

Patent Foramen Ovale Closure and Stroke

To Do or Not to Do and When to Do

Shirin Jalini, MD, FRCPC
Assistant Professor, Division of Neurology
Dept of Medicine
Queen's University

Top three things to be aware
of for effective stroke
prevention

Hypertension hypertension hypertension

- Hypertension is the number one risk factor for stroke and vascular cognitive impairment
- After stroke, BP needs to be consistently below 140/90 (non-diabetic) and 130/80 (diabetic and ICH patients)
- Combo of ACEi and thiazide/ thiazide-like diuretic is preferred.

DOAC Compliance

- **Medication adherence should be continually assessed and reinforced for patients on all oral anticoagulants at each follow-up visit**

Stroke Disparity

System failure: Women's heart and brain health are at risk

Heart & Stroke report reveals significant inequities persist

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- Women are systemically underscreened and undertreated in modifying recognizable risk factors.
- Lack of education/ awareness regarding **atypical symptoms of stroke** in women, leading to failure to seek timely medical attention.

Case 1

- From Cardiology: “Please assess appropriateness for PFO closure in this patient”
 - “42M with TIA and a PFO. Please see to close PFO.”

PFO and Stroke

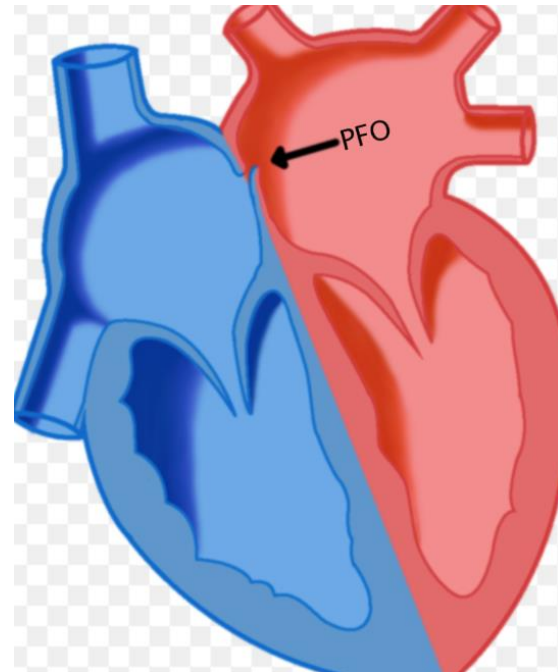
Case 1



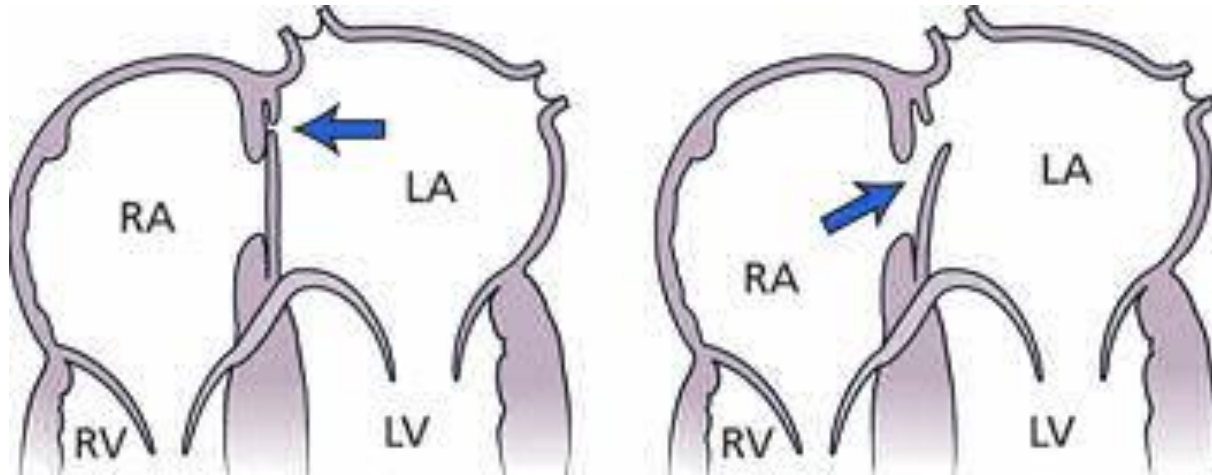
- JM, 42yo M, electrician
- Otherwise healthy, no medication
- 6-weeks ago, he had a spell of word finding difficulties lasting 40minutes.
- CT head: nil acute
- Echo with bubble study: + PFO

