Advances in Stroke Treatment and Prevention

Winter 2026 General Geriatric Healthcare Series
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Disclosures

- None

Outline

- 2026 AHA/ASA Guidelines
- Selected Challenges in Secondary Stroke Prevention
  - ESUS
  - Extended Cardiac Monitoring
  - Timing of Anticoagulation Initiation
  - Management of Recurrent Strokes
  - Cerebral Amyloid Angiopathy

- **2026 AHA/ASA Guidelines for the Early Management of Patients with Acute Ischemic Stroke**

  Shyam Prabhakaran et al, *Stroke*, 2026 Jan 26

Choice of Thrombolytic Agent and Extended Time Windows for IVT

COR	RECOMMENDATIONS
1	In adult patients with AIS presenting within 4.5 hours of symptom onset or last known well and eligible for IVT, tenecteplase at a dose of 0.25 mg/kg body weight (max 25 mg) or alteplase at a dose of 0.9 mg/kg body weight is recommended to improve functional outcomes.
3 No Benefit	In adult patients with AIS presenting within 4.5 hours of symptom onset or last known well and eligible for IVT, tenecteplase at a dose of 0.4 mg/kg body weight is not recommended

COR	RECOMMENDATIONS
2a	In patients with AIS who have salvageable ischemic penumbra detected on automated perfusion imaging and who (a) awake with stroke symptoms within 9 hours from the midpoint of sleep or (b) are 4.5–9 hours from last known well, IV thrombolysis may be reasonable to improve functional outcomes.

American Heart Association.

Abbreviations: AIS indicates acute ischemic stroke; and IVT, intravenous thrombolytics

Prabhakaran, S., et al. 2026 AHA/ASA Guideline for the Early Management of Patients with AIS. *Stroke*.

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Endovascular Thrombectomy for Adults

	COR	RECOMMENDATIONS
Thrombectomy **0 to 6 Hours After Onset of Symptoms, ASPECTS 3 to 10**	1	In patients with AIS from anterior circulation proximal LVO of the ICA or M1, presenting within 6 hours from onset of symptoms, with NIHSS score ≥6, prestroke mRS score of 0 to 1, and ASPECTS 3 to 10, EVT is recommended to improve functional clinical outcomes and reduce mortality
Thrombectomy 6 to 24 Hours After Onset of Symptoms, ASPECTS 6 to 10	1	In patients with AIS from anterior circulation proximal LVO of the ICA or M1 presenting between 6 and 24 hours from onset of symptoms, with NIHSS score ≥6, prestroke mRS score 0 to 1 and ASPECTS ≥6, EVT is recommended to improve functional clinical outcomes and reduce mortality.
Thrombectomy 6 to 24 Hours After Onset of Symptoms, ASPECTS 3 to 5	1	In selected patients with AIS from anterior circulation proximal LVO of the ICA or M1, presenting between 6 and 24 hours from onset of symptoms, with age <80 years, NIHSS score ≥6, prestroke mRS score 0 to 1, ASPECTS 3 to 5, and without significant mass effect on imaging, EVT is recommended to improve functional clinical outcomes and reduce mortality.

American Heart Association.

Abbreviations: AIS indicates acute ischemic stroke; EVT, endovascular thrombectomy; ICA, internal carotid artery; LVO, large vessel occlusion; mRS – modified Rankin scale; and NIHSS, National Institutes of Health Stroke Scale.

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Posterior Circulation Stroke

COR	RECOMMENDATIONS
1	In patients with AIS, with basilar artery occlusion, a baseline mRS score of 0 to 1, NIHSS score ≥10 at presentation, and PC-ASPECTS ≥6 (mild ischemic damage), EVT within 24 hours from onset of symptoms is recommended to achieve better functional outcome and reduce mortality.
2b	In patients with AIS, with basilar artery occlusion, a baseline mRS score of 0 to 1, NIHSS score 6 to 9 at presentation, and PC-ASPECTS ≥6 (mild ischemic damage) the effectiveness of EVT within 24 hours to improve functional outcomes and reduce mortality is not well established.

