Cardioembolic stroke

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It's been
a rough
week, but
I made
it...How
about you?

Objectives:

- Identify cardioembolic strokes.
- Order appropriate tests.
- Choose the most appropriate therapy.
- Identify patients that may benefit from structural heart therapies.

A 79-year-old man was admitted with a middle cerebral artery infarction confirmed by a CT scan of head. He was in atrial fibrillation and had no contraindications to starting anticoagulation. He made a good early recovery. What is the general recommended time to wait prior to starting anticoagulation therapy for this patient?

-

(A) 1 day
(B) 1 week
(C) 2 weeks
(D) 1 month
(E) 6 months

- Twenty-six million people worldwide experience a stroke each year, making it the second-leading cause of mortality and a leading cause of long-term disability.
- One-third of strokes represent intracerebral or subarachnoid hemorrhage, whereas two-thirds represent cerebral ischemia.
- Cardiac embolism causes more severe strokes than

For an accurate diagnosis, which of the following stroke-associated cardiac conditions requires transesophageal echocardiography (TEE) rather than transthoracic echocardiography (TTE)?

- (A) Dilated cardiomyopathy
- (B) Interatrial shunt
- (C) Left atrial thrombus
- (D) Left ventricular thrombus
- (E) Valvular vegetation

A 60-year-old woman with no past history of venous or arterial thrombosis presents to the ED with acute-onset left hemiparesis. The patient takes lisinopril for hypertension and a daily multivitamin. Brain MRI confirms an infarct in the right frontal lobe. MRA of the head and neck is normal. Cardiac rhythm on Holter monitor is also normal. Hypercoagulability studies are unremarkable.

- **A small patent foramen ovale (PFO) is discovered on echocardiography. Minimal right to left shunting is**
- **seen only on Valsalva maneuver. Which of the following is the most appropriate treatment for this patient?**
- (A) Initiate aspirin 325 mg/day
- (B) Initiate warfarin with a target international normalized
- ratio (INR) of 1.5 to 2.5
- (C) Initiate warfarin with a target INR of 1.5 to 2.5
- and aspirin 81 mg/day
- (D) Initiate warfarin with a target INR of 1.5 to 2.5
- and refer for PFO closure
- (E) Initiate warfarin with a target INR of 2 to 3

Risk Factors for Cardioembolic Stroke

- **Atrial Fibrillation**
- AF is a disorder of heart rhythm that affects 33 million people worldwide. AF is associated with a 3- to 5-fold increased risk of stroke. The prevalence of AF increases sharply from 0.1% among adults aged <55 years to almost 10% -15% among those aged >80 years.
- **Recent Myocardial Infarction**
- Acute myocardial infarction (MI) is a long-established risk factor for ischemic stroke. In case series from the 1980s, 2.5% of patients experienced a stroke within 4 weeks of acute MI.
- Current professional guidelines state that anticoagulant therapy is reasonable for patients with ST elevation MI who have evidence of left ventricular mural thrombus, but only a weak recommendation is given for anticoagulation in patients with anterior apical akinesis or dyskinesis but no evidence of thrombus.

Patent Foramen Ovale

- Patent foramen ovale (PFO) affects ≈25% of the general population and may serve as a passageway for paradoxical embolism from the venous to arterial circulation.
- Patients with an unexplained ischemic stroke more often have a PFO than those with known stroke causes.
- Although PFO may be a common stroke risk factor, it is not a strong one, except perhaps in young stroke patients (<50 years).

Aortic Arch Atheroma

- Approximately 45% of individuals aged ≥45 years harbor atherosclerotic plaque in their aorta, and this has been associated with stroke. Large, ulcerated, noncalcified, or mobile atheromas, which occur in ≈8% of the population, have been particularly linked with stroke. In clinical practice, aortic atheromas may be an under-recognized cause of stroke because the imaging modalities required to detect them, such as transesophageal echocardiography, are not routinely performed in stroke patients.

