CLOSURE ONE:
Is there still room for PFO closure?

Pierre Amarenco
INSERM U-698 and Denis Diderot University - Paris VII
Department of Neurology and Stroke Center
Bichat hospital, Paris, France
Presenter Disclosure Information

Pierre AMARENCO, MD
CLOSURE-1

FINANCIAL DISCLOSURE:
Grants/Research Support: Sanofi-Aventis, BMS, AstraZeneca, Merck, Pfizer

UNLABELED/UNAPPROVED USES DISCLOSURE:
None
PFO in the young

A 25-year-old woman had a long flight from Sydney to Paris. The day after she woke up with a fronto-orbital headache. Self-treatment with a triptan with weak success. In the evening: massive, dense left-sided hemiplegia with total resolution within 2 hours. Work-up negative: TCD, Carotid duplex, MRI, MRA, ECG, no hypercoagulation. TEE: PFO and ASA.

Case study
Stroke of Unknown Cause (SUC) or “cryptogenic stroke”

- 15 million people have a stroke each year (WSO)
- 20% are younger than 60 years (3 M)
- 60% have a stroke of unknown cause (1.8 M)
- 60% of them have SUC + PFO (1.08 M)

→ CLOSURE ONE will have a major impact: there is no need to systematically close PFO in pts with SUC and PFO
CLOSURE ONE: final answer?

- 2 more trials: CLOSE in France and PC-Trial in Switzerland
- Causal link has been demonstrated in anecdotal cases
- Did CLOSURE ONE (and CLOSE and PC-Trial) select cases most likely to be causally related with stroke?
- “cryptogenic stroke” or SUC likely includes a broad range of underlying etiologies that may have diluted the true, causal effect of PFO

Courtesy Prof Ariel Cohen, Paris
SUC is the most difficult diagnosis to make

- Classification into SUC category may include pts with
  - Wrong timing of the diagnostic evaluation: if performed too late after stroke onset, the direct signs of the true cause may have disappeared (e.g., arterial dissection, cardiac/aortic thrombus)
  - Incomplete diagnostic testing
  - Low-grade atherosclerotic stenosis or some small vessel disease on neuro-imaging both deemed unrelated to the ischemic stroke
- SUC pts in CLOSURE-1 may have had underlying etiology different from PFO, decreasing the power of the study to detect an effect of PFO closure in pts with PFO causally related to the stroke
How to improve inclusion criteria

• Definition of SUC is vague: we need positive, clear definition of inclusion criteria

• Select patients with a clinical or neuro-imaging “pattern” of cardioembolic stroke, i.e.
  – cerebral infarctions in both hemispheres
  – or in both anterior and posterior circulations
  – or cerebral infarction plus subdiaphragmatic visceral infarction (frequently silent renal or splenic infarction)

• Complete arterial, cardiac and blood evaluation performed immediately after stroke onset (within days, not weeks)
Conclusions

• CLOSURE-1 showed that in pts with SUC and PFO, there is no need for PFO closure because it is not effective and may be associated with major vascular complications, AF or major bleeding

• These results should now be translated in practice for the million of pts with SUC + PFO

• On a case by case basis, after careful evaluation by a vascular neurologist, there may be some patients for whom closing the PFO can be deemed useful, but these cases are very rare