



Heart & Vascular
Center

2024 Northern California Structural Heart Summit



PFO Considerations in Evaluating Cryptogenic Stroke, the Neurologist's Perspective

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Objectives

- Review indications for PFO closure for secondary stroke management
- Define cryptogenic embolic strokes and review appropriate stroke work-up to exclude other causes of stroke
- Explore areas of therapeutic uncertainty in management of stroke/TIA patients with PFO

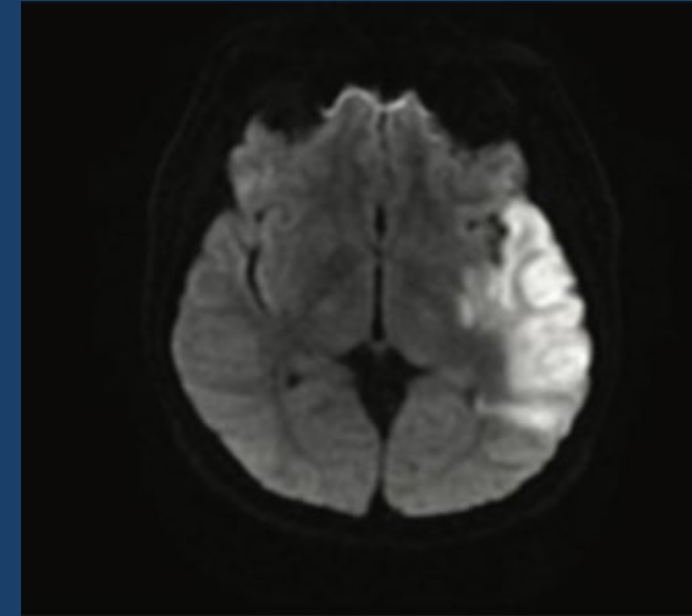


Case Study

40yo man with history of HTN presents with aphasia and R arm weakness, found to have left MCA stroke.

Stroke work-up:

- CTA head/neck: no intracranial stenosis, no carotid stenosis
- Telemetry/Zio patch: no atrial fibrillation
- TTE – **large PFO > 20 microbubbles**
 - BLE duplex with no DVT
- Hypercoagulable work-up negative
- What should be next steps in management?



