Patent Foramen Ovale Closure

Mechanical closure of a patent foramen ovale (PFO) without surgery has been possible since 1992 (1). Highly prevalent (2) but usually clinically silent, a PFO can permit right-to-left shunting of deoxygenated blood and, even worse, allow venous system thromboemboli to cross the atrial septum into the systemic circulation. A substantial proportion of apparently "cryptogenic" strokes may result from such an event (3).

Should a PFO be closed if it seems to have caused a stroke? Reasonable as this approach sounds, there are (as always) risks, costs, and benefits to balance. The closure procedure is invasive, expensive, and not without risk. Even if a PFO is found after a stroke, the connection is circumstantial and usually made by excluding other causes.

Such a situation would seem to constitute ideal equipoise, fertile ground for randomized trials. Unfortunately, trials of PFO closure have been very slow to recruit, complete, and appear in the literature. Until recently, their results were not encouraging, and clinical guidelines have not favored closure, except under stringent circumstances, such as after a second stroke despite ongoing oral anticoagulant therapy (4) or if concomitant deep venous thrombosis is present (5).

Two recently published trials may have tipped the balance (6, 7). In the current *Annals*, 2 updated meta-analyses using these trials, as well as 2 earlier studies, make the case that the totality of available data does favor PFO closure to prevent recurrent stroke in patients who, after work-up, are found to have a PFO and no other apparent cause (8, 9).

The 2 *Annals* meta-analyses are similar in many ways but do have differences. They both identify the same 4 trials of PFO closure versus medical therapy and provide brief descriptions of the included trials. The statistical treatments are mostly similar and use random-effects models to derive pooled effect estimates. The articles report different patient numbers, because one of the included trials used a complex randomization scheme that allowed for different types of anticoagulation and the meta-analysis authors chose different subgroups to include. In the end, both reports conclude that recurrent stroke is substantially reduced by closure of the PFO, by an absolute rate of about 3%. The differences in approach between the 2 meta-analyses make their common conclusion that much more convincing.

Adverse events are discussed, although perhaps not to a sufficient degree. Both reports show that the incidence of atrial arrhythmia increases after PFO closure for reasons that are not yet clear. Perhaps the device itself causes atrial irritation, or the observation might be an artifact of increased surveillance in the closure device–treated groups. Information on this outcome is important, because atrial fibrillation and flutter are themselves risk factors for stroke and would, in most cases, mandate oral anticoagulation, negating one of the perceived advantages of PFO closure.

Device-related complications are not mentioned in either report. Although in all 4 trials combined only 4 patients died, all the deaths occurred in the device closure groups. Rarely, PFO procedures may result in cardiac perforation, pericardial tamponade, device migration, or embolization (10). The long-term effects of these devices are not yet known. Device erosion has been reported in patients with atrial septal defect who had closure with similar, although larger, devices (11).

The article by De Rosa and colleagues (9) includes a good description of the poststroke work-up necessary to identify a candidate for PFO closure. These authors also rightly caution that their findings cannot be extrapolated to patients who have not yet had a stroke, even if they might have a predisposing condition, such as a hypercoagulable state. One might add that these results should be even less supportive of prophylactic closure in patients with a PFO discovered incidentally.

Nonetheless, the logic of preventing recurrent stroke in this manner is undeniable. Patients who have had a stroke for which other causes have been ruled out might understandably want the hole closed without waiting for a second event, a factor that undoubtedly has contributed to the difficulty in trial recruitment. However, in view of the results of 4 randomized trials of reasonable size, current guidelines now seem too restrictive. Perhaps it is time to relax this stringency and consider a first embolic stroke with no other demonstrable cause as reason enough to close a PFO.

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