2. Jones EF, Calafiore P, Donnan GA, Tonkin AM. Evidence that patent foramen ovale is not a risk factor for cerebral ischemia in the elderly. Am J Cardiol 1994;74:596–9.
3. Di Tullio M, Sacco RL, Gopal A, Mohr JP, Homma S. Patent foramen ovale as a risk factor for cryptogenic stroke. Ann Intern Med 1992;117:461–5.
4. Sacco RL, Ellenberg JH, Mohr JP, et al. Infarcts of undetermined cause: the NINCDS Stroke Data Bank. Ann Neurol 1989;25:382–90.
5. Homma S, Sacco RL, Di Tullio MR, et al. Effect of medical treatment in stroke patients with patent foramen ovale: Patent Foramen Ovale in Cryptogenic Stroke study. Circulation 2002;105:2625–31.
6. Maisel WH, Laskey WK. Patent foramen ovale closure devices: moving beyond equipoise. JAMA 2005;294:366–9.
7. ClinicalTrials.gov, National Library of Medicine, National Institutes of Health. Evaluation of the STARFlex septal closure system in patients with a stroke or TIA due to the possible passage of clot of unknown origin through a patent foramen ovale (PFO). Available at: http://www.clinicaltrials.gov/ct/show/NCT00201461?order=1. Accessed January 18, 2006.
8. The Internet Stroke Centre Stroke trials directory. Randomized evaluation of recurrent stroke comparing PFO closure to established current standard of care treatment. Available at: http://www.strokecenter.org/trials/TrialDetail.aspx?tid=482. Accessed January 18, 2006.
9. Minneapolis Heart Institute. CARDIA STAR trial: a United States randomized clinical trial of the CARDIA STAR patent foramen ovale closure system. Available at: http://www.mplsheart.com/pages/Research.asp?ID=10&SID=28. Accessed January 18, 2006.

REPLY

The comment by Harper and Haqqani, namely that a patent foramen ovale (PFO) is unlikely to confer a significant mortality disadvantage, indirectly acknowledges that it might. Paradoxical embolism through a PFO can unequivocally have devastating consequences, including death. Hence, even if no significant risk for mortality has yet been proven, people die from it (1). This must suffice to take the matter seriously. If there was a simple vaccination to close the PFO, it would be a world standard. Implantation of a device in the heart, with an inherent risk for mortality as well, needs proof of superiority over the natural course. This proof (or disproof) is subject to time. About 1,000 patients have been randomized between device closure and natural course in a variety of trials in progress. Device implantation should show any disadvantage quite early as its risks are front-loaded. An advantage, however, takes many years to unveil because events from a PFO are fortunately rare (rarer than we initially thought), but not absent. None of the trials has been stopped prematurely, which speaks against a disadvantage without compromising the hope for an advantage of PFO closure.

The theory of selective mortality of the PFO is indeed not in keeping with the finding that the fewer PFOs in the elderly are larger in size (2). The theory of late spontaneous fusion by increasing left atrial pressure with age could explain that. Conversely, there is hard evidence for the first theory (people do die from PFOs) but not for the second. The fact that patients with mitral stenosis had a passable PFO in <1% according to Harper and Haqqani is not sufficiently explained by either theory. The bulging of the atrial septum into the right atrium in mitral stenosis is likely to render catheter passage from the inferior vena cava more difficult as the PFO is hidden behind this bulge in a region where the septum now is tangential to the catheter path, making probing for the PFO unyielding. Many PFOs go undetected under these circumstances, although they are not fused but simply functionally closed by elevated left atrial pressure and moved out of target for access from the inferior vena cava.

***Bernhard Meier, MD**

*Swiss Cardiovascular Center Bern
University Hospital
Freiburgstrasse
CH-3010
Bern, BE 3010
Switzerland
E-mail: bernhard.meier@insel.ch

doi:10.1016/j.jacc.2006.08.002

REFERENCES

1. Meier B. Patent foramen ovale, guilty but only as a gang member and for a lesser crime. J Am Coll Cardiol 2006;47:446–8.
2. Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. Mayo Clin Proc 1984;59:17–20.

REPLY

We appreciate and acknowledge the interest in our recently reported study (1). In regard to the comments of Schrale et al., we studied subjects in age increments or "cells" of 10 years beginning at age 45, and we did not find an increased stroke risk in even the younger age cells. A recent case control study published by Petty et al. (2) supports our finding that patent foramen ovale (PFO) does not appear to be a risk factor for cryptogenic stroke in the general population.

Also, Harper and Haqqani provide intriguing thoughts regarding the issue of PFO detection rates in older individuals. It is possible that a PFO may close in older subjects, but this postulate is based on many assumptions, including that older people have elevated left atrial pressures. This is an interesting concept that merits systematic evaluation.

***Irene Meissner, MD**

*Mayo Clinic
Department of Neurology
200 First Street SW
Rochester, Minnesota 55905
E-mail: meissner.irene@mayo.edu

doi:10.1016/j.jacc.2006.08.001

REFERENCES

1. Meissner I, Khandheria BK, Heit JA, et al. Patent foramen ovale: innocent or guilty? Evidence from a prospective population-based study. J Am Coll Cardiol 2006;47:440–5.
2. Petty GW, Khandheria BK, Meissner I, et al. Population-based study of the relationship between patent foramen ovale and cerebrovascular ischemic events. Mayo Clin Proc 2006;81:602–8.

Coronary Plaque Burden and Cardiovascular Risk Factors: Single-Point Versus Serial Assessment

In their interesting study, Nicholls et al. (1) recently assessed in a large series of patients the relation between various cardiovascular risk factors and the amount of coronary plaque burden with (*non-serial*) volumetric intravascular ultrasound (IVUS). In this set of high-quality data, male gender, diabetes mellitus, and a history