PFO & Cryptogenic Strokes

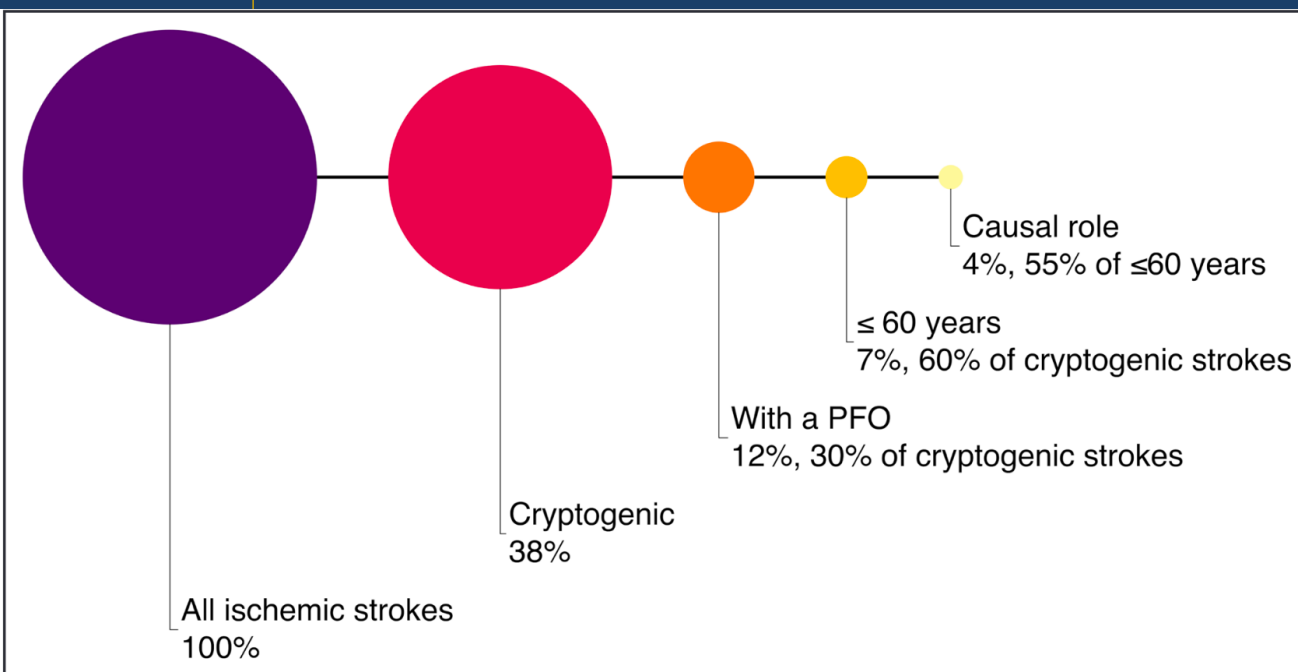


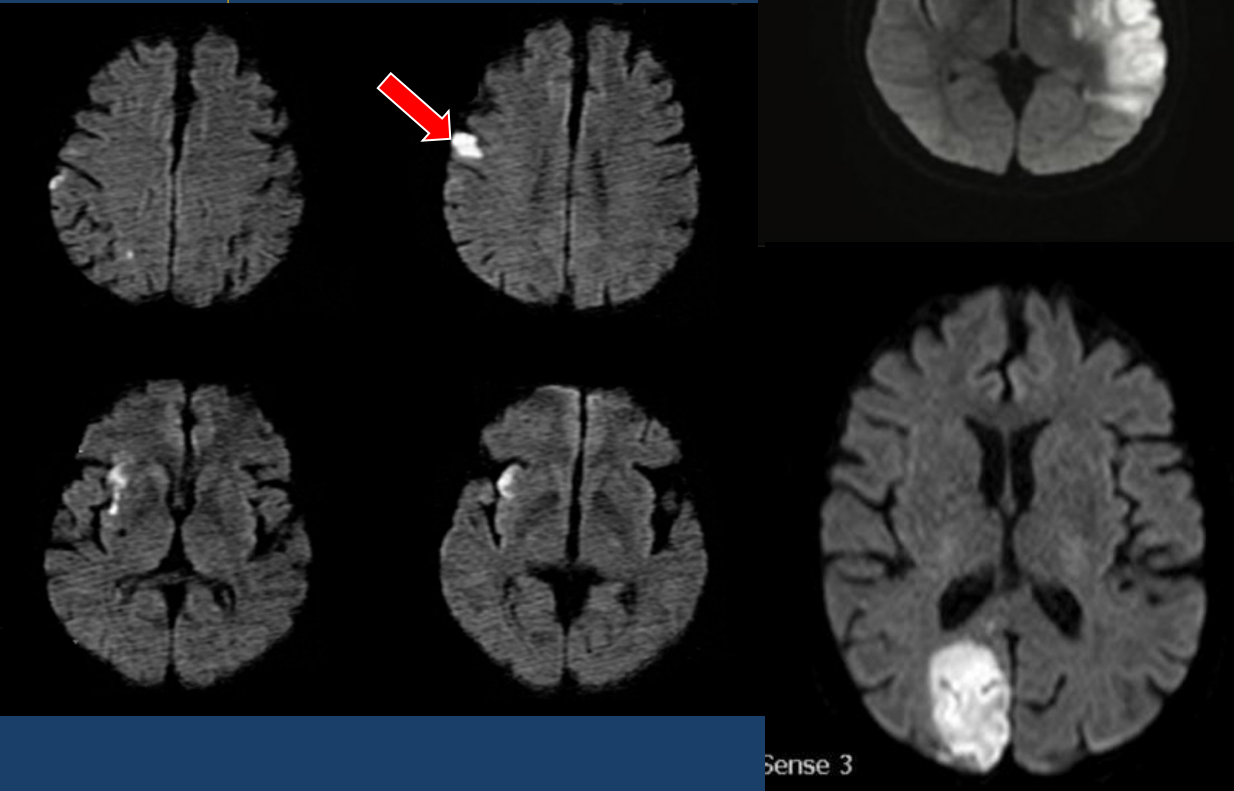
Figure 1. Proportion of ischemic stroke with patent foramen ovale (PFO) as a potential cause.

Proportions are derived from a cohort of 15 239 patients with ischemic stroke from the London Ontario Stroke Registry with complete echocardiograms (unpublished).