American Heart Association.

Abbreviations: AIS indicates acute ischemic stroke; EVT, endovascular thrombectomy; LVO, large vessel occlusion; mRS – modified Rankin scale; and NIHSS, National Institutes of Health Stroke Scale.

Prabhakaran, S., et al. 2026 AHA/ASA Guideline for the Early Management of Patients with AIS. *Stroke*.

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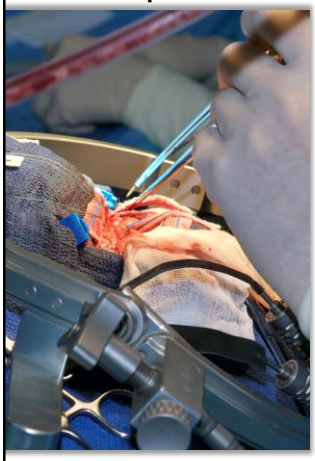
Supratentorial Infarction - Surgical Management



COR	RECOMMENDATIONS
1	**In patients ≤ 60 years of age with unilateral MCA infarctions who deteriorate neurologically within 48 hours from brain swelling despite medical therapy,** **Decompressive craniectomy with dural expansion is beneficial to** • *Reduce mortality AND* • *Improve functional outcome.*

COR	RECOMMENDATIONS
2b	**In patients > 60 years of age with unilateral MCA infarctions who deteriorate neurologically within 48 hours from brain swelling despite medical therapy,** **Decompressive craniectomy with dural expansion may be considered to:** • *Reduce mortality*

American Heart Association.

Abbreviations: MCA indicates middle cerebral artery.

Prabhakaran, S., et al. 2026 AHA/ASA Guideline for the Early Management of Patients with AIS. *Stroke*.

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Antiplatelet Treatment

COR	RECOMMENDATIONS
2a	In patients with minor (NIHSS score ≤5) noncardioembolic AIS or high-risk TIA (ABCD^2 score ≥4) within 24 to 72 hours from stroke onset, or NIHSS score of 4 to 5 within 24 hours from onset, who did not receive IVT, with presumed atherosclerotic cause (≥50% stenosis of intracranial or extracranial stenosis that was likely to have accounted for clinical presentation or acute new infarctions on imaging of presumed large artery atherosclerosis origin), DAPT (clopidogrel and aspirin) for 21 days followed by SAPT is reasonable to reduce the 90-day risk of recurrent stroke.
3: No Benefit	In patients with AIS treated with IVT within 3 hours after symptom onset, adjunctive treatment with IV eptifibatide is not recommended to reduce disability at 3 months.

Abbreviations: AIS indicates acute ischemic stroke; DAPT, dual antiplatelet therapy; IVT, intravenous thrombolytics; NIHSS, National Institutes of Health Stroke Scale; SAPT, single antiplatelet therapy; and TIA, transient ischemic attack.

Prabhakaran, S., et al. 2026 AHA/ASA Guideline for the Early Management of Patients with AIS. *Stroke*.

Rehabilitation in patients with Acute Ischemic Stroke

Road to Recovery

In-hospital

COR	RECOMMENDATIONS
1	In-hospital, formal, interdisciplinary assessment and provision of rehabilitation at a level appropriate for the individual patient is recommended to improve functional recovery.

SSRIs

COR	RECOMMENDATIONS
3 No Benefit	SSRIs are not effective for improving motor recovery or functional status.

