Editorial

Patent foramen ovale: the jury is still out

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This editorial refers to “Transcatheter Closure of Patent Foramen Ovale (PFO) in patients with paradoxical embolism: Periprocedural safety and mid-term follow-up results of three different device occluder systems” by M.U. Braun et al. on page 424

Paradoxical embolism through a patent foramen ovale (PFO) was described first in 1877.1 It was never doubted that this could lead to a stroke. However, it was more than 100 years before it was realized that a PFO is in fact a frequent cause of cerebral embolism and there is a continuous debate as to how these patients should be treated.2,3 In 35–40% of all patients with an ischemic stroke the cause remains “cryptogenic”. Several studies have shown that the prevalence of a PFO in these patients is significantly higher than in control groups. Whereas a PFO is found in 44–66% of patients with cryptogenic stroke, in patients where the cause of stroke is already known it is found in only 9–27%. There is a high recurrence rate despite medical treatment ranging between 2% and 15% per year. As this is a very high risk for young patients, most being younger than 50 years, there is a need for preventative measures.

The options are antiaggregation or anticoagulation therapy and catheter closure of the PFO which is nowadays a routine procedure in many centers all over the world. Surgical closure has also been recommended and performed on a small number of patients. The problem is that none of these treatment options has been evaluated in controlled randomized trials. This is especially true for the medical treatment even though this is often claimed to be the “gold standard”. Several studies have shown that either antiaggregation or anticoagulation is effective in reducing the risk of paradoxical embolism. In fact the results of some studies suggest that neither medical treatment options (antiaggregation or anticoagulation) are effective. In addition, medical treatment incurs a risk of hemorrhagic complications at 9–15% per year (2.5% per year for severe bleeding). Medical treatment for prevention of paradoxical embolism is not only far from being the gold standard but also far from being evidence based medicine.

Catheter closure of PFO is by definition effective in reducing the risk of paradoxical embolism where complete closure can be achieved, at least in the majority of the patients. Nonetheless, the risk of complications arising either through the procedure or from complications related to the device itself during follow-up may be higher than the spontaneous risk without any preventive treatment. If PFO closure could be achieved without risks, we would not have to discuss the clinical value of the procedure. As with medical treatment, we remain far from evidence based medicine.

Currently, there are several trials planned or already in progress, comparing medical treatment and catheter closure. Because there is a general agreement that medical treatment is probably better than nothing, none of these trials are placebo controlled. Surgical closure has probably the same risk as surgical ASD closure (which means 0.5% mortality, 1–2% stroke) and so is also not investigated. As enrolment in these trials is slower than expected, results will not be available within the next 5 years.

As long as we are waiting for the results of randomized trials, evidence based medicine has to be replaced by common sense. Catheter closure will be preferred by the majority of patients because the concept sounds logical and convincing. The important question, which closure device is superior compared to others has been addressed in a retrospective study published by Braun et al. in this issue of the European Heart Journal.4 They compared the acute and subacute results of three different devices (CardioSEAL-STARflex, n = 61, PFO-Star, n = 177 and Amplatzer, n = 69) in 307 patients. They did not find relevant differences in respect to periprocedural complications, echocardiographic findings and clinical mid-term follow-up results between the three devices. This is interesting and in contrast to some other studies as well as our own experience with more than 800 patients, which showed specific risks with specific devices. For example, tamponade has occurred with the PFO-Star and (rarely) the Amplatzer device, arm
fractures with the PFO-Star (but not the CardioSEAL-STARflex and the Amplatzer), thrombus formation in 2–7% on the CardioSEAL-STARflex and the PFO-Star but almost never on the Amplatzer. However, high resolution X-ray to detect device arm fractures was not performed in this study, the results of routine TEE follow-up regarding thrombus formation not reported and the method and completeness of clinical follow-up not given. Nevertheless, this is an important study demonstrating that the overall complication rate of catheter PFO closure is probably very low.

The future of stroke prevention in PFO patients using catheter techniques will depend mainly upon our ability to eliminate all procedural and post-procedural adverse events and — until this can be achieved — upon patient selection. In clinical practice patients but also physicians especially neurologists like to ask for closure of the PFO in all young stroke patients even if another cause has been found in order “to eliminate every factor”. One should keep in mind that in a patient with another potential cause of stroke such as atrial fibrillation or carotid stenosis, this is more likely to be the source of the stroke than the PFO. That is because a PFO alone is in contrast to atrial fibrillation or a carotid stenosis — not a risk factor. It is the combination of a PFO and a risk of thrombus formation in the venous system which causes the event. Unfortunately we are still only able to identify the occasional patient with a thrombogenic disorder who is at risk of suffering a paradoxical embolism. Most often this diagnosis is made retrospectively by a history of recurring events. If, however, a thrombogenic disorder has been diagnosed already by laboratory tests, this case should not be excluded from catheter closure because it is likely to be most beneficial. As it is well known that these patients carry a high risk for thrombus formation (and embolism) despite medical treatment additional anticoagulation treatment may be required.

References