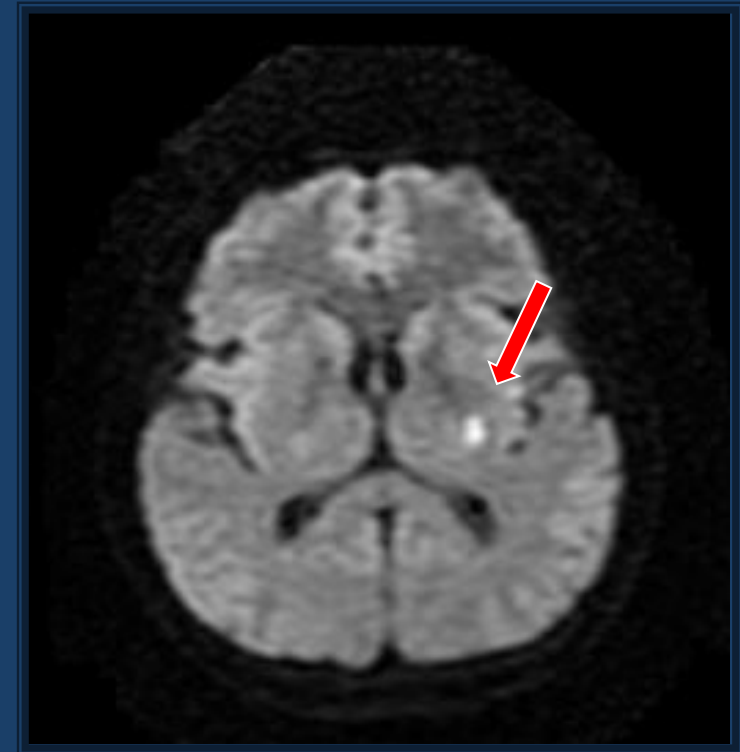
- About 15-25% of adult population has a PFO
- Higher rate of PFOs in patients with cryptogenic strokes
 - Prevalence may be 45% in young stroke patients
- Cryptogenic stroke vs embolic stroke of undetermined source (ESUS)
- PFO-associated Stroke mechanisms:
 - Paradoxical embolism
 - Intracardiac thrombus (within PFO or on atrial septal aneurysm)
- Unclear role of PFO in older patients with stroke

Embololic vs Lacunar Stroke

Embololic



Lacunar (Small vessel)



Sense 3



PFO Closure Trials

Does percutaneous closure of a PFO reduce stroke recurrence risk compared to medical therapy alone?