- **Prosthetic Heart Valves**
- The prevalence of moderate-to-severe valvular heart disease is ≈2.5% in the general population and 12% in those aged ≥75 years. Patients with a mechanical valve have a 4.0% annual risk of stroke, which decreased with the use of oral anticoagulation to 0.8% for aortic valves and 1.3% for mitral valves

Infective Endocarditis

- Infective endocarditis affects ≈1 per 10 000 individuals in high-income settings. It is a relatively uncommon stroke risk factor, but the magnitude of association between infective endocarditis and stroke greatly exceeds that of more common stroke risk factors.
- Approximately 1 in 5 cases of endocarditis are complicated by stroke, and multiple studies have found a >20-fold relative increase in stroke risk in the month after a diagnosis of bacteremia or infective endocarditis.
- Diffusion MRI studies have shown that cerebral microembolisms are present in almost every IE cases.
- Mitral valve involvement is associated with a high risk of stroke, especially if anterior leaflets are infected. SA, candida, and HACEK (*Haemophilus species, Aggregatibacter species, Cardiobacterium hominis, Eikenella corrodens*, and *Kingella species*) group organisms are linked to higher embolism risk.
- Embolism risk increases if the size of left-sided vegetation is greater than 1 cm.
- Stroke frequency is significantly reduced after 2 to 3 weeks of effective IV antibiotic

Other Causes

- There are several rare causes of embolism, such as papillary fibroelastoma, myxoma, and mitral calcification. Each accounts for <1% of cardioembolic strokes.

Diagnostic Criteria for Cardioembolic Stroke

- Although the factors above place patients at an increased risk of cardioembolic stroke, these patients also experience other types of ischemic stroke because of shared risk factors. How can one distinguish a cardioembolic stroke from other etiologic subtypes of ischemic stroke?
- **Clinical Presentation**
- Classically, cardioembolic strokes present with the sudden onset of neurological deficits that are maximal at onset, whereas strokes caused by small-vessel occlusion (lacunar strokes) or large artery atherosclerosis may have a more stuttering course. Cardiac embolism often lodges in distal arteries supplying the cerebral cortex while small-vessel occlusion affects subcortical tissue, so cardioembolic stroke can be differentiated from lacunar stroke by cortical signs, such as aphasia or visual field deficits.
- However, clinical characteristics alone cannot reliably classify the underlying cause of ischemic stroke.Thus, accurate classification also requires integration of neuroimaging, cardiac, and vascular evaluation.

Neuroimaging Profile:

- The vast majority of these cardioembolic strokes involve lesions in a cortical territory. In contrast, lacunar stroke is by definition restricted to a subcortical location.
- About half of cardioembolic strokes involve multiple cerebral arterial territories (ie, both internal cerebral arteries or 1 internal cerebral artery as well as the basilar artery), which distinguishes cardiac embolism from artery-to-artery embolism because of large artery atherosclerosis in the cerebral circulation.

Evaluation:

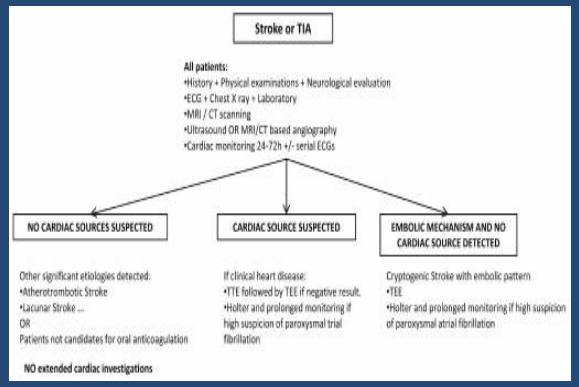
ALWAYS DO:

- Vascular imaging of the extracranial (cervical) carotid arteries to rule out carotid stenosis and Transthoracic echocardiography to rule out high-risk sources of cardiac thrombus.
- a 12-lead ECG to rule out AF or recent MI and inpatient cardiac telemetry or 24-hour Holter monitoring to rule out AF.
- CONSIDER:
- TEE especially in young patients

Prolonged ambulatory monitoring

- For patients with non-lacunar infarcts, long-term monitoring should be considered if no other clear stroke etiology is found. Starting all such patients on a NOAC without confirming the presence of AF does not prevent ischemic strokes better than aspirin alone and poses increased risk of brain hemorrhages by 4 to 6.5 folds

- Monitoring strategies include Holter (24 to 72 hours), mobile cardiac outpatient telemetry devices (up to 4 weeks). These



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Risk factors for Atrial fibrillation

- Older than 60 years of age
- Diabetes
- High blood pressure
- Coronary artery disease
- Cardiomyopathy
- Pericardial inflammation
- Prior Myocardial infarction.
- Congestive heart failure
- Structural heart disease (valve problems or congenital defects)
- Prior open-heart surgery
- Untreated atrial flutter.
- Thyroid disease
- Chronic lung disease
- Sleep apnea
- Excessive alcohol or stimulant use
- Serious illness or infection

Risk scores

- Despite the tendency to overestimate embolic risk, CHA_2DS_2-VASc has become the most commonly used embolic risk score recommended by both European and American AF management guidelines .
- The cutoff score for using OACs in NVAF is ≥1 per European guidelines and ≥2 per the US guidelines; patients with a score of 1 can be managed with either OAC or antiplatelet per the latter.