PFO Basics.....

and its relation to ischemic stroke

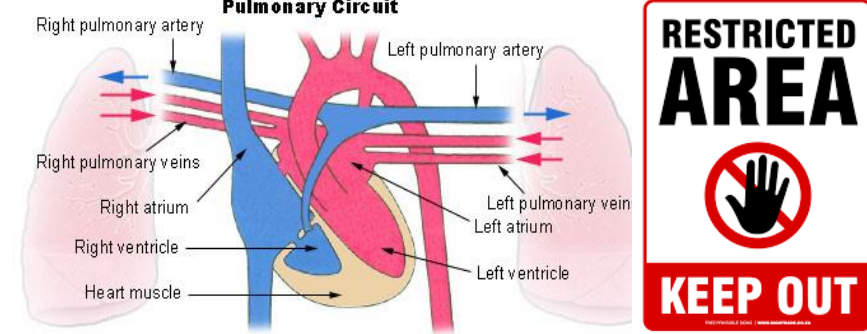


Patent Foramen Ovale



- Found in approximately 25% adults.

PFO-related Stroke: Paradoxical Embolism



- Defined as migration of thrombus from the **systemic venous circulation** to the **arterial circulation** through a right-to-left shunt, leading to stroke, MI or any peripheral embolism
- “Paradoxical” bc venous-origin thrombi are responsible for a systemic arterial thrombotic event.
 - Ordinarily, venous origin thrombi pass through the right heart into the pulmonary circulation and are trapped into the pulmonary arterial-arteriolar-capillary bed
 - Paradoxical embolism occurs when there is a direct connection between the otherwise distinct a-v circulation, such as in PFO

