Cryptogenic Stroke and Patent Foramen Ovale: Matched Cohorts in Observational Studies Remain Matched

To the Editor:

Serena et al\(^1\) are to be congratulated on a comprehensively and carefully conducted trial of the incidence of stroke recurrence in cryptogenic stroke patients with and without patent foramen ovale (PFO). The study showed equal recurrent stroke rates at 2-years follow-up (~6\% in each group).

Unfortunately, however, the conclusion they draw from their study, that patent foramen ovale is not a risk factor for stroke recurrence in this population, is flawed. Moreover, the authors make adverse comments about PFO closure which are not warranted.

What the study, in fact, shows us is that if you take a matched cohort and perform a purely observational study, the cohort remains matched at follow-up. In the CODICIA study, although the groups differed according to presence or absence of PFO, they were matched in respect of the inclusion event—stroke in all cases. There was no difference in treatment between the groups during the study; therefore, it is not surprising that the stroke recurrence rate after 2-years follow-up was equal in both groups.

This meticulously undertaken study therefore unfortunately tells us little about the influence of PFO on recurrent cerebrovascular events. It merely tells us that whatever risks were attributable to PFO in the one group were matched by the risks attributable to “factors unknown” in the (genuinely) cryptogenic other group.

Indeed this phenomenon has already been seen in a large trial. Homma et al\(^2\) assessed cryptogenic stroke patients in the warfarin-aspirin recurrent stroke study. Of 265 patients with cryptogenic stroke, the 2-year stroke recurrence rates were 14.8\% versus 15.4\% for those with and without PFO respectively.

Because it is not possible either to control for or eradicate “factors unknown,” the only study that can currently demonstrate the importance of PFO in stroke recurrence is one which eliminates PFO from half of a randomized cohort. We fully agree with the authors about the importance of randomized trials in this area, and await with interest the outcomes of the recently completed CLOSURE and PC trials.

Disclosures

None.

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