High–dose mobilization

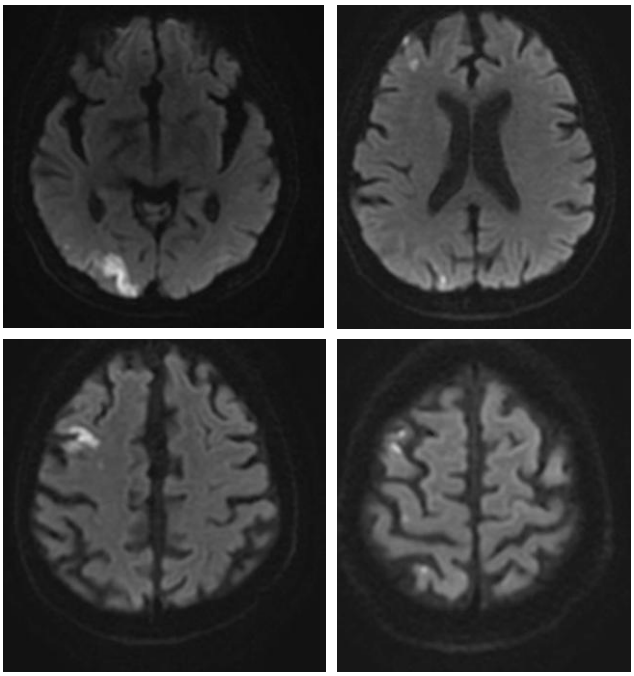
COR	RECOMMENDATIONS
3 Harm	High-dose, very early mobilization within 24 hours of stroke onset is not recommended to improve the odds of a favorable outcome at 3 months and may be harmful.

Abbreviations: SSRIs indicates selective serotonin reuptake inhibitors.

Prabhakaran, S., et al. 2026 AHA/ASA Guideline for the Early Management of Patients with AIS. *Stroke*.

Case Presentation

- 76-year-old with HTN, HLD, tobacco use in remission, COPD presented with acute mental status change, slurred speech, and left facial droop.
- Vessel imaging was negative for hemodynamic stenosis and TTE showed diastolic dysfunction, no regional wall motion abnormalities, mild left atrial enlargement, and no PFO



- In-hospital telemetry was unremarkable and subsequent 2-week cardiac event monitor was also negative for A fib
- BNP while hospitalized was 1071 pg/mL

Embolic Stroke of Undetermined Source (ESUS)

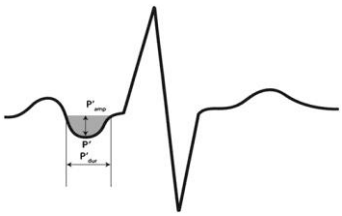
- Non-lacunar
- No proximal arterial source (<50% stenosis)
- No cardioembolic source (A fib, LVT, vegetation, myxoma, etc)
- No other specific known cause (arteritis, dissection, vasospasm)

Potential Causes

- Occult A fib
- Aortic atheroma
- Paradoxical embolism
- Hypercoagulable state
- Unstable atherosclerosis

Atrial Cardiopathy

- Structural/functional changes in the atria resulting in pro-thrombotic condition
- Markers
  - Left atrial enlargement
  - Atrial fibrosis on cardiac MRI
  - Elevated pro-BNP
  - Increased P wave terminal force velocity in lead V1
  - A fib



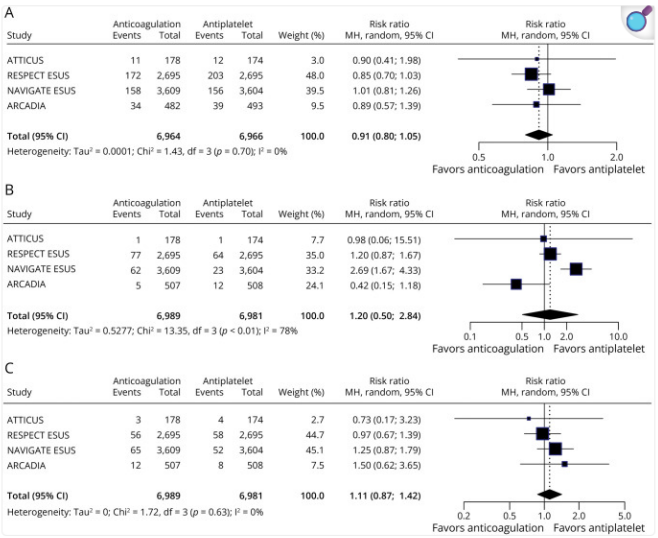
Kamel H, Stroke, 2018; 49(4): 980
Fonseca AC, 2018; 49(3): 734

Role for Anticoagulation?