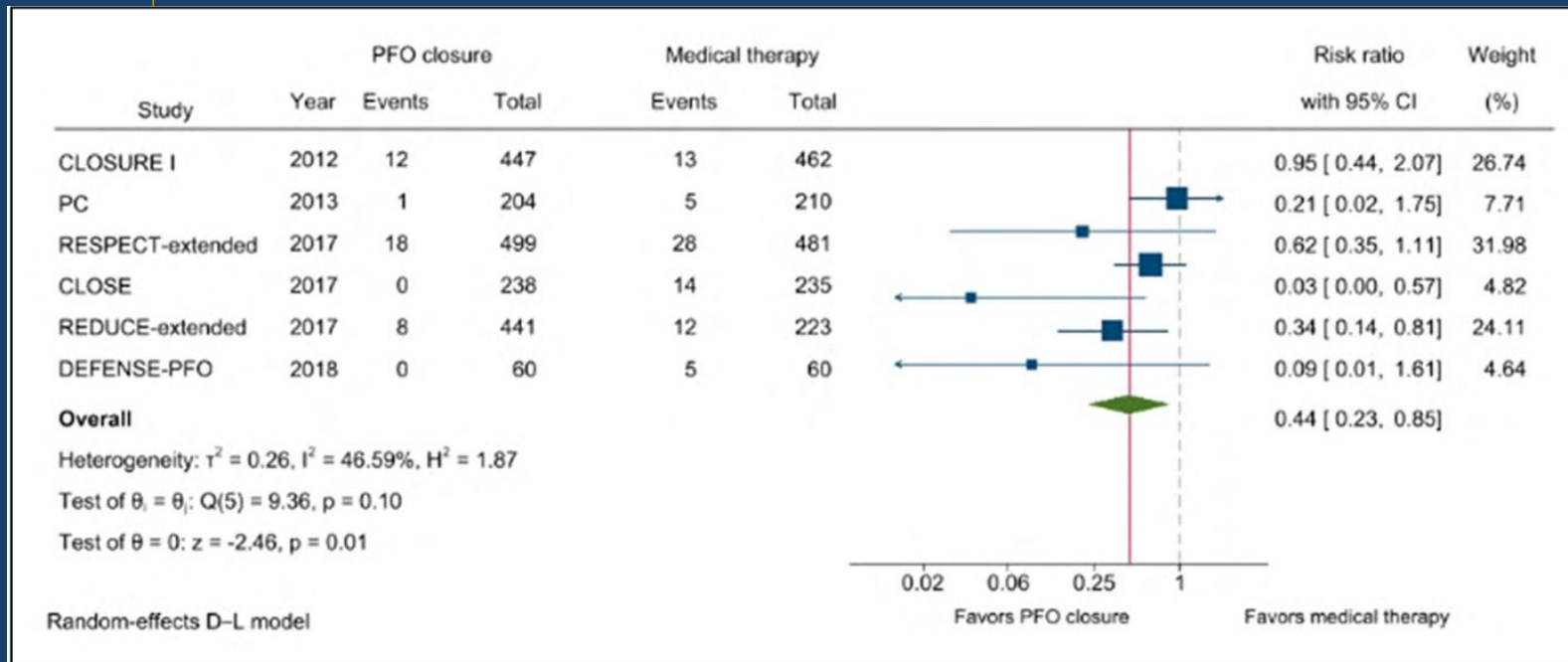


Figure 1. Study-level meta-analysis of randomized clinical trials comparing anticoagulation and antiplatelet strategies in the prevention of recurrent ischemic strokes.

PFO closure moderately reduces risk of recurrent stroke

- RR 59% over 5 years
- ARR 0.62% per year

NNT 32 to prevent 1 stroke over 5 years

There is a small risk of developing atrial fibrillation





Stroke

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<https://doi.org/10.1161/STR.0000000000000375>

AHA/ASA GUIDELINE

2021 Guideline for the Prevention of Stroke
With Stroke and Transient Ischemic Attacks
From the American Heart Association

Recommendations for PFO		
Referenced studies that support recommendations are summarized in online Data Supplements 38 and 39.		
COR	LOE	Recommendations
1	C-EO	1. In patients with a nonlacunar ischemic stroke of undetermined cause and a PFO, recommendations for PFO closure versus medical management should be made jointly by the patient, a cardiologist, and a neurologist, taking into account the probability of a causal role for the PFO.
2a	B-R	2. In patients 18 to 60 years of age with a nonlacunar ischemic stroke of undetermined cause despite a thorough evaluation and a PFO with high-risk anatomic features,* it is reasonable to choose closure with a transcatheter device and long-term antiplatelet therapy over antiplatelet therapy alone for preventing recurrent stroke. ^{552–557}

