PATENT FORAMEN OVALE: NOT TO CLOSE

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One quarter of autopsied patients has a probe patent foramen ovale (PFO). The relation between PFO and stroke is still controversial. The PFO-ASA study observed, that only the presence of both PFO and atrial septal aneurysm (ASA) was a significant predictor of a recurrent stroke.The Patent Foramen Ovale and Cryptogenic Stroke Study (PICSS) found no association between the presence of patent foramen ovale alone and recurrent stroke or death and in contrast to the PFO-ASA study, there was no association between recurrent stroke and death in patients with both PFO and ASA. The SPARC (a population-based study) suggested that PFO and large patent foramen ovale were not independent risk factors for ischemic stroke in older subjects. On contrary, a prospective case-control study (500 consecutive patients with a stroke from one institution) demonstrated, that the presence of PFO was significantly associated with cryptogenic strokes in the younger than 55 and older than 55 age groups. Some authors propose that only the co-existence of large PFO (>4 mm), right-to-left shunting at rest, increased septal motility and atrial septal aneurysm are associated with an increased risk of strokes.

Arguments against closing:the PFO prevalence is high in the normal population but the estimated annual risk of cryptogenic stroke in healthy people is only 0.1%. The existing data are conflicting with regards to the relationship between ischemic stroke and PFO making the choice of treatment modalities, especially the surgical options, controversial.

Antiplatelets: the observations of french PFO-ASA study (isolated PFO and a stroke or TIA), support the aspirin therapy (the risk of stroke recurrence was only 2.3% as opposed to 4.2% in the group with no PFO or ASA. The PICSS study did not demonstrate superiority of warfarin to aspirin on the risk of subsequent stroke or death among patients with cryptogenic stroke and PFO.

Invasive interventions: the percutaneous device closure can result in minor complications 7.9% of cases and major complications (death, cardiac tamponade or fatal pulmonary emboli) with 1.5% incidence. The recently published italian PFO closure found that cardiac arrhythmias are frequent.

The CLOSURE-I enrolled 900 patients with cryptogenic stroke or TIA randomized equally to PFO closure using the Starflex device with 24 months of aspirin and six months of clopidogrel or to best medical therapy — aspirin or warfarin or a combination. During two years of follow-up, the cumulative incidence of the primary end point (a composite of stroke or TIA, death during the first 30 days, or death from neurologic causes between day 31 and two years) was not statistically different between the two groups. Of note, different source of stroke, unrelated to paradoxical embolism, was seen in most of the recurrent TIA or strokes in the study. Both major vascular complications and atrial fibrillation, mostly periprocedural, were significantly more common in the intervention group. The device did not offer a greater benefit than medical therapy alone for the prevention of recurrent stroke or TIA. Composite endpoint: device 5.5% medical therapy 6.8%.

At the Transcatheter Cardiovascular Therapeutics 2012 conference, the results of RESPECT (Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment)) trial were summarized. Patients (cryptogenic stroke within the last 9 months) were randomly assigned to either occlusion of the PFO (Amplatzer occluder) or medical treatment with antiplatelet drugs or warfarin. The primary endpoint was nonfatal recurrent stroke, fatal recurrent stroke, and early death after randomization. In this trial 464 pts. were occluded, 481patients received medical treatment. In the RESPECT trial, the 46.6% reduction in the risk of stroke was not statistically significant when assessed in the intention-to-treat analysis. However, when the investigators analyzed the data among patients treated per protocol, the 63.4% reduction in stroke was statistically significant, as was the 72.7% reduction in stroke when analyzed by patients who actually received the device.

The PC Trial included 414 patients also randomized to PFO closure or medical therapy. Patients were included in the study if they were younger than 60 years of age and had a clinically or neuroradiologically verified ischemic stroke or transient ischemic attack with a documented intracranial ischemic lesion. There was a nonsignificant 37% relative reduction in the primary end point of death from any cause, nonfatal stroke, transient ischemic attack, and peripheral embolism.There was also a non-significant 80% reduction in the risk of stroke.

Patent foramen ovale and migraine: a retrospective cohort study of 150 patients with migraine and PFO demonstrated that percutaneous PFO closure resulted in a high rate of migraine improvement, particularly in migraine with aura (34% of patients headache free, and 48% with significant improvement). But the MIST (prospective, double-blind, randomized, controlled, multicenter trial) to evaluate PFO closure with the Starflex device in patients with frequent migraine with aura refractory to 2 types of preventive medication and without a prior stroke or transient ischemic attack showed no difference at 6 months between PFO closure and sham treatment for the primary endpoint of headache cure. Prospective studies assessing the effect of patent foramen ovale closure on migraine headache are underway. The PREMIUM trial is a prospective, randomized, sham-controlled, double-blind, multicenter study to evaluate safety and efficacy of the Amplatzer occluder and standard of care medical treatment compared to standard of care medical treatment only. They are going to involve patients with migraine, with or without aura. The MIST II trial is also a prospective, randomized, sham-controlled, double blind, multicenter study to evaluate safety and efficacy of the Biostar occluder.

In light of the above observations and pending completion of other trials, percutaneous closure of PFO as a preventive intervention for stroke or treatment modality for migraine cannot be recommended.

References

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