PATENT FORAMEN OVALE (PFO): TO CLOSE OR NOT TO CLOSE?

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Over the past 15 years, there have been an increasing number of papers dealing with PFO and stroke, but the nature of the relationship between this common cardiac abnormality and stroke is still a matter of controversy. Therapeutic options include antiplatelet drugs, oral anticoagulants, and transcatheter closure of the foramen. There are no studies showing the efficacy or superiority of any one of these strategies. This article summarizes the arguments that speak against the use of PFO closure in patients with PFO-associated stroke.

1. The association between PFO and stroke remains controversial.

Many but not all case-control studies have established a statistical association between PFO and cryptogenic stroke. This association appears to be stronger in patients with large R-L shunt and in those who have an atrial septal aneurysm (ASA) in addition to a PFO. A recent population-based case-control study challenged the association between PFO and cryptogenic stroke. The authors of this study concluded that the role of PFO may have been overestimated in previous studies because of selective referral of cases and under-recognition of PFO among comparison groups of patients referred for echocardiography for clinical indications.

Contrasting with many case-control studies, longitudinal studies have been unable to show an increased risk of first or recurrent stroke in patients with PFO receiving medical therapy, whatever the degree of shunt. Some longitudinal studies suggested an increased risk of first stroke in patients with an ASA and one study showed and increased risk of stroke recurrence in young adults with both PFO and ASA. Thus, the recent finding that PFO may not be a significant predictor of first or recurrent stroke contrasts with the increasing number of reports on transcatheter closure of the foramen.

Another important point is that statistical association, as demonstrated by case-control or longitudinal studies, does not automatically establish a cause-and-effect relationship. Statistical association may also result from confounding, that is to say the presence of an as-yet unknown confounding factor, which could be associated with PFO, as well as with stroke.

2. The actual mechanisms by which of PFO causes stroke are still debated.

Many think that stroke results from paradoxical embolism of thrombotic material from the venous bed into the arterial circulation. Direct evidence for this comes from case reports in which a thrombus was visualized within a PFO, at autopsy or echocardiography. Such cases, however, are very unusual, either because this mechanism of stroke is rare, or because the chances of a thrombus being « caught » at exactly the right moment are very low. For paradoxical embolism to occur, a venous source of embolism is needed. Accordingly, demonstrating venous thrombosis is a key criterion for an indirect or presumed diagnosis of paradoxical embolism. In our experience, evaluation of patients with cryptogenic stroke and PFO rarely reveals a venous source of thrombus, and several studies corroborate this finding. Failure to document a venous source of embolism may mean that paradoxical embolism has not occurred, but may also reflect our inability to detect venous thrombi, because of their location (for example in a pelvic vein) or small size. Conversely, just demonstrating venous thrombosis does not mean that paradoxical embolism has occurred (or will occur again), because venous thrombosis may just be a consequence of immobilization due to the stroke rather than the cause of stroke. Other potential mechanisms include direct embolization of thrombi formed in situ and paroxysmal arrhythmia, but these mechanisms have not been documented. Thus, in most patients with PFO-associated stroke, there is no evidence of paradoxical embolism, intracardiac thrombosis, or arrhythmias. This suggests that other mechanisms (unrelated to PFO) may be operant in many cases. In addition, it should be kept in mind that PFO is a common finding in the normal population and must coexist by chance alone in one third of young adults with ischemic stroke. Consequently, there are inevitably patients in whom stroke is erroneously attributed to a PFO.

3. PFO closure may not a relevant treatment in many patients.

Transcatheter PFO closure can prevent paradoxical embolism, but this treatment will not be relevant if a PFO-unrelated mechanism of ischemic stroke is the cause. As previously discussed, paradoxical embolism can and does occur, but the proportion of PFO-associated strokes which is due to paradoxical embolism is unknown and could be very low. Therefore, closure of the foramen does not mean that further strokes will be prevented. Indeed, recurrent events may occur after PFO closure even in the absence of a residual shunt. In addition, if paradoxical embolism is the actual mechanism of recurrent stroke in PFO patients, PFO closure will only prevent arterial embolism, not venous thrombo-embolism, which is the actual cause of paradoxical embolism. Therefore, stopping antithrombotic treatment after PFO closure may not be appropriate.

4. PFO closure is not without risk and has not been shown to be superior to medical treatment to decrease stroke recurrence.

Closure of the PFO is not without risk. These include complications related to vascular access, cardiac perforation with and without tamponade, air embolism, device embolization, arrhythmias, and intracardiac thrombus formation, some of which may be responsible for periprocedural stroke. Low rates of stroke recurrences have been reported in recent series of patients treated with PFO closure, but we don't know whether these rates would have been higher in similar patients treated medically with antiplatelet drugs or oral anticoagulants. Non- randomized comparisons of medical treatment with PFO closure will not answer the question/solve the problem, precisely because the non-randomized study design may confound the results and introduce bias. All therapeutic options have risks and unless randomised clinical trials can define who should be treated with what (if anything), and for how long, we could end up exposing patients to unnecessary complications of treatment. Fortunately, several RCTs are underway in the USA and Europe.

5. Guidelines from professional societies all recognized that data on the risks and benefits of PFO closure are insufficient.