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Transcranial Doppler: Cinderella in the Assessment of Patent Foramen Ovale in Stroke Patients

To the Editor,

In the recently published *Controversies in Stroke* on the best treatment of patients with patent foramen ovale (PFO) and stroke, much emphasis is put on the association of PFO with atrial septal aneurysm as a marker of increased stroke risk as compared with PFO alone, whereas PFO size seems to be a negligible variable.¹⁻³ Data in support of this contention mainly come from a large, multicenter, French study⁴ where 581 patients were included and assessed with transesophageal echocardiography. PFO was sized by counting the bubbles appearing in the left atrium after antecubital injection of agitated saline and PFO size failed to represent a significant predictor of recurrence. However, as is clearly stated in the paper, the interrater disagreement for the amount of shunting was substantial (about 26%), and the technique employed in the French study has been shown to yield a very low level of accuracy to quantify right-to-left shunt (RLS) when compared with direct invasive measurement of the leaflets' separation.⁵ Therefore, from the data of the French study one cannot conclude that the amount of shunt is irrelevant, because it was measured in an inappropriate way. On the other hand, a number of studies have suggested that it is precisely the amount of shunt as assessed in the cerebral vessels by contrast enhanced transcranial Doppler (c-TCD) that may constitute the principal determinant of stroke occurrence⁶ and relapse.⁷

It is therefore surprising that PFO assessment with TCD is systematically neglected in the already quoted as well as in other authoritative editorials which have recently appeared in the literature.⁸ Yet, if the persistent patency of the fossa ovalis is to be considered important for the passage of venous emboli, there should be no argument that the amount of blood diverted to the brain is a crucial factor. For an embolus to get to the brain from a peripheral vein, a number of conditions may be relevant in addition to PFO size, such as the orientation of the caval ostium in the right atrium, the persistence of an Eustachian valve, the relative eccentricity of ostium primum and ostium secundum, and, finally, the anatomy of supraaortic vessels. All these factors may contribute to modify the proportion of the shunted blood that gets into the brain. In any case, the greater the shunt to the brain, the greater the likelihood that a peripheral embolus can threaten the brain vessels. Therefore it may be useless to measure the degree of shunt across the atrial chambers, but it becomes crucial to have an estimate of it in the target organ, the one we want to protect.

Despite these obvious considerations, the assessment of RLS with TCD has been systematically overlooked in the published trials.

I would like to advocate the routine use of c-TCD for the assessment of RLS as a precious tool to help stratify patients according to their risk profile. The technique is simple, standardized, much less disturbing to the patients than transesophageal echocardiography, and, although to my knowledge there is no epidemiological data on the amount of shunt which can be found in normal people, from the paper of Serena et al⁶ it appears that the so-called "curtain" pattern is encountered exclusively in cryptogenic stroke patients, thus providing some clue for the ability to distinguish "innocent" from "suspected" (ie, potentially harmful) shunts.

Furthermore, c-TCD is ideal for follow-up studies, because it is easily repeatable and sensitive enough to detect also minor residual shunts, such as after PFO closure or in doubtful cases if a pulmonary fistula is suspected.

In conclusion, in the contemporary era of evidence-based medicine, every piece of information should receive due recognition for its contribution to the general knowledge. In the hot debate on patent foramen ovale, transcranial Doppler merits a place not less than transesophageal echocardiography in the assessment of patients with cryptogenic stroke. It is desirable that it will be incorporated in future trials addressing the natural history of or the comparison between different treatments in PFO-associated stroke. Its unique ability to measure the shunt in the brain vessels will hopefully provide some light to the still hazy landscape of PFO-associated strokes.

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