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Author

Tobis, Jonathan M

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Editorial Comment

Putting Cryptogenic Stroke into Perspective

Jonathan M. Tobis, MD

Professor of Medicine, Division of Cardiology, UCLA

Key Points

- In patients who have a cryptogenic stroke and have their PFO closed, the recurrence rate of “cerebral ischemia” is much greater in patients who are older than 55 years.
- Most of these recurrent events (2 strokes and 4TIAs) in the older age group were due to identifiable causes.
- These findings corroborate the long-term results from the RESPECT randomized clinical trial of PFO closure versus medical therapy.

It should come as no surprise, even in the cryptogenic stroke population, that patients are more likely to have strokes as they get older. The question is whether these recurrent strokes in people who have already had one cryptogenic stroke, are due to the usual causes of stroke such as atherosclerosis or atrial fibrillation, or whether patients with a PFO that has not been closed, may be subject to an increased rate of recurrent stroke because of a higher propensity for thrombophlebitis and varicose vein formation with venous thrombosis as people get older.

The accompanying paper is an observational report from 2 centers where a PFO was closed in 458 patients following a cryptogenic stroke or a TIA. The patient population was divided into two groups based on age greater or less than 55 years. They found that the recurrence rate of “ischemia” was higher in the older age group but the numbers are small (6 vs 1 event, but only 2 strokes). Since all of these patients had their PFO closed, the 2 strokes were due to the development of atherosclerosis or atrial fibrillation. The 5 TIAs are harder to classify since it is impossible to distinguish a TIA from a migraine aura. In addition, it is impossible to know whether these predispos-

ing factors were the cause of the primary stroke, and not the presumed paradoxical embolus through their PFO.

In the RESPECT clinical trial, patients were enrolled if they were less than 60 years old at the time of their incident event and there was no apparent cause for the stroke. Long-term follow-up for these patients has been reported in abstract form at TCT 2015. These data also showed that patients were more likely to have a recurrent stroke as they got older. In this regard, the current observational report from Italy is consistent with the data from the RESPECT trial. However, the RESPECT trial was able to probe further because it was a randomized study and separated patients into those who had PFO closure versus those with continued medical therapy. The subsequent stroke event, confirmed by MRI, was adjudicated as to whether the 2nd stroke was due to a known cause such as atherosclerosis or atrial fibrillation, or whether the recurrent event was still cryptogenic. Those patients who did not have their PFO closed were much more likely to have a recurrent cryptogenic stroke compared to the group who had their PFO closed with an Amplatzer occluder.

This observational study from Italy is useful because it emphasizes that stroke of known cause is more likely to occur as patients get older even in the group of patients who had a cryptogenic stroke at an earlier age. But the long-term results of the RESPECT trial goes beyond that and emphasizes that if the PFO was closed, it will decrease the frequency of recurrent cryptogenic stroke presumably due to paradoxical embolism through the patent foramen ovale.

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Conflict of interest: Nothing to report.

*Correspondence to: Dr. Tobis, Jonathan, Emeritus Director of Interventional Cardiology, UCLA, B976 Factor Building CHS, 10833 Le Conte Avenue, Los Angeles, CA 90095. E-mail jtbis@mednet.ucla.edu

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