Patent
Prevention
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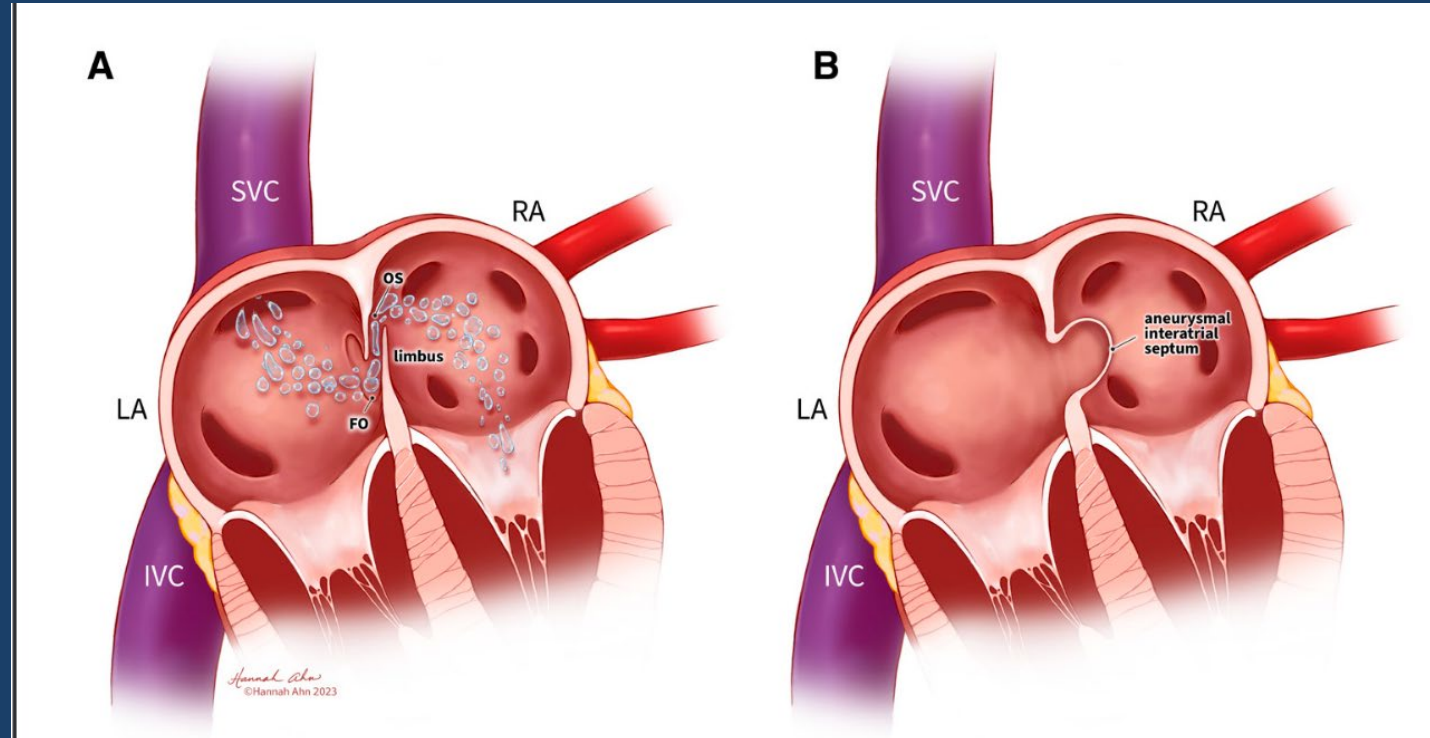
Criteria for PFO closure

- 18-60 year old with embolic stroke of unknown source
- MRI brain or CT head to rule out non-embolic appearing stroke
- Negative work-up for other etiologies:
 - **CTA or MRA head/neck** to rule out atherosclerotic disease, vasculopathy, dissection
 - Prolonged **Cardiac rhythm monitoring** to evaluate for afib (*)
 - **TTE/TEE** showing PFO and NO other cardioembolic source of infarct
 - **Hypercoagulable studies** (i.e. **antiphospholipid antibodies**; prothrombin gene, Factor V Leiden mutation, Protein C/S)



High-Risk PFO Features

PFO Size



Large PFO > 20 microbubbles
Presence of atrial septal aneurysm (ASA)

Who benefits from PFO closure?

Patients aged < 60 years with cryptogenic embolic-appearing infarct and PFO with high-risk anatomic features (i.e. large shunt, atrial septal aneurysm)

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

Table 2. Proposed Flexible Clinical Practice Approach to Classifying Patent Foramen Ovale Causal Association in Patients With Embolic Infarct Topography and Without Other Major Stroke Sources^a

Risk source	Features	RoPE Score	
		Low ^b	High ^b
Very high	A PFO and a straddling thrombus	Definite	Definite
High	(1) Concomitant pulmonary embolism or deep venous thrombosis preceding an index infarct combined with either (2a) a PFO and an atrial septal aneurysm or (2b) a large-shunt PFO	Probable	Highly probable
Medium	Either (1) a PFO and an atrial septal aneurysm or (2) a large-shunt PFO	Possible	Probable
Low	A small-shunt PFO without an atrial septal aneurysm	Unlikely	Possible

Abbreviations: PFO, patent foramen ovale; RoPE, the Risk of Paradoxical Embolism Score.

^a The algorithm in this table is proposed for use in flexible clinical practice, when application of an entire formal classification system is not being conducted.

^b The RoPE score includes points for 5 age categories, cortical infarct, absence of hypertension, diabetes, prior stroke or transient ischemic attack, and smoking. A higher RoPE score (≥ 7 points) increases probability of causal association.