Stroke risk stratification in non valvular AF

Definition and Scores for $CHADS_2$ and CHA_2DS_2-VASc	Score
$CHADS_2$	
Congestive HF	1
Hypertension	1
Age ≥75 y	1
Diabetes mellitus	1
Stroke/TIA/TE	2
Maximum score	6
CHA_2DS_2-VASc	
Congestive HF	1
Hypertension	1
Age ≥75 y	2
Diabetes mellitus	1
Stroke/TIA/TE	2
Vascular disease (prior MI, PAD, or aortic plaque)	1
Age 65–74 y	1
Sex category (i.e., female sex)	1
Maximum score	9

Annual Stroke Risk

CHA_2DS_2-VASc Score	Stroke Risk %	
0	0	
1	1.3	
2	2.2	
3	3.2	
4	4.0	
5	6.7	
6	9.8	
7	9.6	
8	12.5	
9	15.2	

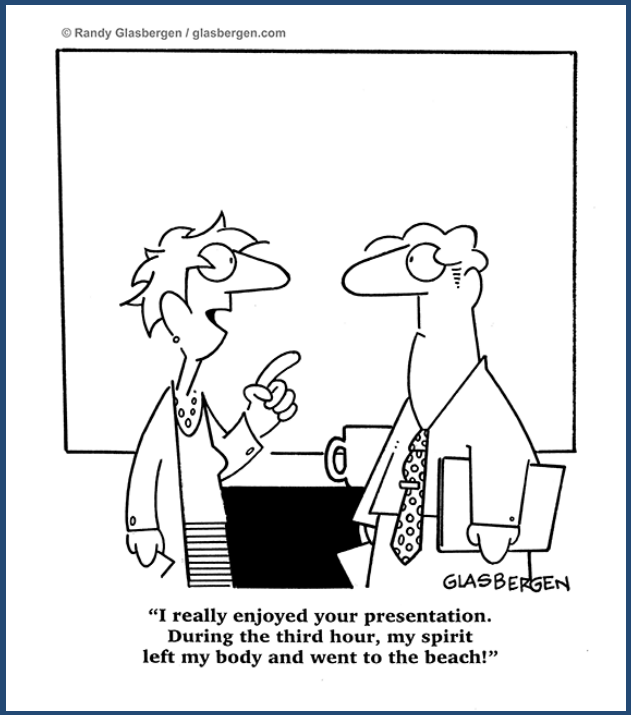
HAS-BLED score

Condition	Points
H - Hypertension	1
A - Abnormal renal or liver function (1 point each)	1 or 2
S - Stroke	1
B - Bleeding	1
L - Labile INRs	1
E - Elderly (> 65 years)	1
D - Drugs or alcohol (1 point each)	1 or 2

HAS-BLED score	Bleeds per 100 patient-years
0	1.13
1	1.02
2	1.88
3	3.74
4	8.70
5	12.5

Note: HAS-BLED has been validated for warfarin, but not for the new anticoagulants.

Pisters R et al. Chest 2010;138(5):1093-1100.



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Vitamin K Antagonists Versus Antiplatelet Drugs

- The mainstay of preventive therapy for cardioembolic stroke is anticoagulation. AF is the most common risk factor for cardioembolic stroke, and in 8 trials involving ≈10 000 patients with chronic nonvalvular AF and no previous stroke, adjusted-dose warfarin therapy significantly decreased the risk of ischemic stroke compared with aspirin (odds ratio, 0.53).

Non Vitamin K antagonist oral anticoagulants (NOACS)

- Since 2008, oral anticoagulant drugs other than vitamin K antagonists have been available. Non–vitamin K antagonist oral anticoagulants (NOACs) work as either direct thrombin inhibitors (dabigatran) or inhibitors of factor Xa (rivaroxaban, apixaban, and edoxaban).
- In randomized trials involving patients with AF, these drugs performed similar to warfarin in regard to ischemic stroke risk) while significantly reducing the risk of hemorrhagic stroke.

What about Subclinical Afib?

- It remains unclear whether patients with subclinical AF would similarly benefit from anticoagulation for stroke prevention. To ascertain the significance of these dysrhythmias, the ASSERT study (Asymptomatic Atrial Fibrillation and Stroke Evaluation in Pacemaker Patients and the Atrial Fibrillation Reduction Atrial Pacing Trial) enrolled 2580 patients with a recently implanted pacemaker or defibrillator, at least 1 stroke risk factor, and no previous AF. Patients with a single episode of AF lasting ≥6 minutes during the first 3 months

What if Afib is ablated?

