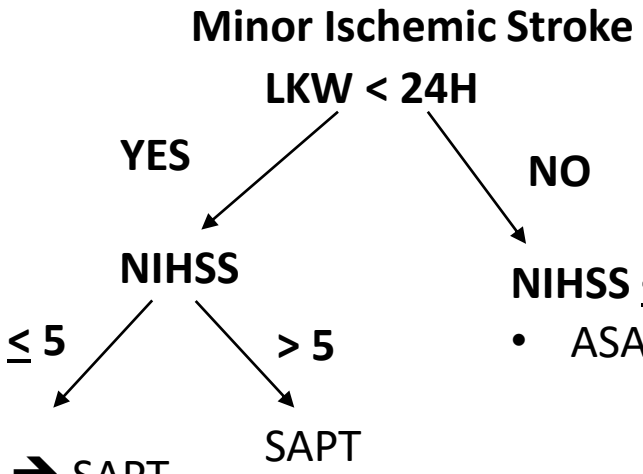
- ASA + Clopidogrel X 21-90 days ➔ SAPT

OR

- ASA + Ticagrelor* X 30 days ➔ SAPT (**$ABCD^2 > 6$*)**
- Typically use a loading dose to get therapeutic quickly
- Start Within 24H LNW (benefit really in preventing another event in first 24H)

- **Want to treat highest risk patients with DAPT more aggressively to prevent recurrent event**
- **Only want short course of DAPT usually <21-90s**
  - After which bleeding risk > benefits of stroke protection

Antiplatelet Choice for Minor Stroke (Noncardioembolic)



NIHSS ≤ 5 + LKN 24-72 H + >50% atherosclerosis

- ASA + Clopidogrel X 21-90 days ➔ SAPT

Dual Antiplatelet:

- ASA + Clopidogrel X 21-90 days ➔ SAPT

OR

- ASA + Ticagrelor X 30 days ➔ SAPT

Intracranial Atherosclerosis (ICAD)

- TIA/stroke (within 30 days) attributable to severe stenosis (70-99%) ➔ aspirin 325 mg + clopidogrel 75 mg for 90 days (based on SAMMPRIS trial)[1] and then continue with monoantiplatlet treatment

- ICAD carries high risk of recurrent stroke (~12-20% within 1 year)

- Trend towards being more aggressive with antithrombotics

CAPTIVA

Comparison of Anti-coagulation and Anti-platelet Therapies for Intracranial Vascular Atherostenosis (CAPTIVA)

- Subjects with will be randomized 1:1:1 to one year of treatment with:
  - Ticagrelor (180 mg loading dose, then 90 mg twice daily) + aspirin (81 mg daily)
  - Low dose rivaroxaban (2.5 mg twice daily) + aspirin (81 mg daily)
  - Clopidogrel (600 mg loading dose, then 75 mg daily) + aspirin (81 mg daily)

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Blood Pressure

An office BP goal of <130/80 mm Hg is recommended for most patients to reduce the risk of recurrent stroke and vascular events

- **Some exceptions**: ICAD, flow-limiting stenosis, orthostatic syncope, very elderly

More important the degree of BP lowering than specific agent

- Data showing benefits with thiazides, ACE, ARBs for lowering BP to reduce recurrent stroke

Hyperlipidemia

- Go to statin = atorvastatin 80 mg
- Pt with TIA/ischemic stroke with no known CAD or major cardiac sources of embolism and LDL-C >100 mg/dL, atorvastatin 80 mg daily is indicated to reduce risk of stroke recurrence (**SPARCL 2006 trial**)
- Pts with TIA/ischemic stroke with atherosclerotic disease (intracranial, carotid, aortic, or coronary), statin (+ ezetimibe, if needed) to a goal LDL-C of <70 (**TST 2020 trial**)
- Pts with stroke + another major ASCVD risk factor on maximally tolerate statin and ezetimibe, consider PSCK9i (up to 60% further lowering)

