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Transcatheter closure of patent foramen ovale: an updated meta-analysis of randomized controlled trials

Dear Editor,

The association between patent foramen ovale (PFO) and unexplained cryptogenic stroke has been well established in multiple studies.[1] Over ensuing years, PFO has been considered as a source of the paradoxical thromboembolic phenomenon that could increase the risk of stroke. Closing the shunt between the right and left atrium via transcatheter closure devices was suggested as a treatment to decrease the risk of stroke recurrence. Numerous randomized control trials (RCTs) and meta-analysis compared medical therapy alone (antiplatelet and/or anticoagulation) with transcatheter closure. The majority of these studies favored closure of PFO over medical therapy.[2-9] Initial RCTs such as CLOSURE I, PC, and RESPECT[10-12] did not show significant benefit in reducing stroke recurrence when compared with medical therapy alone. However, the extended follow-up of the RESPECT study, in addition to CLOSE and Gore REDUCE, showed reduction in stroke recurrence with PFO closure combined with antiplatelet therapy compared with medical therapy alone.[13-15] Recently, the DEFENSE-PFO trial was published and we sought to update a recently published meta-analysis [9] to include all of these RCTs.

Using the electronic databases MEDLINE, Embase, and Cochrane Library, we searched for clinical trials that randomized patients with cryptogenic stroke to percutaneous PFO closure versus medical therapy. Two authors extracted the data on patient characteristics and outcomes at the longest follow-up available. The primary efficacy outcome was recurrent stroke. Random-effects risk ratios (RRs) were estimated using a DerSimonian and Laird method. Heterogeneity was calculated using the I^2 test and publication bias using Egger's test. Statistical analyses were conducted using RevMan 5.3.

Six trials met our inclusion criteria with a total of 3560 patients included in the analysis and a mean follow-up of 3.25 years. From 1889 patients in the PFO closure group, 37 (1.9%) had a recurrent stroke compared with 78 (4.6%) patients in the medical therapy group (n = 1,671). This difference in recurrent stroke rate was statistically significant, favoring PFO closure (pooled RR for recurrent stroke = 0.43, 95% CI: 0.30, 0.63, I^2 = 57%, P < 0.0001) [Figure 1]. The occurrence of atrial fibrillation (AF) was reported in all studies. AF occurred in 79 (4.1%) patients in the PFO closure group compared with 12 (0.7%) patients in the medical therapy group (RR = 4.58, 95% CI: 2.47, 8.51, I^2 = 0%, p < 0.0001) [Figure 2].

The findings of this meta-analysis suggest that PFO closure significantly decreased the risk of recurrent stroke in patients with cryptogenic stroke and PFO compared with medical therapy alone. These results are consistent with previously published reports with higher patient numbers and longer follow-up periods. Despite convincing evidence that supports PFO closure, current US practice guidelines did not endorse this practice as of yet.[16] Regardless, PFO closure should be a team approach that includes neurologists and cardiologists, including interventional and congenital cardiologists. Patient selection based on suitable anatomy for PFO closure is an imperative step prior to referring patients for PFO closure. There are several limitations to

Figure 1: Recurrence of stroke in the patent foramen ovale (PFO) closure group compared to medical therapy

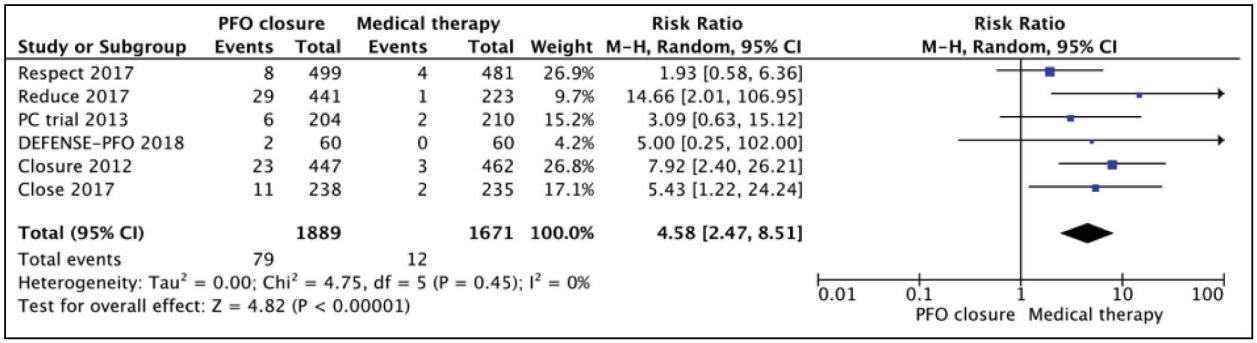

Figure 2: The occurrence of atrial fibrillation (AF)

the current analysis. The medical treatment in the medical therapy group was inconsistent among studies. Some studies used antiplatelet therapy alone whereas others used anticoagulation. Different medical regimens can alter the PFO closure efficacy in preventing recurrent stroke. Another interesting observation is that the PFO closure group had higher risk of AF after PFO closure compared with the medical therapy group. However, this increase in AF did not translate into higher stroke rates. Higher rate of AF could be explained by the mechanical irritation from the PFO closure device of the left atrial wall, which could be due to sizing or deployment problems.

In summary, PFO closure is associated with lower rates of recurrent stroke in patients presenting with cryptogenic stroke and higher rate of AF following the closure. Further studies are required to scrutinize the appropriate medical therapy after PFO closure.

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Conflicts of interest

There are no conflicts of interest.

Fahed Darmoch, Yasser Al-khadra[1], Homam Moussa Pacha[2], Mohamad Soud[2], M Chadi Alraies[3]

Beth Israel Deaconess Medical Center/Harvard, School of Medicine Boston, Massachusetts, [1]Cleveland Clinic Foundation, Cleveland, Ohio, [2]MedStar Washington Hospital Center, Washington, D.C., [3] Wayne State University, Detroit Medical Center, Detroit Heart Hospital, Detroit, Michigan, USA

Address for correspondence: Dr. M Chadi Alraies, Wayne State University, Detroit Medical Center, 311 Mack Ave, Detroit, MI 48201, Phone: +1 (216) 255-0008, E-mail: alraies@hotmail.com

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