CASE 1

Case 1

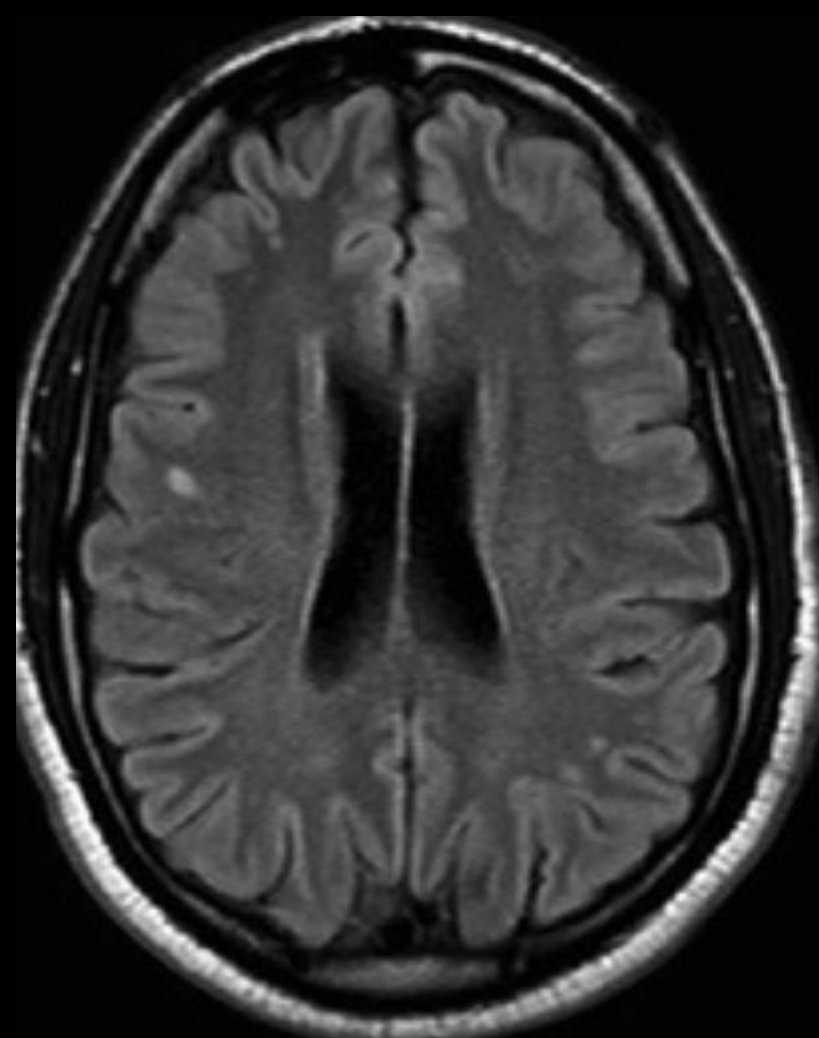
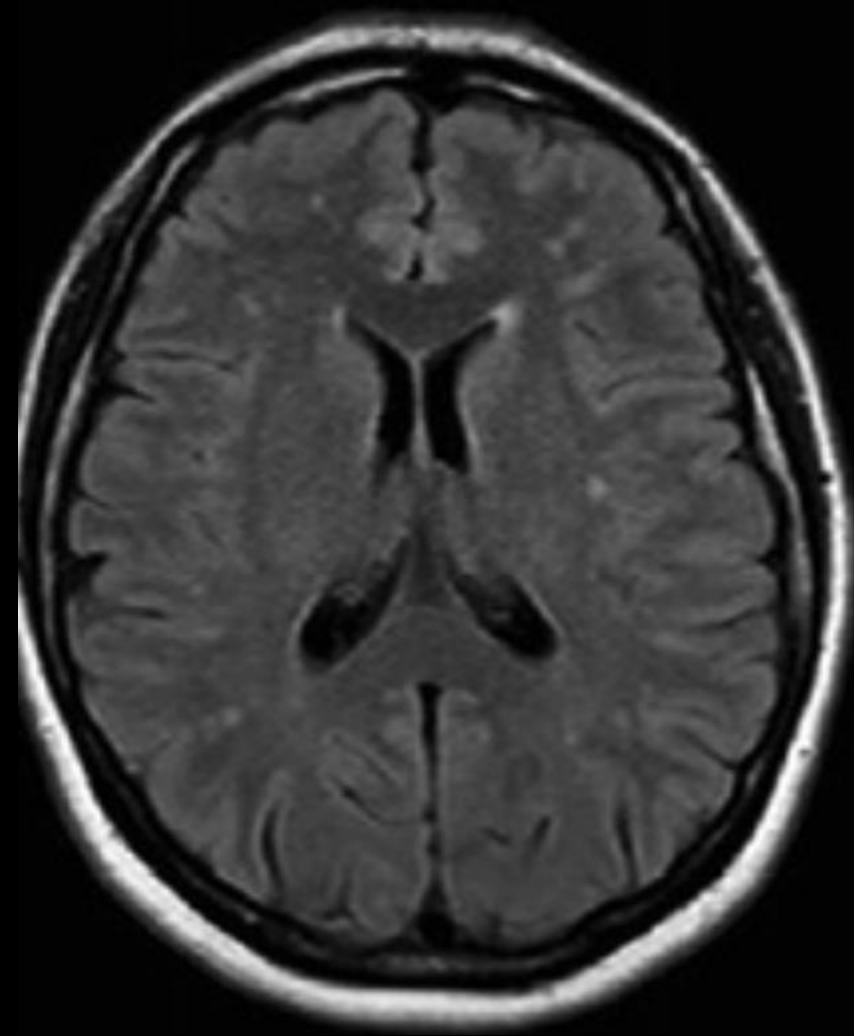
Question 1: Is the spell a vascular event

Case 1

- + headaches in the past (1/mth)
- 2 with visual scotomas
- + Daughter has + migraines

- This episode: began with typical visual scotoma, progressed to stuttering, “foggy head”, very slow to talk, followed by headache.





Case 1

- Patient's spell is most likely consistent with migraine.
- No PFO closure is indicated.
- Reassurance provided.