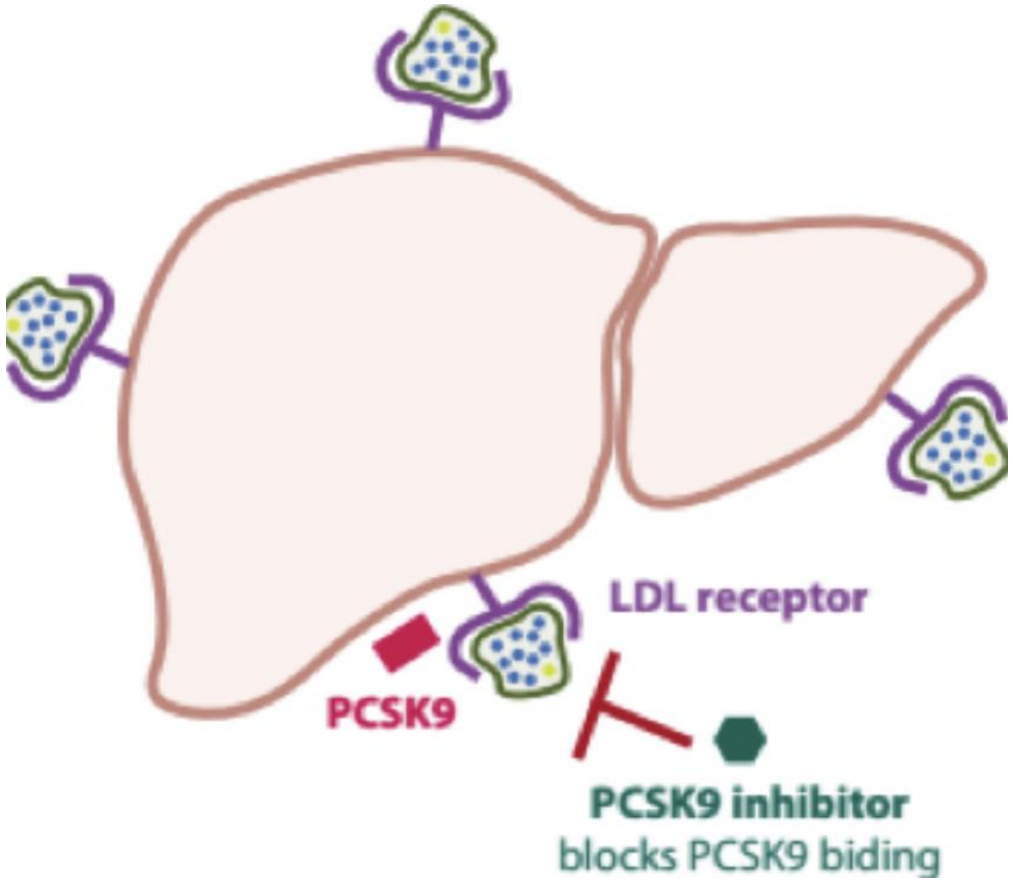

Image: https://sitn.hms.harvard.edu/flash/2015/a-potential-new-weapon-against-heart-disease-pcsk9-inhibitors/

Hyperglycemia

- Glycemic control should be **individualized**
  - Most patients, especially those <65 years of age and without life-limiting comorbid illness, achieving a goal of HbA1c ≤7% is recommended to reduce risk for **microvascular complications**

- Unclear usefulness of achieving intensive glucose control (HgA1c <7%) beyond acute phase for preventing future stroke

Lifestyle

- Mediterranean-diet
- Aerobic activity
- Weight loss recommended; goal BMI <26
- Smoking cessation
- Limiting ETOH use (≤ 14 drinks/week for men and ≤ 7 drinks/week for women)

MOC REFLECTIVE STATEMENT (BRIEF TAKE HOME NOTES FOR REFERENCE)

- The American Heart Association released 2026 guidelines that now further expand the eligibility for intravenous thrombolysis and endovascular therapy for management of acute ischemic stroke.
- Every transient ischemic attack and ischemic stroke patient require a baseline work-up. An unrevealing baseline work-up requires more in-depth testing specific to the patient (e.g., ILR, bubble study).
- Dual antiplatelet use has limited indications in ischemic stroke (intracranial atherosclerotic disease and high-risk TIA/nondisabling stroke) and is used for a limited time.
- Risk factor modification is also critically important in reducing recurrent ischemic stroke.

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