- Abundant Trial Data
  - RE-SPECT ESUS: Dabigatran vs Aspirin
  - NAVIGATE-ESUS: Rivaroxaban vs Aspirin, stopped early
  - ARCADIA: Apixaban vs Aspirin, stopped early
- Recurrent stroke: 5.4% vs 5.9%, non-significant
- Major bleeding: 2.1% vs 1.5%, non-significant
- Mortality: 1.9% vs 1.7%, non-significant

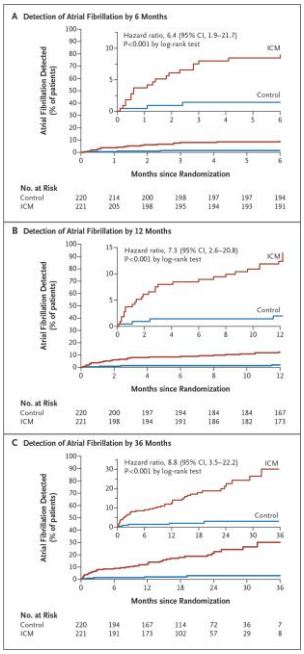
Diener HC, *N Engl J Med*, 2019; 380(20): 1906
Hart RG, *N Engl J Med*, 2018; 378(23): 2191
Kamel H, *JAMA*, 2024; 331(7): 573

Figure 3. Anticoagulation vs Antiplatelet Therapy in Embolic Stroke of Undetermined Source.



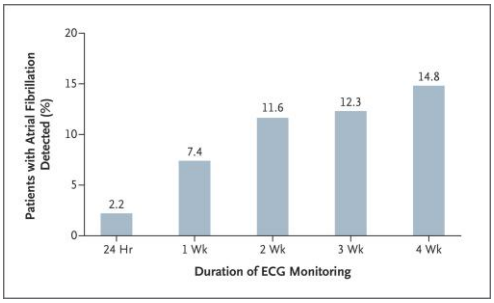
Detecting Atrial Fibrillation

- CRYSTAL-AF
  - Cryptogenic stroke, no AF on initial monitoring
  - Loop recorder vs conventional follow up
  - 8.9% vs 1.4% AF detection at 6 months



Sanna T, *N Engl J Med*, 2014; 370(26): 2478

- EMBRACE
  - Cryptogenic stroke, no AF on initial monitoring
  - 30-day external monitor vs 24-hour Holter
  - 16.1% vs 3.2% AF detection within 90 days



Gladstone DJ, *N Engl J Med*, 2014; 370(26): 2467

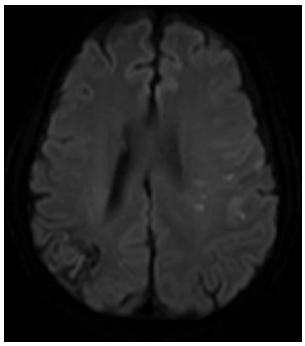
Areas of uncertainty

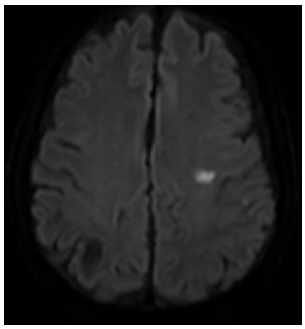
- Duration of A fib
  - <30 seconds?
  - <5 minutes?
- Other atrial tachyarrhythmias
- Historical or provoked A fib