CASE 2

Case 2

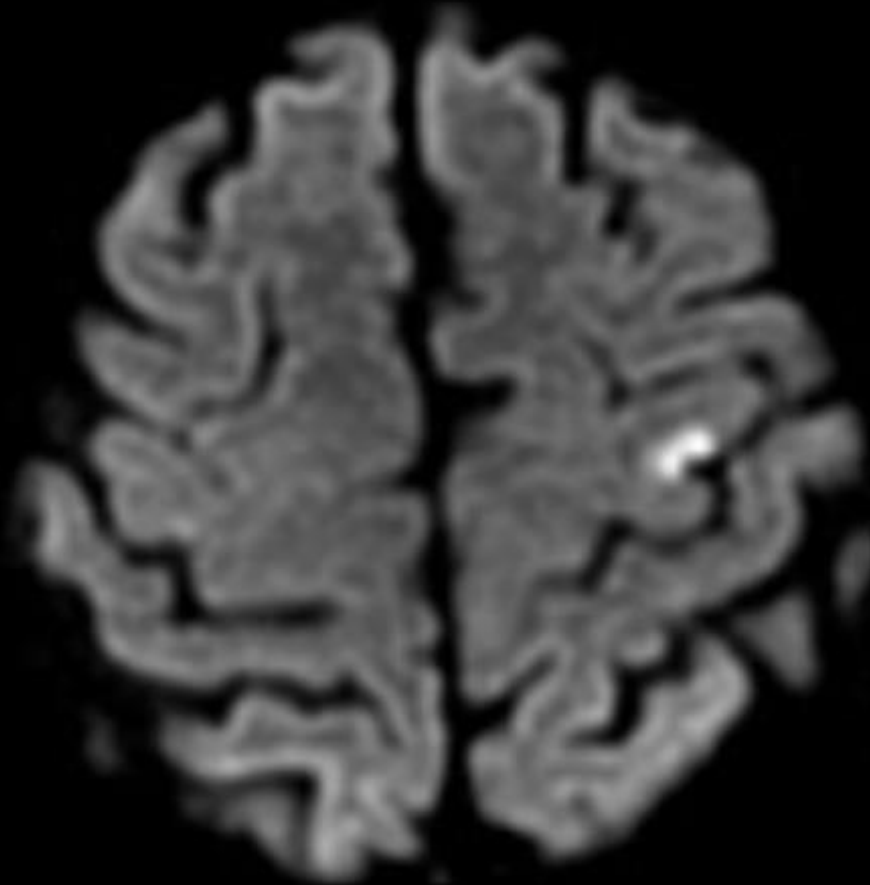
From ED Dept

- 55 year old with 1 hr of R weakness. Exam normal. CT/CTA normal in ED.

Case 2

- SS, 50M, construction worker.
- PMH: Hypertension, DM2, TIA, CAD, Smoking
- 4 days ago, profound right sided weakness, no other deficits. Resolved. No headache





Case 2

- Stroke work-up:
 - **CT angiogram:** No ICA stenosis
 - **Echo:** LVH, Regional wall motion abnormality in the inferior wall. Bubble test + for atrial shunt, consistent with probable PFO
 - **Holter:** No atrial fibrillation
 - **HbA1C:** 7.9%
 - **LDL:** 1.3



Case 2

My patient with stroke has a PFO...now
what?

- In a stroke patient with a PFO, the **principal challenge is to determine if a PFO is a an incidental PFO or a culprit PFO**

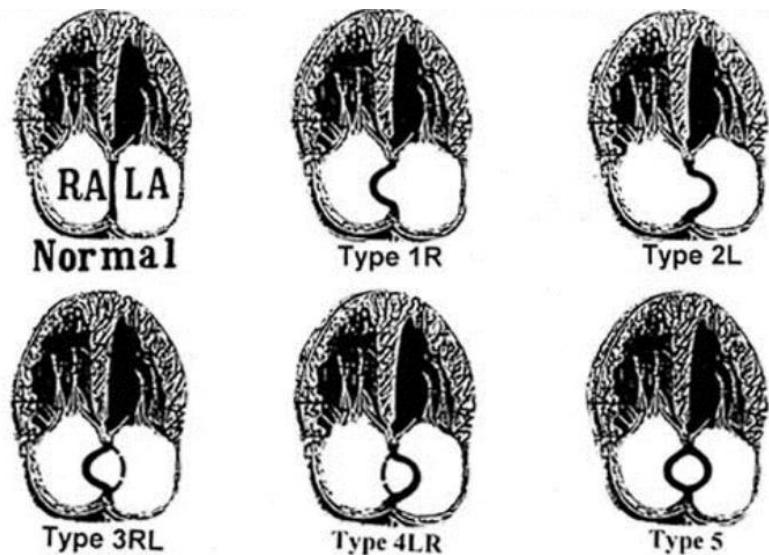
Not all PFOs in stroke need to be closed.