- For now, guidelines recommend against cessation of anticoagulant therapy after catheter AF ablation.


I don't care if my PowerPoint presentation has 320 slides. You are staying until it's over.

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Left atrial appendage occlusion

Connection Between Non-Valvular AF-Related Stroke and the Left Atrial Appendage

WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

AF Creates Environment for Thrombus Formation in Left Atrium

- Stasis-related LA thrombus is a predictor of TIA[1] and ischemic stroke[2].
- In non-valvular AF, >90% of stroke-causing clots that come from the left atrium are formed in the LAA[3].

1. Stoddard et al. Jim Heart J. (2003)
2. Goldman et al. J Jim Soc Echocardiogr (1999)
3 Blackshear JL Odell JD, Jinnals of Thoracic Surg (1996)

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Everyday Challenges of Oral Anticoagulation

Warfarin

Bleeding risk
Daily regimen
High non-adherence rates
Regular INR monitoring
Food and drug interaction issues
Complicates surgical procedures

Direct Oral Anticoagulants (DOACs)

Bleeding risk
Daily or 2x/daily regimen
High non-adherence rates
Complicates surgical procedures
Limited reversal agents
High cost

83% of patients with AF would be willing to try a different treatment to help reduce their risk of stroke·

[1]National Online Survey conducted by The Harris Poll of more than 200 people (aged 45 and older) living with AF.

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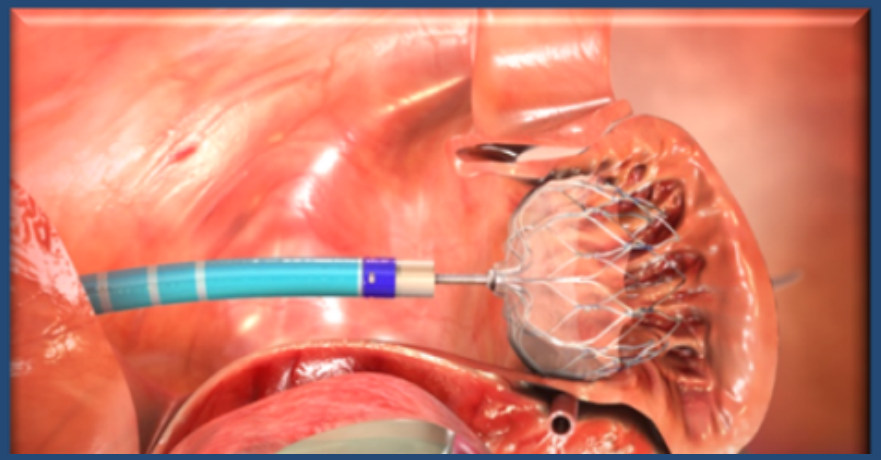
WATCHMAN LAAC Device: A One-Time Procedure

- One-time implant that does not need to be replaced
- Performed in a cardiac cath lab/EP suite by a Heart Team
- Transfemoral Access:
  - Catheter advanced to the LAA via the femoral vein
  - Does not require open heart surgery
- General anesthesia (typical)
- 1 hour procedure (typical)
- 1-2 day hospital stay (typical)



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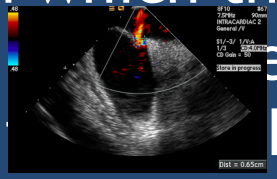
- These patients typically need OAC for 6 weeks after the procedure to prevent device thrombosis, followed by dual antiplatelets for another 4.5 months after which they are maintained on aspirin.

WATCHMAN Patient Criteria

1. Patient has Non-Valvular Atrial Fibrillation (NVAF)
2. Patient has an increased risk for stroke and is recommended for oral anticoagulation (OAC)
3. Patient is suitable for short-term warfarin therapy but deemed unable to take long-term OAC
4. Patient has an appropriate rationale to seek a non-pharmacologic alternative to warfarin.

- **Prosthetic Heart Valves**
- Few data from randomized clinical trials exist to guide therapy for stroke prevention in patients with prosthetic heart valves. On the basis of the available observational data, guidelines provide detailed recommendations for vitamin K antagonist therapy according to the type and position of the replaced valve. The RE-ALIGN trial (Dabigatran Etexilate in Patients With Mechanical Heart Valves), a phase 2 randomized trial of dabigatran versus

PFO and stroke

- The major mechanism of ischemic stroke in the setting of PFO is “paradoxical embolism,” in which the thromboembolic material originating from veins in  eaches the cerebral circulation after passing he PFO.