- Guidelines suggest 30 days of monitoring
  - Cryptogenic or suspected cardioembolic stroke
- Consider longer term monitoring after initial 30 days
  - Age>50 years
  - Biomarkers of atrial cardiopathy (left atrial enlargement, atrial fibrosis, elevated pro-BNP, increased P wave terminal force velocity in lead V1)
  - Frequent ectopy (particularly atrial tachycardia) on initial monitoring
  - Family history of A fib
  - Recurrent cryptogenic stroke

Case Continued

- Patient presents with expressive language deficits that developed while flying home from an international trip
- In the ED he is noted to be in A fib/RVR

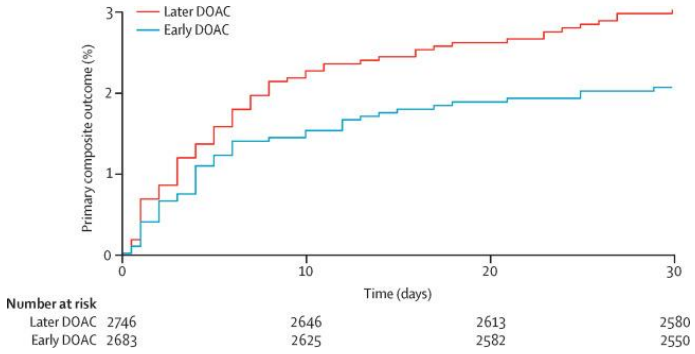




Timing of Anticoagulation

- Earlier evidence suggesting increased risk for early (<4 days) and late (>14 days) anticoagulation initiation
- ELAN, TIMING, OPTIMAS, START trials
- CATALYST meta-analysis
  - Modest reduction in recurrent stroke with early (≤4 days) vs late (>4 days) DOAC initiation (1.7% vs 2.6%)
  - No increase in symptomatic ICH

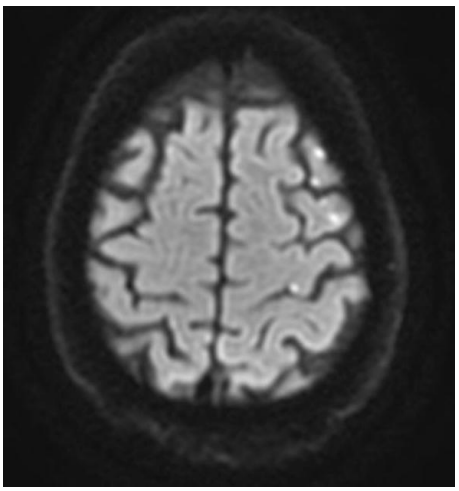
King BT, *Int J Stroke*, 2019; 14(9): 977
Oldgren J, *Circulation*, 2022; 146(14): 1056
Fischer U, *N Engl J Med*, 2023; 388(26): 2411
Werring DJ, *Lancet*, 2024; S0140-6736(24)
Dehbi HM, *Lancet*, 2025; 406(10498): 43



- Specific scenarios
  - Small-moderate stroke: start 24-96 hours
  - Large infarct: start 4-7 days
  - Consider waiting
    - Symptomatic hemorrhagic transformation
    - Uncontrolled HTN
    - Malignant edema
  - Bridging with aspirin, DVT prophylaxis ok

Case Continued

- Patient started on apixaban
- Returns 6 months later with right sided numbness that largely resolved at the time of presentation
- Had been taking apixaban consistently, no other provoking factors



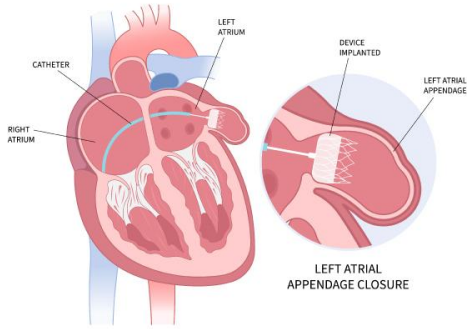
Management of Recurrent Strokes (Anticoagulation Failure)

- Assess for medication adherence, appropriate dosing, drugs affecting DOAC metabolism
- Switch to warfarin or alternative DOAC?
- Add antiplatelet?