Culprit PFO>> Incidental PFO

- 1) Presence of atrial septal aneurysm**

Presence of atrial septal aneurysm

- The atrial septum is the membrane separates the left and right upper chambers of the heart.
- An atrial septum that bulges and travel abnormally into either or both atria with each heartbeat is considered to have an aneurysm.
- These may potentiate stroke risk ¹⁻² in PFO patients bc:
 - Are associated with larger defect size
 - Hemodynamically facilitate access of venous thromboemboli arriving into the R atrium thru the PFO



1 N Engl J Med. 2001;345(24):1740-1746
2 Stroke 2018;49(6):1541-1548

Culprit PFO>> Incidental PFO

- 1) Presence of atrial septal aneurysm
- 2) Increased right-to-left shunt flow
(permanently or transiently)**

Increased right-to-left shunt flow

- The **greater the volume of right-to-left flow across the PFO, the greater the chance a venous thromboembolus will cross the interatrial shunt** rather than move directly from the right atrium to the right ventricle
- Causes: ¹⁻³
 - PFO Size (larger the size, larger the chances of cross over).
 - Chronic right atrial hypertension
 - Valsalva
 - Mueller maneuver attributable to obstructive sleep apnea.



1 N Engl J Med. 2017;377(11):1011-1021.

2 J Am Coll Cardiol. 2018;71(20): 2335-2342.

3 EuroIntervention. 2019;14(13): 1389-1402.

Culprit PFO>> Incidental PFO

- 1) Presence of atrial septal aneurysm
- 2) Increased right-to-left shunt flow
(permanently or transiently)
- 3) Presence of, or disposition to, venous thrombosis**

Presence of, or disposition to, venous thrombosis

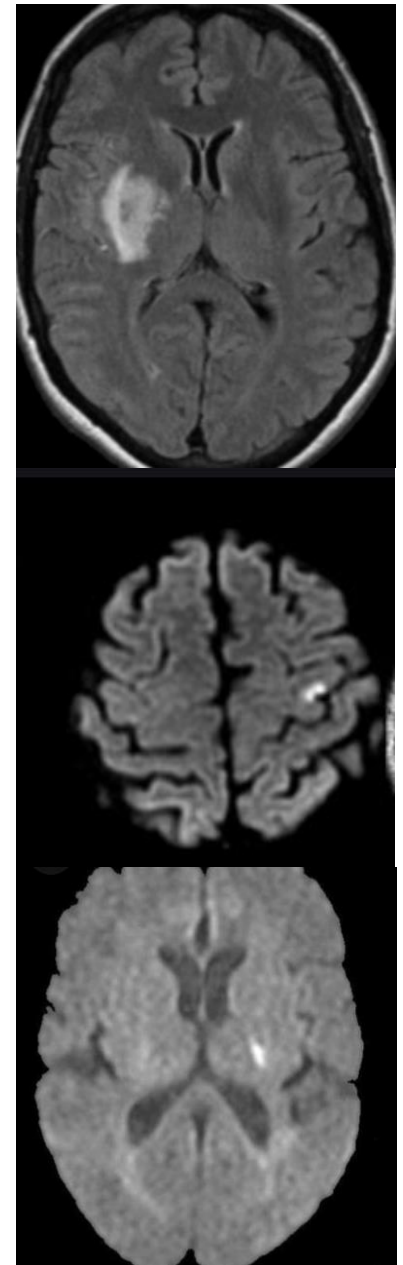
- DVT documented within 3 days of stroke
- Recent immobility
- Dehydration
- Lab findings of venous hypercoag state
- Anatomic causes of venous congestion (may-turner)
- History of previous VTE

Culprit PFO>> Incidental PFO

- 1) Presence of atrial septal aneurysm
- 2) Increased right-to-left shunt flow (permanently or transiently)
- 3) Presence of, or disposition to, venous thrombosis
- 4) **Recipient brain artery or territory typical of embolism.**

Recipient brain artery or territory typical of embolism.

