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Letter to the Editor

Author's Reply to Cryptogenic Stroke, Patent Foramen Ovale Closure, and Mid to Long-term Outcomes: Rising Shadows of Doubt

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▸ See the letter "Cryptogenic Stroke, Patent Foramen Ovale Closure, and Mid to Long-term Outcomes: Rising Shadows of Doubt" in volume volume 53 on page 648.

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Dear Editor.

We sincerely appreciate the letter by Dell'Angela and Nicolosi[1] for our recently published article regarding a percutaneous patent foramen ovale (PFO) closure after a PFO-associated stroke.[2] They raised the concern about whether percutaneous PFO closure would be beneficial in terms of the safety of PFO closure.

Dell'Angela and Nicolosi[1] emphasized that there is no net clinical benefit based on the results of the recent meta-analysis.[3] Initial three randomized trials (CLOSURE 1, PC, RESPECT) failed to prove the benefits of percutaneous PFO closure for inadequate patient selection (a large number of patients with transient ischemic attacks [TIAs]), a high rate of procedural failure, limited follow-up period and inadequate study design. Percutaneous PFO closure also showed excess complication rates with the procedure in early trials. Therefore, it is not appropriate to conclude that PFO closure has no advantage over medical treatment using the meta-analysis results, including the initial three randomized controlled trials (RCTs). Additionally, in this meta-analysis, the net clinical benefit was defined as the cumulative incidence of stroke/transient ischemic attack, major bleeding, atrial fibrillation (AF)/flutter, or serious procedural and device complications. However, it is questionable whether defining the composite net clinical outcomes by including the AF or flutter is appropriate.

Recent evidence suggests that percutaneous PFO closure increases the risk of new-onset AF, and concern has been raised about this procedure's safety. The risk of AF was found to be device dependent. Risk of AF was not different with the Amplatzer PFO occluder (Abbott, Chicago, IL, USA) (relative risk [RR], 2.10; 95% confidence interval [CI], 0.80–5.56; p=0.13) but was significant with the STARFlex (NMT Medical, Boston, MA, USA) (RR, 7.92; 95% CI, 2.40–26.61; p<0.01).[4] Most cases of AF in the trials occurred early (<45 days) after device implantation and consisted of a single paroxysmal episode that resolved spontaneously, medically, or with cardioversion. Only 3.8% of AF episodes after the procedure were reported to progress to permanent AF.[5] Recently, the long-term risk of developing AF following PFO closure through the Danish nationwide cohort data was reported.[6] The 5-year risk of

Conflict of Interest
Dr. Jung-Sun Kim is a consultant for the Abbott. Oh-Hyun Lee has no conflicts of interest.

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AF was 7.8% (95% CI, 5.5–10) in the PFO closure cohort and 3.1% (95% CI, 2.0–4.2) in the PFO diagnosis cohort. The hazard ratio (HR) of AF comparing PFO diagnosis was 2.3 (95% CI, 1.3–4.0) within the first three months and 0.7 (95% CI, 0.3–1.7) after three months. Therefore, this study suggested that PFO closure was not associated with a substantially increased long-term risk of developing AF beyond the procedure-related short-term risk.

Real-world, long-term outcomes of PFO closure were reported.[7][8] Among a total of 442 patients who underwent PFO closure using Occlutech Figulla Flex II Occluder device (Occlutech GmbH, Jena, Germany), two patients suffered recurrent transient ischemic attack (with no residual R-L shunt detected) after a follow-up of 9.2 years.[7] A total of 4.7% of the cumulative incidence of supraventricular tachycardia (SVT)/AF (2.5% transient SVT/AF during hospitalization and 2.2% for one year after discharge) was shown. Abrahamyan et al.[8] also reported excellent long-term safety and effectiveness outcomes for PFO closure conducted by Amplatzer PFO occluder. Over a mean follow-up of 9.1 (standard deviation, 3.8) years, 4% experienced TIA, 1.5% stroke, and 7.6% AF. The composite outcome of stroke/TIA/death was observed in 10.9% of patients (1.22 events per 100 person-years).[8]

Nevertheless, the safety issue still needs to be resolved entirely in the PFO closure, and we agree with the opinion that well-designated, large, multi-center, and long-term follow-up studies, including strict patient selection, are needed.

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