Clinical Insights

A PUBLICATION DELIVERING CONCISE CLINICAL DATA

AMPLATZER™ PFO OCCLUDER

PFO CLOSURE OR MEDICAL THERAPY IN PATIENTS WITH PFO AND CRYPTOGENIC STROKE - SUMMARY OF A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS[1]

METHODS

This analysis evaluated the relative impact of 3 treatment options for patients aged <60 years with a PFO who had a cryptogenic stroke (CS):

- PFO closure plus antiplatelet therapy (APT)
- APT alone
- Anticoagulation

For this analysis, publications from studies comparing any combination of these therapies were identified by a literature search. Data were evaluated by network meta-analysis to determine the relative treatment impact on key outcomes such as ischemic stroke risk, mortality, major bleeding and other significant safety events.

STUDIES

Data from 8 studies were included (see Table), comparing PFO closure versus APT (n=6), PFO closure versus anticoagulation (n=1), and anticoagulation versus APT (n=3). The CLOSE study included comparisons between all 3 treatment options. The median follow-up duration was 3.9 years. Across the PFO closure studies, the AMPLATZER PFO Occluder was the most frequently used device (used in all patients in the PC Trial, RESPECT and DEFENSE PFO studies and in 52% of patients in the CLOSE study).

STUDIES INCLUDED IN THE ANALYSIS

Study	Number of Patients
PFO closure plus antiplatelet vs antiplatelet therapy	
CLOSURE 1 (Furlan et al., 2012)[2]	909
CLOSE (Mas et al., 2017)[3]	473
PC Trial (Meier et al., 2013)[4]	414
RESPECT (Saver et al., 2017)[5]	980
REDUCE (Sondergaard et al. 2017)[6]	664
DEFENSE PFO (Lee et al. 2018)[7]	120
PFO closure plus antiplatelet vs anticoagulation	
CLOSE (Mas et al., 2017)[3]	353
Anticoagulation vs antiplatelet therapy	
PICSS (Homma et al. 2002)[8]	203
CLOSE (Mas et al., 2017)[3]	361
Shariat et al. (2013)[9]	44

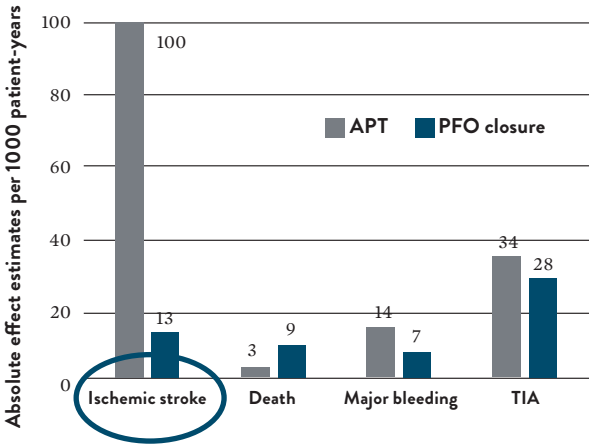
OUTCOMES

Based on data from the included studies, the absolute effect estimates per 1000 patient-years were estimated (see Figure for ischemic stroke, death, major bleeding and TIA) for each of the comparisons between the treatment options. Although several event rates showed numerical differences, the evidence was not always strong enough to conclude that there were probable treatment effects (e.g. due to low event rates and/or indirect evidence). The authors concluded that the following outcomes are associated with probable treatment effects of PFO closure plus APT:

- Ischemic stroke prevention:
  - PFO closure plus antiplatelet therapy probably results in a substantial reduction in the risk of recurrent ischemic stroke compared with APT by ~8.7% over 5 years (Figure A).
  - PFO closure and anticoagulation provide similar ischemic stroke prevention (Figure B).
- Major bleeding:
  - PFO closure probably reduces the risk of major bleeding compared with anticoagulation by ~2% over 5 years (Figure B).
  - PFO closure and APT have similar major bleeding risk (Figure A).
- During the first year, PFO closure plus antiplatelet therapy results in a ~ 1.8% increased risk of persistent atrial fibrillation and a ~ 3.6% increased risk of device-related adverse events compared with APT alone.

