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LETTER TO THE EDITORS

Personalized approach as the best treatment strategy in patients after cryptogenic stroke and PFO

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There are convincing data that interventional closure of patent foramen ovale (PFO) reduces the risk of recurrent stroke in patients with previous cryptogenic stroke (newly known also as embolic stroke of undetermined source, ESUS). This approach is supported by new evidence from four trials (RESPECT, REDUCE, CLOSE and DEFENSE-PFO) which showed reduced stroke rates after PFO closure. Pooling the data from these four trials with positive results and two published earlier with not significant results (PC Trial and CLOSURE I), Vukadinović et al. [1] showed that interventional PFO closure results in relative risk reduction (RRR) for recurrent stroke for about 60% compared with antiplatelet/anticoagulant therapy only.

The device used in CLOSURE I trial (StarFlex) is not manufactured anymore. Additionally, patients with lacunar strokes were also included in this trial, in which pathophysiology is more likely based on microatheroma rather than on embolic genesis. Including also patients with lacunar strokes was in variance with other trials. Therefore, excluding the data from CLOSURE I trial seems to be somehow interesting, as this can be viewed as a sensitivity analysis. Running the meta-analysis without the data from this trial, the estimated pooled risk ratio is further reduced from 0.38 (95% CI 0.18–0.82, $p=0.01$, $I^2=55\%$) to 0.27 (95% CI 0.11–0.67, $p=0.005$, $I^2=50\%$). These results convince even more that PFO is a substantial risk factor for recurrent stroke as closing it results in RRR of 73%.

We agree that diagnosis of transitory ischemic attack (TIA) sometimes could represent a challenge due to variable symptoms which could mislead classifying to TIA. Accordingly, TIA definitely does not represent an easy endpoint like stroke. Nevertheless, we considered to combine TIA and stroke, increasing the power of analysis. Furthermore, TIA was also an inclusion criteria used in many of the trials and might be pathophysiologically related to PFO as well.

One concern after PFO closure represents the four to five-fold increased risk of new atrial fibrillation in which patients after stroke requires anticoagulant therapy. According to the design of the trials, patients received single or dual antiplatelet therapy for 3–6 months after occluder implantation. Additional anticoagulant therapy may put these patients at an increased risk of bleeding. However, most cases of new AF from CLOSE trial had an onset shortly after implantation and were of short duration. This implicates that the nature of this AF lies probably in some kind of local inflammation during the endothelialization process rather than in increased filling pressure as in patients with arterial hypertension or heart failure, where AF episodes tend to last longer and had more chronic patterns and probably a higher burden of morbidity and mortality.

Despite convincing results for stroke prevention by PFO closure, a personalized approach in each individual is needed, where the probability that observed PFO might be the passage for embolus should be comprehensively evaluated. A longer screening for occult AF is needed before PFO closure. In trials, all patients were under 60 years of age. The rationale behind this concept was to exclude the presence of advanced atherosclerosis as a competitive mechanism for stroke. Of note, both biological and chronological age should be considered, as one with previous cryptogenic stroke and sign of embolic stroke based on imaging could be 70 years old but without any sign of atherosclerosis, even no plaques detected by ultrasound. Presence of PFO in such a person would strongly suggest PFO closure as the best treatment strategy. Before PFO closure, confirmation of embolic pattern based on imaging should be considered as an obligation. Lack of standardization regarding antiplatelet and anticoagulant therapy among the trials does not allow any conclusion on which treatment strategy should be chosen.

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Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

Reference

1. Vukadinović D, Schirmer SH, Vukadinović AN et al (2018) Interventional closure vs. medical therapy of patent foramen ovale for secondary prevention of stroke: updated meta-analysis. Clin Res Cardiol. https://doi.org/10.1007/s00392-018-1334-z