- Typical recipients of emboli within the brain are the **main arterial trunks** (causing large superficial-deep infarcts/large deep infarcts) OR **small distal arterial branches** (causing isolated superficial infarcts)
- Emboli less likely to veer into small, single deep penetrator arteries (isolated small deep infarcts)



Culprit PFO>> Incidental PFO

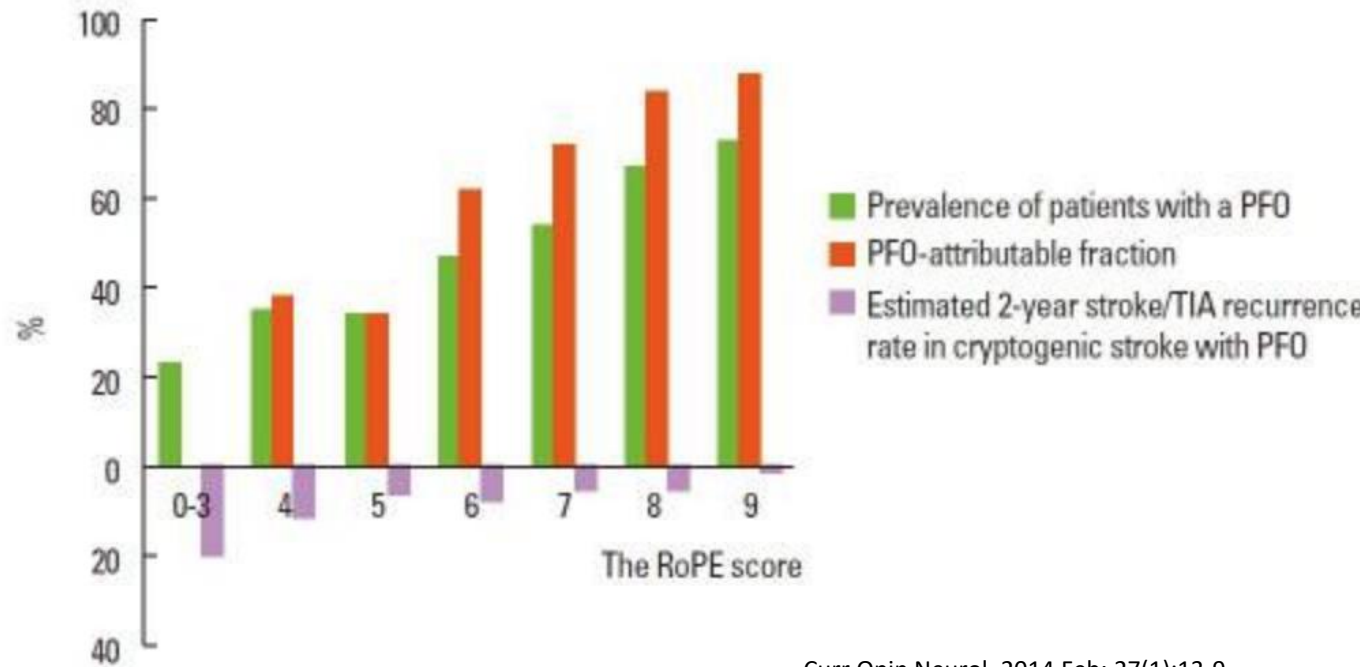
- 1) Presence of atrial septal aneurysm
- 2) Increased right-to-left shunt flow (permanently or transiently)
- 3) Presence of, or disposition to, venous thrombosis
- 4) Recipient brain artery or territory typical of embolism.
- 5) **Absence of risk factors for atherosclerosis**

Absence of risk factors for atherosclerosis

- Mild atherosclerosis is a frequent and competing cause of stroke
- **PFO as a causative mechanism is supported by the absence of demographic and medical-history of atherosclerotic risk factors i.e.**
 - younger patient age
 - absence of hypertension, hyperlipidemia, diabetes, and tobacco use

RoPE SCORE

| Characteristics | 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 (year) | |
| 18-29 | 5 |
| 30-39 | 4 |
| 40-49 | 3 |
| 50-59 | 2 |
| 60-69 | 1 |
| ≥ 70 | 0 |
| Maximum score | 10 |



Curr Opin Neurol. 2014 Feb; 27(1):13-9.

- Highest score: Increased likelihood that PFO is responsible for the stroke. NOT recurrence risk
- The higher the ROPE score, the lower the recurrence risk. Generally, recurrent stroke risk is greater score <5 than >5.

