Reply

We thank Drs. Schwerzmann and Meier for their interesting comments on our study (1). However, we disagree with their suggestion of possibly biased results.

In autopsy studies, patent foramen ovale (PFO) prevalence ranged from 15% (2) to 29% (3). Previous data showed that PFOs not detected by high-quality transthoracic echocardiography are smaller and associated with small right-to-left shunts (4); therefore, they are far less likely to be associated with embolic stroke features (5). Moreover, our stroke risk estimates were almost identical to those from the SPARC (Stroke Prevention: Assessment of Risk in a Community) study (6), which used transesophageal echocardiography and reported a PFO prevalence of 24.3%. Therefore, although underdetection of smaller PFOs may have occurred in our study, the hazard ratio (HR) for PFO and ischemic stroke is very unlikely to have been artifactually low because of it.

It was shown that PFO has been associated with stroke not only in the young but also in the elderly (7). In our study, 195 subjects were between the ages of 40 and 59; PFO prevalence in them was 17.4%, and the HR for ischemic stroke did not reach independent statistical significance after adjustment for other stroke risk factors. We mentioned that our results do not exclude the possibility that higher-risk subjects with PFO may exist because of associated cofactors. Younger age could be one of these cofactors, or be more frequently associated with them. However, an independent stroke risk from a PFO in the younger group was not apparent in our study over a follow-up of approximately seven years. As for any study, our results only apply within the context of the study population examined and the duration of follow-up considered.

Among the risk factors included in the same multivariate model with PFO, not reported because of space limitations, increasing age (HR 1.06, 95% confidence interval [CI] 1.03 to 1.09 per year), arterial hypertension (HR 1.89, 95% CI 1.02 to 3.50), and diabetes mellitus (HR 2.93, 95% CI 1.79 to 4.81) were independently associated with ischemic stroke, whereas hypercholesterolemia (HR 0.91, 95% CI 0.56 to 1.49), cigarette smoking (HR 1.06, 95% CI 0.65 to 1.75), and atrial fibrillation (HR 1.90, 95% CI 0.46 to 7.88) were not. With the exception of atrial fibrillation, present in only 2.6% of the study cohort, risk factors appeared to affect the stroke risk in expected fashion. Therefore, there is no reason to believe that this may have been a source of bias in our results.

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