Patent foramen ovale: close or not?

Dott.ssa Chiara Pane
Università degli Studi di Napoli Federico II
Patent foramen ovale: PFO

- Prevalence: 27.3% ¹
- Mean size 5 mm
- Large shunt size:
  - atrial septal aneurym ASA (30%)
  - prominent valvula Eustachii
- Diagnosis
  - c-Transthoracic echo TTE
  - c-Transesophageal echo TEE
  - c-Transcranial Doppler TCD

During the strain phase, the interatrial septum bows into the right atrium.
PFO and Stroke risk

- PFO prevalence\(^1\)
  - control 10%
  - stroke with risk factor 21%
  - CRIPTOGENETIC STROKE (25 % of stroke) 54%

- PFO and CRIPTOGENETIC STROKE OD 2.9 (<55 years of age)\(^2\)

- Stronger risk PFO and Atrial Septal Aneurysm (ASA)
  PFO and large shunt size\(^3\)

Cryptogenic stroke

• Ca. 25% (10-40%) of patients with ischemic stroke have no probable cause found after standard workup (TTE, 24-hour Holter monitoring, MRI or CT of the infarct in the brain / neck and brain arteries, blood work).

• Embolic strokes of undetermined source (non lacunar brain infarcts without substantial proximal arterial stenosis or major cardioembolic sources) represent 80 to 90% of all cryptogenic ischemic strokes.

• Occult paroxysmal atrial fibrillation is increasingly recognized as a source of cryptogenic stroke, especially in older patients (>60 y. of age).

• Low risk of recurrence with aspirin: 1-2% per year.

20-30% of healthy population has PFO

20-40% of acute ischemic strokes are cryptogenic

Prevalence of PFO in cryptogenic stroke is around 50%
Pathophysiology: PFO and stroke

• Paradoxycal embolism¹
• “In situ” thrombosis: hypercoagulability more prevalent in patient with PFO and Stroke²
• Dysrhythmia: ASA in associated with atrial fibrillation ³

Pathogenic and incidental PFO
Risk of Paradoxical Embolism (RoPE) score

Figure 1. RoPE score interpretation. A higher RoPE score indicates a higher likelihood that stroke or TIA was related to a PFO and a low likelihood of recurrence. A lower RoPE score indicates a higher likelihood that stroke or TIA was caused by factors unrelated to PFO and higher likelihood of recurrence.

PFO closure and Stroke: 2012-2016

NO PFO CLOSURE INDICATION

- CLOSURE by Furlan et al. 2012
  - 2 years/447 vs 462 patients
  - Therapy group aspirin or warfarin
  - STAR-flex device

- PC by Meier et al. 2013
  - 4 years/204 vs 210 patients
  - antiplatelet or anticoagulant
  - Amplatzer device

- RESPECT by Carroll et al. 2013
  - 2.6 years/499 vs 481 patients
  - antiplatelet or warfarin
  - Amplatzer device

LIMITS

- Treatment group received antiplatelet or anticoagulant according to the physician preference
- Different device used
- Short follow up period
- Variation in baseline risks
Evidence until 2017

CLOSURE OF PFO IN NOT SUPERIORI TO ANTIPLATELET OR ANTICOAGULATION IN PREVENTING RECURRENT STROKE/TIA

Guidelines from International Societies regarding cryptogenic stroke and PFO

- The 2012 American College of Chest Physicians (ACCP) guidelines recommended antiplatelet therapy for patients with CS and a PFO and stated that anticoagulation was not indicated. In patients with CS and PFO who had evidence of DVT, the ACCP guidelines recommended VKA therapy for 3 months and consideration of PFO closure over no VKA or aspirin therapy.

- The 2014 American Heart Association/American Stroke Association (AHA/ASA) guidelines state that there are insufficient data to establish whether anticoagulation is equivalent or superior to aspirin for secondary stroke prevention in patients with PFO. For patients with an ischemic stroke or TIA and a PFO who are not undergoing anticoagulation therapy, antiplatelet therapy is recommended. When anticoagulation is contraindicated, an inferior vena cava filter is reasonable.

- 2016 American Academy of Neurology (AAN) practice advisory state that clinicians should not routinely offer percutaneous PFO closure to patients with cryptogenic ischemic stroke in the absence of another indication for anticoagulation, clinicians may offer antiplatelet medications instead of anticoagulation to patients with cryptogenic stroke and PFO.
PFO closure: 2017 NEWS
PFO closure and Stroke: 2017

PFO CLOSURE INDICATION

- **CLOSE By Mas et al. 2017**
  - 5.3 year/ 238 vs 235 patients
  - only patient PFO and ASA (excursion>10 mm)/large shunt (>30 microbubbles)
  - variety of closure devices
  - anticoagulant more efficacious than antiplatelet
  - \(P = 0.03\)

- **REDUCE by Sondergaard et al. 2017**
  - 3.2 years/ 441 vs 223 patients
  - PFO moderate (6-25 microbubbles) or large (>25 microbubbles)
  - Helex or cardioform septal occluders
  - \(P = 0.002\)

- **RESPECT EXT by Saver et al. 2017**
  - extension of follow-up at 5,9 years of same 980 patients
  - PFO >20 microbubbles
  - Amplatzer device
  - \(P = 0.046\)
Clinical Significance

- PFO is a frequent finding in cryptogenic stroke patients.
- High RoPE scores are associated with a higher likelihood of a causal relationship between PFO and stroke.
- Patent foramen ovale closure is indicated and reduced recurrent stroke/transient ischemic attack compared with medical therapy.
- The estimated absolute risk reduction of stroke recurrence with PFO closure versus antiplatelet treatment is about 1–1.3% per year.
- PFO closure was associated with higher risk of new-onset atrial fibrillation/flutter (1.5-5.9%).
- Meta-analysis indicates that PFO closure is significantly more efficacious in patients with high-risk PFO (moderate to large PFO and ASA\textsuperscript{1}, large shunts\textsuperscript{2} or male gender\textsuperscript{2}).

Flow chart

Cryptogenic stroke
- PFO present

- Age < 60 y.
  - Large shunt or with atrial septal aneurysm
    - PFO closure

- Age < 60 y.
  - Small-moderate shunt
  - RoPE Score > 5
    - PFO closure

- Age < 60 y.
  - Small-moderate shunt
  - RoPE Score ≤ 5
    - Consider PFO closure vs. medical therapy

- Age ≥ 60 y.
  - Medical therapy
Open Questions

- What is the role of ASA and shunt size in determining the benefit of PFO closure?
- Can patients not included over 60 years of age, or those with a competitive cause of ischemic stroke benefit from PFO closure?
- What is the clinical relevance of atrial fibrillation induced by PFO closure?
- What is the optimal duration of antiplatelet therapy following PFO closure?
- What is the role of oral anticoagulants compared with PFO closure?
  
  Meta-analysis of non-randomized studies and the CLOSE trial suggest that oral anticoagulants may be superior to antiplatelet drugs to prevent stroke recurrence in patients with PFO-associated stroke.
- Can any device be better?
  
  Stroke recurrence varied across device type being lower with AMPLATZER PFO Occluder and Helex/Cardioform Septal Occluders.

Every end is a new beginning