- In case of PFO and otherwise cryptogenic embolism, PFO should be closed if recurrence occurs despite medical treatment. These patients should continue taking

- PFO closure may be reasonable in some instances after the first embolic episode. Cerebral MRI, obtained during the index stroke, documenting one or more previous embolic (cortical) infarcts, contraindications to use of long-term anticoagulants or antiplatelets and high-risk features of PFO would support PFO closure especially in the young patient with high-flow RLS.

FDA approval

- Based on extended follow-up results of the RESPECT and REDUCE trials, the FDA approved the Amplatzer PFO Occluder on October 28, 2016 and the Gore Cardioform Septal Occluder on March 30, 2018 for PFO closure in the United States “to reduce the risk of recurrent ischemic stroke in patients, predominantly between the ages of 18 and 60 years, who have had a cryptogenic stroke due to a presumed paradoxical embolism, as determined by a neurologist and cardiologist following an evaluation to

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The Risk of Paradoxical Embolism (RoPE) score.

TABLE 1. RoPE SCORE CALCULATOR	
Patient Characteristic	**Points**
No history of hypertension	+1
No history of diabetes	+1
No history of stroke or TIA	+1
Nonsmoker	+1
Cortical infarct on imaging	+1
Age (y)	
18–29	+5
30–39	+4
40–49	+3
50–59	+2
69–69	+1
≥ 70	+0
Total RoPE score	0–10

- Should be reluctant to close a PFO with a score of less than 7.
- Lower scores have a higher risk of recurrent stroke irrespective of PFO closure due to

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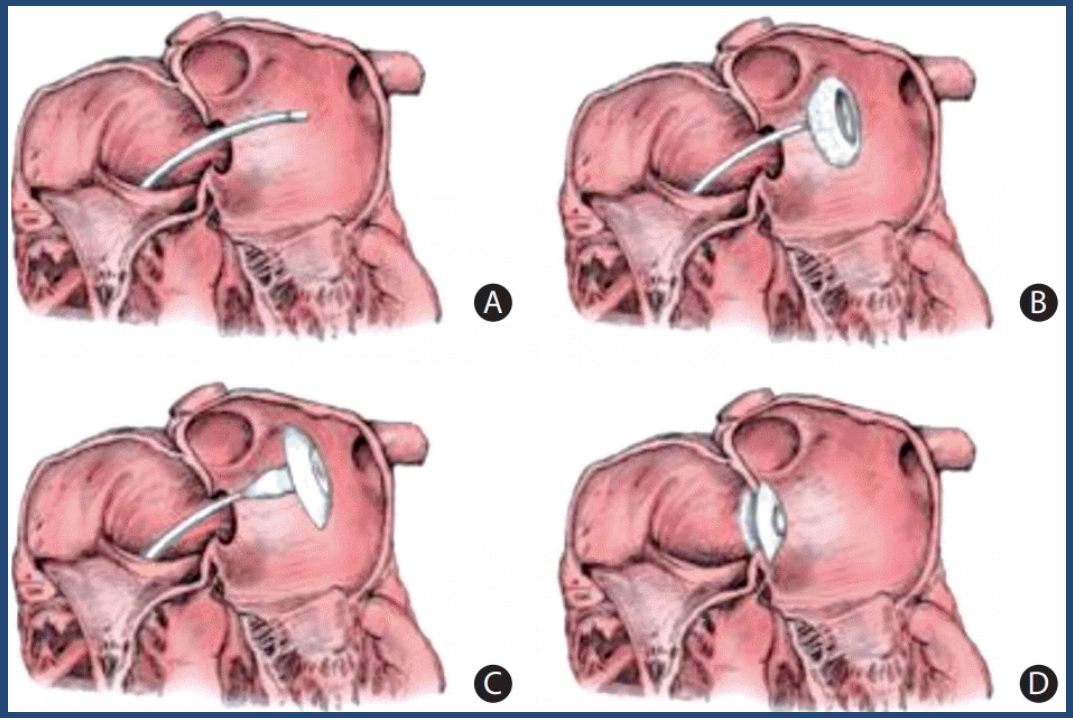
A
B
C
D

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- (C) Initiate warfarin with a target INR of 1.5 to 2.5
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- (D) Initiate warfarin with a target INR of 1.5 to 2.5
- and refer for PFO closure

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