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Methods

Objective

To assess whether (1) PFO closure with device plus (chronic) antiplatelet therapy on one hand, and (2) oral anticoagulants on the other hand, are superior to antiplatelet therapy, to prevent stroke recurrence in patients 16 to 60 years old with cryptogenic stroke and PFO with atrial septal aneurysm or PFO with large shunt.

Trial design

- Academic-driven, multicenter (32 sites in France and 2 sites in Germany), randomized, open-label, three-arm superiority trial with blinded adjudication of outcome events.
- Funded by the French Ministry of Health.
- 900 patients: 80% power to detect a 50% reduction in the rate of the primary outcome (3.5%/yr in the reference arm) in at least one experimental arm, 5-year study, $\alpha=5\%$.
- 663 patients included from Dec. 2008 to Dec. 2014. Follow-up until Dec. 2016. Mean follow-up 5.3 years (3544 patient-years).

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Key inclusion criteria

- Recent (≤ 6 months) ischemic stroke, confirmed by neuroimaging, mRS ≤ 3
- Strictly defined causes of stroke other than PFO ruled out by appropriate investigations
- PFO with ASA > 10 mm (TTE), PFO with large shunt > 30 microbubbles (TTE, TEE) confirmed by echo core lab before randomization

Key exclusion criteria

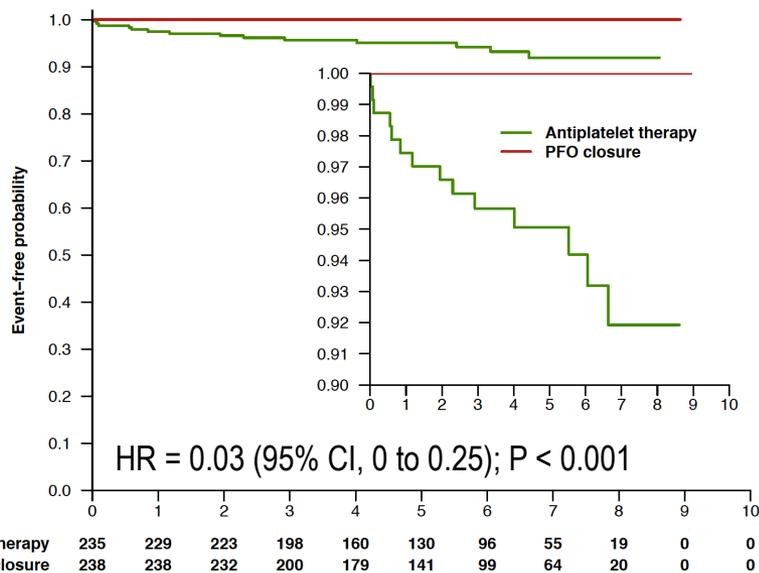
- Contraindication to oral anticoagulants and PFO closure
- Contraindication to antiplatelet therapy
- Increased bleeding risk
- Expected poor compliance or inability to attend follow-up visits
- Anatomical to device placement

Outcomes

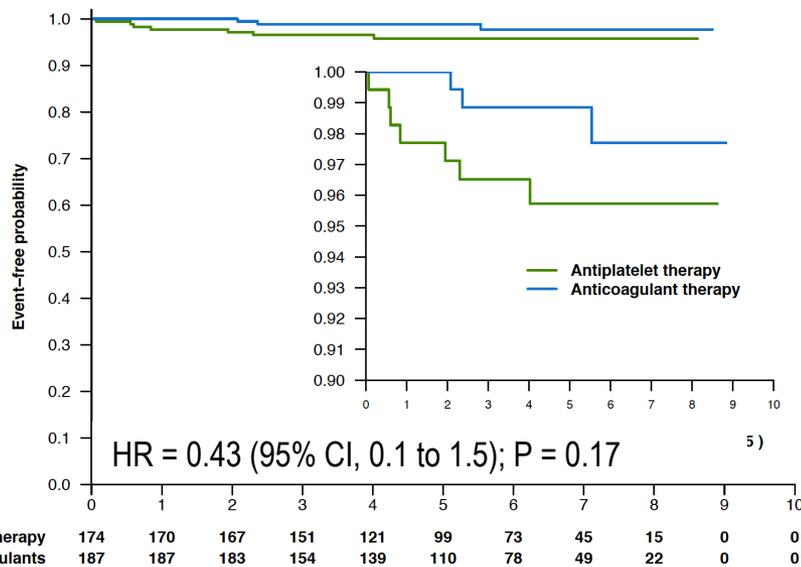
- **Primary** : fatal or nonfatal stroke
- **Secondary** : composite of ischemic stroke, TIA, or systemic embolism, all-cause mortality, vascular death, success of device implantation and success of PFO closure
- **Safety** : major procedural complications and major hemorrhagic complications

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PFO closure vs. Antiplatelet therapy



Oral anticoagulants vs. Antiplatelet therapy



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Conclusion

- PFO closure plus long-term antiplatelet therapy reduced the risk of stroke recurrence in patients 16 to 60 years old with cryptogenic stroke and PFO with atrial septal aneurysm or PFO with large shunt, compared with antiplatelet therapy alone.
- PFO closure was associated with an increased risk of new onset atrial fibrillation.
- Oral anticoagulants did not reduce significantly the risk of stroke recurrence compared with antiplatelet therapy. However, there was a trend pointing toward superiority of oral anticoagulants over antiplatelet therapy.