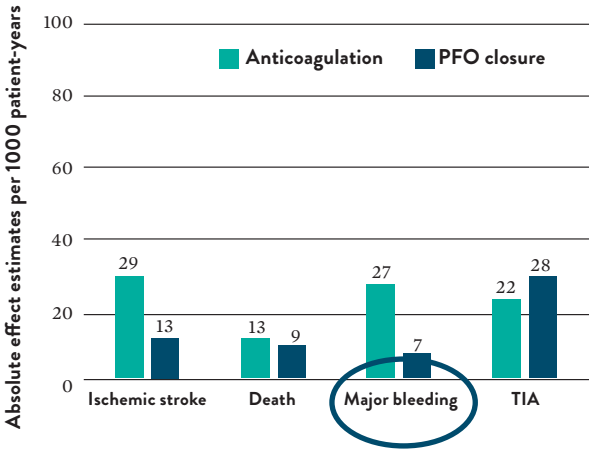
  The analysis did not find differences in the risk of pulmonary and systemic embolism between the treatments.

PFO CLOSURE VERSUS ANTIPLATELET



A

PFO CLOSURE VERSUS ANTICOAGULATION



B

CONCLUSIONS

The study concluded that PFO closure plus antiplatelet therapy in CS patients <60 years has the following effects:

- Compared with APT: A substantial reduction in the risk of ischemic stroke with similar major bleeding risk.
- Compared with anticoagulation: Similar stroke risk with a modest reduction in major bleeding risk.
- A modest risk of persistent atrial fibrillation and device- or procedure-related adverse events compared with APT alone.

REFERENCES

1. Mir H et al. Patent foramen ovale closure, antiplatelet therapy or anticoagulation in patients with patent foramen ovale and cryptogenic stroke: a systematic review and network meta-analysis incorporating complementary external evidence. *BMJ Open* 2018;8:e023761
2. Furlan AJ, Reisman M, Massaro J, et al. Closure or medical therapy for cryptogenic stroke with patent foramen ovale. N Engl J Med 2012;366:991–9.
3. Mas JL, Derumeaux G, Guillon B, et al. Patent Foramen Ovale Closure or Anticoagulation vs. Antiplatelets after Stroke. N Engl J Med 2017;377:1011–21.
4. Meier B, Kalesan B, Mattle HP, et al. Percutaneous closure of patent foramen ovale in cryptogenic embolism. N Engl J Med 2013;368:1083–91.
5. Saver JL, Carroll JD, Thaler DE, et al. Long-Term Outcomes of Patent Foramen Ovale Closure or Medical Therapy after Stroke. N Engl J Med 2017;377:1022–32.
6. Søndergaard L, Kasner SE, Rhodes JF, et al. Patent Foramen Ovale Closure or Antiplatelet Therapy for Cryptogenic Stroke. N Engl J Med 2017;377:1033–42.
7. Lee PH, Song JK, Kim JS, et al. Cryptogenic Stroke and High-Risk Patent Foramen Ovale: The DEFENSE-PFO Trial. J Am Coll Cardiol 2018;71.
8. Homma S, Sacco RL, Di Tullio MR, et al. Effect of medical treatment in stroke patients with patent foramen ovale: patent foramen ovale in Cryptogenic Stroke Study. Circulation 2002;105:2625–31.
9. Shariat A, Yaghoubi E, Farazdaghi M, et al. Comparison of medical treatments in cryptogenic stroke patients with patent foramen ovale: A randomized clinical trial. J Res Med Sci 2013;18: (2): 94–98ST.

Abbott Vascular International BVBA
Park Lake, Culliganlaan 2b, 1831 Diegem, Belgium

Abbott