Case 1: ROPE Score if he had a stroke

| | | |
|-----------------------------|--|---|
| History of hypertension | <input checked="" type="radio"/> No +1 | <input type="radio"/> Yes 0 |
| History of diabetes | <input checked="" type="radio"/> No +1 | <input type="radio"/> Yes 0 |
| History of stroke or TIA | <input checked="" type="radio"/> No +1 | <input type="radio"/> Yes 0 |
| Smoker | <input checked="" type="radio"/> No +1 | <input type="radio"/> Yes 0 |
| Cortical infarct on imaging | <input type="radio"/> No 0 | <input checked="" type="radio"/> Yes +1 |
| Age | <input type="text" value="42"/> | years |

8 points

84% chance that stroke is due to PFO.

6% risk of 2 year recurrence of stroke/TIA.



42M
Healthy

Case 2: ROPE Score

| | | |
|-----------------------------|-------|--------|
| History of hypertension | No +1 | Yes 0 |
| History of diabetes | No +1 | Yes 0 |
| History of stroke or TIA | No +1 | Yes 0 |
| Smoker | No +1 | Yes 0 |
| Cortical infarct on imaging | No 0 | Yes +1 |
| Age | 50 | years |

3 points

0% chance that stroke is due to PFO.

20% risk of 2 year recurrence of stroke/TIA.



