Editorial / *Editöryal Yorum*

Should we close PFOs?

PFO'yu kapatalım mı?

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Patent foramen ovale (PFO) has the potential for right-to-left shunt, paradoxical embolization and, therefore, ischemic stroke.[1] Additionally, studies have shown that prevalence of PFO in patients with cryptogenic stroke is significantly higher compared to the normal population.[1,2] The association between PFO and increased risk for cryptogenic ischemic stroke is stronger in patients who are younger than 55 years old.[3,4] When there is a coexistent atrial septal aneurysm, the association between PFO and increased risk for ischemic stroke may be stronger.[3,4] Cramer and co-workers[5] have found that young adults with cryptogenic ischemic stroke are more likely to have both PFO and pelvic deep venous thrombosis. Considering these studies, there is strong evidence that young people with PFO are more prone to have ischemic stroke. However, currently, we cannot conclude that closing PFO in patients who have ischemic stroke is clearly beneficial, as evidence from recently-conducted studies reveals no clear benefit of doing so in these patients.[6-8] It is known, then, that PFO has a cause-effect relation with ischemic stroke, while PFO closure has no clear benefit. There may be several mechanisms to explain this discrepancy.

Firstly, we might carefully select certain types of PFO which may have more propensity to cause right-to-left shunt, and therefore ischemic stroke, because PFO which is spontaneously causing large right-to-left shunt may have greater potential to be the culprit. To detect this type of PFO, we should give the contrast medium from a lower extremity vein because PFO can transport the blood coming through the inferior vena cava. It is to be expected that PFO allowing blood passage on provocation is less likely to be a reason for ischemic stroke. However, current evidence suggest that predictors of high risk for recurrence among patients with PFO and cryptogenic ischemic stroke are uncertain. Evidence conflicts regarding the role of an atrial septal aneurysm, and there is little evidence that the size of the PFO defect affects ischemic stroke risk.[9,10]

Abbreviation:

PFO Patent foramen ovale

Secondly, having done thousands of PFO closures, we have realized that a PFO closure device itself might be a source of proarrhythmogenia and thromboembolism. Therefore, advancements in closure device technology may improve the success rate of PFO closure in protecting from ischemic stroke, and newer-generation devices might be less irritating to the atrial wall, thus reducing the rate of atrial arrhythmia following PFO closure.

The last point that needs to be stressed is the potential sources of thromboembolism. If thromboembolism occurs, there must be a thrombus either in the lower extremity veins or in the pelvic veins. Therefore, young patients with cryptogenic ischemic stroke and PFO should be evaluated for lower-extremity or pelvic venous thrombosis before PFO closure. If there is no evidence of deep venous thrombosis, PFO closure may be futile.[11]

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In the current issue of the Archives of the Turkish Society of Cardiology, Ates et al.[12] performed a study included 47 patients (25 female, mean age: 38.7 years), and the authors found that during the follow-up period (mean 14±6.4 months) there were no deaths, strokes, or transient ischemic attacks among the patients. Recently-published studies report that the rate of recurrent ischemic stroke in the medical arms ranged from 0.6% to 1.5% per year.[9-11] It is clear that 14-month follow-up is very short for 47 patients; however, I believe that the authors intend to publish longer duration follow-up results of this study. I particularly wonder about the longer follow-up results of those patients with class-4 right-to-left shunt (6 patients, 12.7%), and those with class-3 shunt (14 patients, 29.8%).[12] Regarding this study,[12] the other point to comment on is the 24-hour Holter monitorization. 24-hour monitorization is usually not sufficient to detect a paroxysmal atrial fibrillation, and cannot rule out the possibility of its occurrence.

To date, 3 randomised controlled studies of transcatheter PFO closure versus medical management have been published.[6-8] All 3 included patients up to 60 years old who had no identified cause for the index event other than paradoxical embolism. Lacunar strokes and transient ischemic attacs were included in the CLOSURE-1 and PC trials, but not in the RESPECT trial. Although the point estimates favored device closure to various degrees in each trial, none of the studies demonstrated a statistically significant finding for their primary end point in an intention-to-treat analysis. Serious procedural complications occurred in 0% to 4.2% of patients who underwent PFO closure in the 3 trials. Subgroup analysis of the RESPECT trial showed a significant benefit for device closure among patients with atrial septal aneurysms or substantial shunts, but these findings were not supported by the CLOSURE 1 trial. The PC Trial also showed no trend for an advantage of device closure among those with atrial septal aneurysms and did not report the subgroup with substantial shunts. AF occurred in 5.7% of CLOSURE 1 patients treated in the device arm, and in 0.7% of medically treated patients.[6-8]

As a result, in the future, investigation of the embolic source, careful selection of patients with PFO and ischemic stroke, and culprit PFO closure with a newer-generation device may result in more effective protection against recurrent thromboembolic cerebrovascular accidents.

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