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Patent Foramen Ovale and Ischemic Stroke in Patients With Pulmonary Embolism

TO THE EDITOR: Le Moigne and colleagues (1) assessed the frequency of patent foramen ovale (PFO) and recent ischemic stroke in patients with symptomatic pulmonary embolism. They concluded that the PFO group had a higher incidence of recent ischemic stroke than the non-PFO group. We commend the authors for their work, but the importance of appropriate PFO screening and diagnosis needs to be emphasized.

According to clinical studies, the prevalence of PFO is 20% in the adult population. Different ultrasonography-based imaging methods exist for detecting right-to-left shunts, and all of them involve use of an agitated saline bubble study unless the PFO is apparent by color Doppler imaging. These imaging methods include transthoracic echocardiography (TTE), transesophageal echocardiography (TEE), transcranial Doppler (TCD), and intracardiac echocardiography.

Transesophageal echocardiography is considered the reference standard, and studies comparing the accuracy of the different ultrasonography-based methods for diagnosing PFO often use it as the reference. However, the most precise method for diagnosing PFO involves passage of a guidewire through the interatrial septum during right heart catheterization. Transesophageal echocardiography can either miss or misdiagnose PFO in approximately 10% of patients (2). Moreover, when compared with TEE, conventional TTE has a sensitivity of 46% and a specificity of 99% for diagnosing an intracardiac right-to-left shunt (although the sensitivity and specificity of TTE modestly improve when this study is performed with harmonic imaging). These findings imply that TTE misses a substantial number of PFOs (3).

The suboptimal sensitivity of TTE for detecting a right-to-left shunt explains why the prevalence of PFO in the study cohort (13%) is lower than expected. Imaging with TCD is more sensitive for detecting right-to-left shunts than TTE or TEE and is therefore our preferred initial screening method (4). If TCD imaging indicates a shunt, its location is then documented by TEE.

These findings imply that most, if not all, of the 20 patients who presented with acute pulmonary embolism and recent ischemic stroke in the non-PFO group in Le Moigne and colleagues' study were PFO carriers with false-negative results. If a more sensitive test had been used, such as TCD or TEE, a right-to-left shunt might have been diagnosed. How else can one explain the simultaneous occurrence of recent ischemic stroke and pulmonary embolism? If all 20 patients with stroke in the non-PFO group had PFO, the PFO group accordingly would have increased from 42 to 62 participants and the prevalence of PFO in the overall study would have been 20% (62 of 315). This value corresponds with the prevalence of PFO in the general population, which would strengthen the findings of their study.

We urge future investigators to use a method that is more sensitive for PFO screening than TTE or TEE, such as TCD. Doing so will allow for conclusions based on more accurate data, which are especially important in a syndrome with a substantial effect on mortality (5).

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IN RESPONSE: Dr. Kumar and colleagues emphasize that the prevalence of PFO in our cohort (13%) was lower than expected compared with the previously reported prevalence of 20% in the general population (1). As discussed in our article and reported by others, 1 explanation may be that TTE contrast testing has low sensitivity compared with TEE, the gold standard for diagnosing PFO (2, 3). Moreover, our patients' low echogenicity (which was related to their age and comorbidities, such as emphysema) may have decreased the sensitivity of TTE. The choice to use TTE when assessing PFO was based on our scientific rationale. Because paradoxical embolism is an important mechanism of ischemic stroke in patients with concomitant PFO and pulmonary embolism, the high specificity of TTE for diagnosing PFO was of prime importance. Our patients' clinical context also helped guide our decision to use TTE, which is the noninvasive reference diagnostic imaging study for PFO and the most accurate tool for assessing right ventricular function.

Dr. Kumar and colleagues note that TCD imaging is their preferred initial screening method for detection of right-to-left shunts. It is undoubtedly more sensitive than TTE for de-

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tecting PFO in patients with cryptogenic stroke (4). However, in this population, TTE seems to provide false-negative results not only for patients without PFO with stroke but also patients with PFO without stroke (4). This factor is even more relevant in our population of patients with pulmonary embolism in whom the primary scientific hypothesis was that the paradoxical embolism mechanism is related to an intracardiac shunt. In addition, TCD imaging has not been evaluated in this specific population of patients with pulmonary embolism.

We agree that TCD imaging could be part of the strategy for diagnosing PFO in patients with pulmonary embolism, but this method needs to be assessed in this population.

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