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Letters

TO THE EDITOR

Paradoxical Brain Embolism, Not Only From a Patent Foramen Ovale

We read with interest an article by Kijima et al. (1), which highlights the fact that not only a patent foramen ovale (PFO) can be responsible for a cryptogenic stroke. Right-to-left shunting (RLS) through an PFO is undeniably the major cause of paradoxical embolism. However, rarely, it can also be caused by RLS at pulmonary level due to pulmonary arteriovenous malformation (PAVM). A PAVM is a direct communication between the branches of the pulmonary artery and pulmonary veins. Large or multiple PAVMs can cause cyanosis and exertional dyspnea, but usually patients are asymptomatic. Regardless of their size, PAVMs can affect the central nervous system causing migraines, transient ischemic attacks, strokes, or abscess. The reported incidence of strokes in patients with PAVM is 18% to 32% and up to 60% in cases of multiple PAVMs (2). It has also been shown that recurrent strokes occur more often in patients with PAVMs than with PFO (probably because of continuous RLS). Classical diagnostic tools used to confirm PAVM are contrast-enhanced computed tomography or magnetic resonance imaging and pulmonary angiography. Chest radiography suggests PAVM only in about 45% of patients.

It should be underscored that PAVMs can be also diagnosed using contrast transesophageal echocardiography (c-TEE) and contrast transcranial Doppler (c-TCD), which are considered the "gold standard" for revealing an PFO. In the case of an extracardiac shunt, c-TEE with a Valsalva maneuver shows bubbles entering the left atrium 3 to 8 cardiac cycles after they were seen in the right atrium. In contrast, in cardiac RLS, the "3-beat rule" is used, which means that bubbles should appear in the left atrium between first and third cardiac cycles (3). In addition, RLS can be identified by the use of c-TCD. The technique is based on the detection of an intravenously injected contrast within intracranial arteries. In case of an RLS, the contrast enters the arterial circulation and produces microembolic signals. Microembolic signals passing pulmonary shunts appear later in the cerebral circulation than those passing cardiac shunts. The time window characteristic for PAVMs is about 15 s (11 s for intracardiac shunts), but it depends on the heart rate (duration of about 6 heart beats) (3).

In conclusion, it is of great importance to distinguish the level of RLS in c-TEE and c-TCD. It seems that PAVM can be responsible for some "false-positive" results of c-TEE or c-TCD. Finally, it is reasonable to consider c-TCD or c-TEE after every PFO closure to identify potential persistent RLS. For complete prevention of recurrent strokes caused by paradoxical embolism, it is necessary to not only close a PFO, but all existing shunts.

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REPLY: Paradoxical Brain Embolism, Not Only From a Patent Foramen Ovale

We appreciate the valuable commentary on our paper by Drs. Sabiniewicz and Wozniak-Mielczarek. A right-to-left shunt (RLS) caused by a pulmonary arteriovenous malformation (PAVM) and that caused by a patent foramen ovale (PFO) is most often diagnosed with echocardiographic modalities using agitated saline bubble contrast techniques. These include contrast transthoracic echocardiography, contrast transesophageal echocardiography, and contrast

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transcranial Doppler (TCD). For contrast transthoracic echocardiography and transesophageal echocardiography, a PFO is distinguished from bubbles passing through the pulmonary circulation based on the timing of the appearance of contrast in the left atrium, which is called the "3-beat rule." However, there are exceptions to this general rule. A large PAVM can produce early appearance of bubbles that look exactly like what is seen with a PFO (1). Therefore, the rules defined by the timing of the appearance of bubbles tend to be misleading and often provide an inadequate diagnosis. Theoretically, when a PFO is combined with a PAVM, bubbles through a PFO appear in the left atrium before the appearance of bubbles through a PAVM.

TCD can be performed with an adequate Valsalva maneuver especially when aided by visual feedback using a manometer, and is the most sensitive method to detect an RLS (2). One criticism of TCD is that it does not distinguish the etiology of an RLS. However, the degree of an RLS caused by a PFO tends to increase from rest to Valsalva, whereas an RLS caused by a PAVM does not (3). This is another reason why quantitative measurement of the degree of an RLS with TCD is preferable to transesophageal echocardiography.

Distinguishing the level of an RLS is important and a PAVM can mimic an RLS caused by a PFO. It is not straightforward to distinguish one from the other and sometimes (20%) these 2 etiologies coexist. A PFO or PAVM should be closed as secondary prevention for cryptogenic stroke, but either should be closed as primary treatment for hypoxemia.

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Midterm Safety and Efficacy of ABSORB Bioresorbable Vascular Scaffold Versus Everolimus-Eluting Metallic Stent

An Updated Meta-Analysis

One of the principal aims in developing bioresorbable vascular scaffolds (BVS) was reduction in the long-term risk of stent-related complications, including very late (>1 year) stent thrombosis (ST). However, recent data suggest that the risk of very late ST may persist, or even be increased, in BVS compared with current-generation metallic drug-eluting stents (DES) (1). Because randomized trials have not been powered adequately to detect differences in individual endpoints, including device thrombosis, we conducted an updated meta-analysis of randomized trials and comparative observational studies to evaluate the safety and efficacy of the commercially available ABSORB BVS system (Abbott Vascular, Abbott Park, Illinois) compared with everolimus-eluting metallic stents (EES) at the midterm follow-up.

Published data searches were performed through electronic databases and abstract lists from international congresses over the past 2 years. Study inclusion criteria were: 1) randomized controlled trial or comparative observational study; 2) comparison of clinical outcomes between BVS and EES; 3) minimum of 100 patients treated with BVS; and 4) minimum of a 2-year follow-up for ≥90% of included patients. Where published articles and conference presentations referred to the same study, the most recent follow-up data were prioritized. The primary endpoint was target lesion failure (TLF), defined as a composite of cardiac death, target vessel myocardial infarction (TV-MI) or ischemic-driven target lesion revascularization (ID-TLR). Secondary endpoints included individual components of TLF, definite or probable ST and patient-oriented composite endpoint (POCE) consisting of all-cause death, any MI, and repeat revascularization. Data were analyzed by random effects modeling in StataMP 14.0 (StataCorp, College Station, Texas). Summary statistics are reported as pooled odds ratios (OR) with 95% confidence intervals (CI). Statistical heterogeneity was