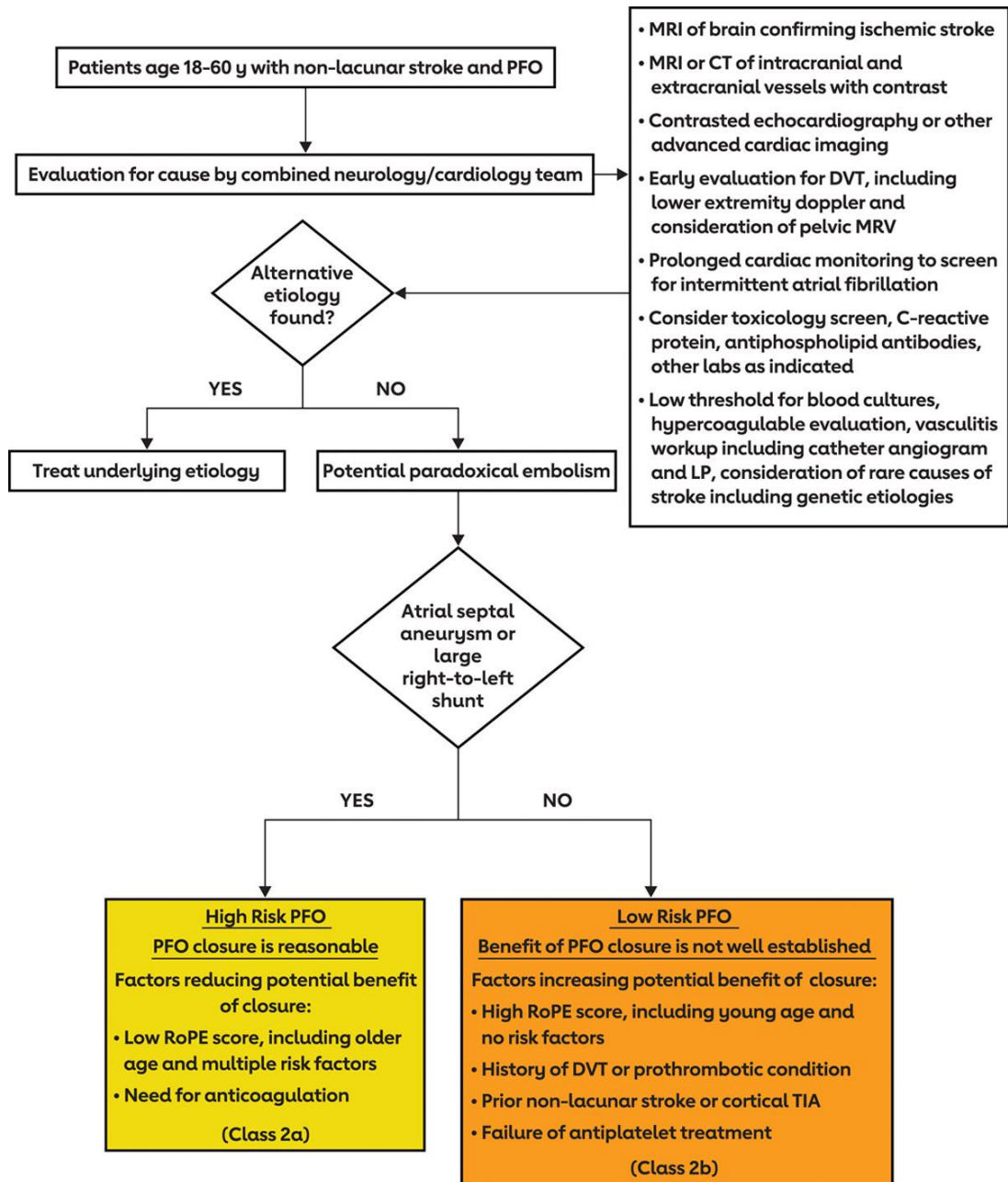
Case 2

- No PFO closure indicated.
- Incidental PFO.
- Dx: Cryptogenic Embolic Stroke
- ASA, secondary prevention of vascular risk factors.



The Role of PFO Anatomical Features

- Over the last couple of years, there is emphasis on anatomical features of PFO to as an important feature for deciding for or against closure.
 - Atrial Septal Aneurysm (ASA)
 - Large Shunt (variably defined in clinical trials, usually >15-20 microbubbles crossing)



Case 3

- 35 yo nurse presents on Code Stroke with acute vertigo, imbalance, slurred speech and left sided dysmetria.
- NIHSS 3.
- CT/CTA normal.
- + IV thrombolysis
- PMH: ADHD
- Meds: vitamins





Case 3



- Stroke Workup
 - No family history of stroke
 - **CTA:** No dissection of vessels, no atherosclerosis, Normal intracranial vessels
 - **TTE:** PFO, **TEE:** PFO with ASA
 - **Leg Doppler:** no DVT
 - **2 week Holter:** No Afib
 - **Drug Screen:** Negative
 - **Arterial hypercoagulable workup:** Negative antiphospholipid antibodies, Jak2 mutation
 - **Venous hypercoagulable workup:** Negative protein C+S, antithrombin, prothrombin, factor 5 Leiden
 - **Infectious and Inflammatory:** Negative blood cultures, Lyme, Syphilis, HIV, ENAs Screen, ANCA, RhF, normal CRP, ESR

Case 3: ROPE score

History of hypertension

No +1

Yes 0

History of diabetes

No +1

Yes 0

History of stroke or TIA

No +1

Yes 0

Smoker

No +1

Yes 0

Cortical infarct on imaging

No 0

Yes +1

Age

35

years

9 points

88% chance that stroke is due to PFO.

2% risk of 2 year recurrence of stroke/TIA.





Patients age 18-60 y with non-lacunar stroke and PFO

Evaluation for cause by combined neurology/cardiology team

- MRI of brain confirming ischemic stroke
- MRI or CT of intracranial and extracranial vessels with contrast
- Contrast echocardiography or other advanced cardiac imaging
- Early evaluation for DVT, including lower extremity doppler and consideration of pelvic MRV
- Prolonged cardiac monitoring to screen for intermittent atrial fibrillation
- Consider toxicology screen, C-reactive protein, antiphospholipid antibodies, other labs as indicated
- Low threshold for blood cultures, hypercoagulable evaluation, vasculitis workup including catheter angiogram and LP, consideration of rare causes of stroke including genetic etiologies



Alternative etiology found?

YES → Treat underlying etiology

NO → Potential paradoxical embolism

Atrial septal aneurysm or large right-to-left shunt



High Risk PFO
PFO closure is reasonable
 Factors reducing potential benefit of closure:

- Low RoPE score, including older age and multiple risk factors
- Need for anticoagulation

(Class 2a)

Low Risk PFO
Benefit of PFO closure is not well established
 Factors increasing potential benefit of closure:

- High RoPE score, including young age and no risk factors
- History of DVT or prothrombotic condition
- Prior non-lacunar stroke or cortical TIA
- Failure of antiplatelet treatment

(Class 2b)

Case 3

- Good candidate for PFO closure.
- Successful percutaneous closure without complications.
- Lifelong ASA.



Summary

- PFO closure in stroke can be confusing!
- It is important to firmly establish the diagnosis of ischemic stroke before looking for PFO.
- A minority of stroke patients with PFO require PFO closure.
- The type of stroke matters! Lacunar versus embolic.
- Patient age and profile matters! Young versus older, risk factors versus no risk factors.
- Anatomical features of the PFO matters! ASA, Large shunt.
- Extensive investigations are required to rule out other etiologies
- We are more than happy to see these patients!

- Thank you!
- Questions?