- 6-year retrospective cohort study of 46,000 patients
  - 2,900 developed recurrent stroke (~1% annual risk)
  - Switching to warfarin (HR 1.96) and different DOAC (HR 1.62) associated with increased risk of recurrence
  - Addition of antiplatelet did not reduce risk
  - Predictors of recurrent stroke: diabetes, large artery atherosclerosis, taking other cyp450/p-glycoprotein modulators

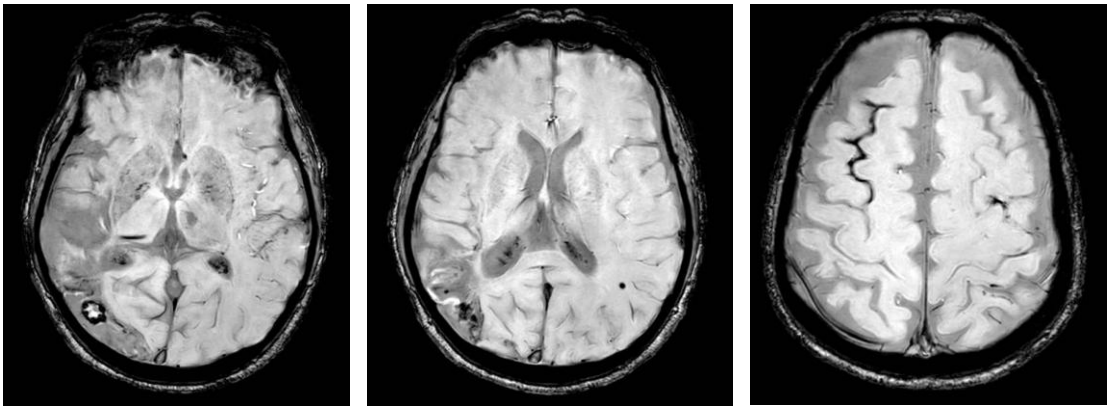
Ip YMB, *Neurology*, 2023; 101(4): e358

- Left Atrial Appendage Closure
  - 2-year observational studies found significantly reduced CE stroke (HR 0.273) with LAAC
  - Rate of recurrence 2.0 per 100 patient-years vs 7.8 per 100 patient-years



Preda A, *Can J Cardiol*, 2026; S0828-282X(26)
Galea R, *Eur J Neurol*, 2025; 32(9): e70365

Case Continuation



- Patient presents to an outside hospital with headache and left arm numbness
- Imaging demonstrates a right parietal ICH, with additional microbleeds and superficial siderosis

Cerebral Amyloid Angiopathy

- Deposition of amyloid beta-peptide
- Sporadic, rare genetic cases (APP), apoe2 and e4 increase susceptibility
- Microbleeds, lobar ICH, convexity SAH/superficial siderosis
- Transient focal neurologic episodes (“amyloid spells”)
- CAA-related inflammation

- Avoiding antithrombotic exposure
  - Warfarin (7-10 fold risk) > DOAC > antiplatelet
  - High risk indications
    - Mechanical valve
    - Life-threating thrombosis (PE, critical limb ischemia, etc)
    - Hypercoagulable state (cancer, APS)
  - Strong consideration for LAAC

Case Conclusion

- Patient underwent successful LAAC
- Remained on apixaban for 6 weeks post-procedure, then DAPT x 6 months after TEE demonstrated well seated device

Summary

- Patients should be rapidly assessed for early IVT and EVT after presenting with AIS symptoms.
- Diagnosis of ESUS should trigger a deeper diagnostic workup for occult A fib and other etiologies, but patients should not be empirically treated with anticoagulation.
- In patients with A fib, consider early initiation of a DOAC unless high risk features are present.
- Consider referral for LAAC if patients develop recurrent stroke despite appropriate anticoagulation therapy but probably don't change anticoagulant therapy.
- Avoid anticoagulation exposure for patients with CAA.

- Questions?