correspondence

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## 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

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## 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

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# 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