PROBABLE or POSSIBLE associated with substantial net benefit from PFO closure (90% and 62% relative risk reduction respectively)

UNLIKELY: no benefit of PFO closure





Therapeutic Uncertainty: PFO and cryptogenic embolic strokes

- Age > 60 years
- TIA
- Patients with indication for long-term anticoagulation (defined thrombophilia, unprovoked DVT/PE)
- Best antithrombotic therapy (antiplatelet vs anticoagulation) with or without closure



Suggested Diagnostic Algorithm for Selecting Patients for PFO Closure

Neurology AND cardiology evaluation is recommended for cryptogenic stroke patients before PFO closure decision is made

Neurologist:

- Was index event an ischemic stroke?
- Does stroke have features consistent with embolic mechanism?
- Rule out competing causes with comprehensive stroke work-up

Cardiologist:

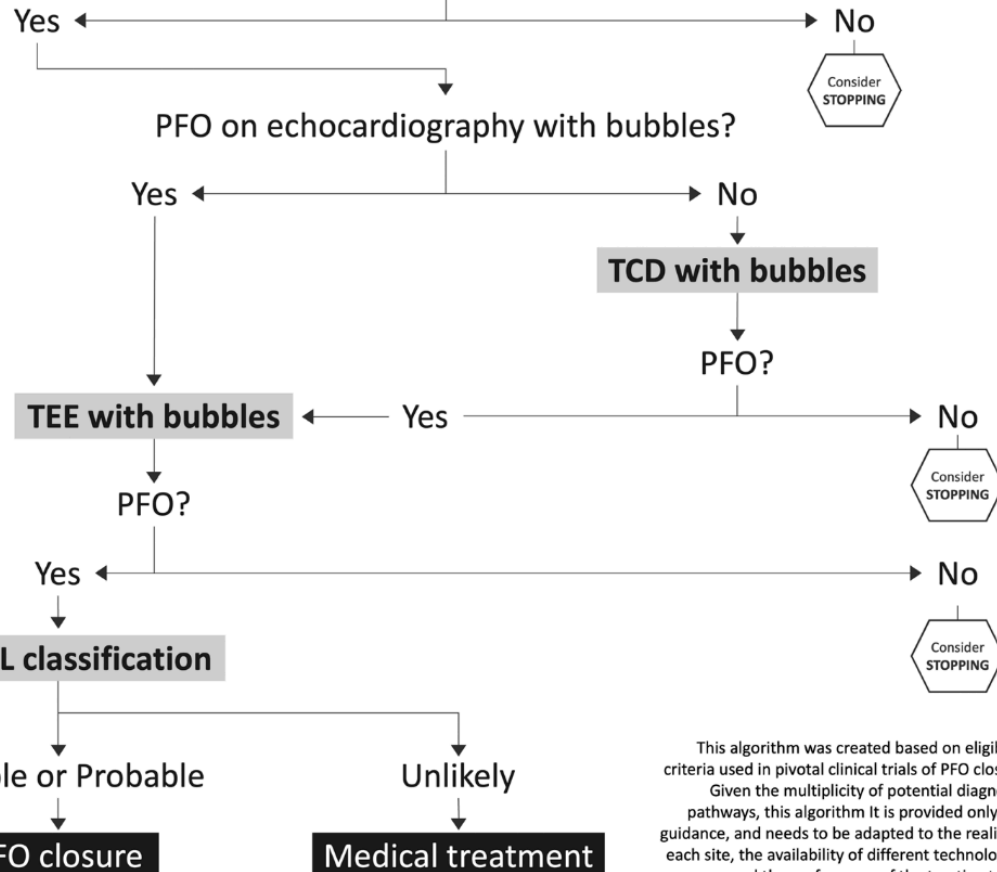
- What are the characteristics of the PFO?
- Assess technical aspects related to procedure

Ischemic Stroke

Basic stroke workup

Brain and intracranial/extracranial vessel imaging, standard of care cardiac monitoring, transthoracic echocardiography. Consider agitated saline injection in <60 years

ESUS (non-lacunar) and < 60 years



This algorithm was created based on eligibility criteria used in pivotal clinical trials of PFO closure. Given the multiplicity of potential diagnostic pathways, this algorithm is provided only as a guidance, and needs to be adapted to the reality of each site, the availability of different technologies, and the preferences of the treating team.

THANK YOU

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