

# Letter to the Editor

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## Letter by Hołda Regarding Article, “Patent Foramen Ovale Closure Versus Medical Therapy for Cryptogenic Ischemic Stroke: A Topical Review”

To the Editor:

Saver et al,<sup>1</sup> in their extensive review, synthesized knowledge pertaining to the role of patent foramen ovale (PFO) in cryptogenic stroke. However, some newly discovered facts were omitted by authors. The PFO channel, together with atrial septal aneurysm, was correctly identified as being interatrial septum structures whose presence increases the risk of ischemic stroke in paradoxical embolism mechanisms (associated with PFO) and local blood stasis on the left atrial side of the septum (associated with atrial septal aneurysm).<sup>2</sup> Unfortunately, the recently described septal entity—atrial septal pouch—was not recognized by Saver et al.<sup>1</sup> This structure turns out to be a new cryptogenic stroke risk factor that may revolutionize diagnosis and management of cryptogenic strokes in young patients.<sup>3</sup>

It is well known that the presence of PFO channel is age dependent. This fact was also highlighted by Saver et al.<sup>1</sup> However, the PFO channel does not simply disappear in older people. There is a theory of continuous, lifelong remodeling of the interatrial septum, a process in which the constant friction between PFO channel elements leads to its partial fusion. A diverticulum that arises by this mechanism, atrial septal pouch, can be located on either right or left (left-sided septal pouch [LSSP]) side of the interatrial septum, and there is no connection through the pouch between atria. A smooth septum forms as a result of further closing of the pouches.<sup>4</sup> The prevalence of LSSP is estimated to be 47%.<sup>4</sup>

Shortly after the anatomic description of the atrial septal pouch, the LSSP was linked to ischemic stroke. Several dozen case reports have described the presence of the thrombus inside the LSSP in ischemic stroke patients. Almost all morphological features of LSSP (eg, its downward orientation and the presence of secondary diverticula) predispose patients to local blood stasis and thrombosis inside the pouch.<sup>4</sup> A recent cross-sectional study confirmed the role of LSSP in cryptogenic stroke in young adults. After adjusting for other risk factors, the presence of an LSSP was found to be associated with an increased risk of cryptogenic stroke (odds ratio, 2.02; 95% CI, 1.19–3.41;  $P=0.001$ ).<sup>3</sup>

The presence of LSSP may be easily diagnosed using transesophageal echocardiography after agitated saline injections and the Valsalva maneuver.<sup>3</sup> Nevertheless, LSSP can be misidentified as a PFO channel (or vice versa) by inexperienced echocardiographers. This misidentification can influence later management and secondary stroke prevention.

Saver et al<sup>1</sup> described 5 clinical features increasing the probability that a PFO is related to cryptogenic stroke with venous

thrombosis in the first place. This major causative factor for paradoxical embolism will not be present in patients with LSSP because there is no connection between both atria in such a variation.<sup>4</sup> Instead, local thrombosis within the pouch is thought to be the main pathophysiological mechanism behind LSSP as an ischemic stroke source. Several factors may contribute to this phenomenon. First, all conditions leading to peri-wall atrial blood stasis such as high ventricular pressure, mitral stenosis, heart failure, and atrial fibrillation increase the risk of LSSP thrombosis.<sup>3</sup> Moreover, the LSSP may be by itself arrhythmogenic substrate responsible for triggering atrial fibrillation.<sup>5</sup> The brisk laminar blood flow of the right pulmonary veins is thought to be a protective mechanism against clot formation within the LSSP, and its disturbance may be prothrombotic.<sup>4</sup>

Management options for LSSP are not yet known. Like in patients with PFO channel, treatment options for secondary stroke prevention in patients with LSSP may include antiplatelet therapy, anticoagulant therapy, or interventional LSSP damage/closure. Future studies and daily clinical practice should consider the fundamental differences between PFO and LSSP; features that share the same location but anatomically and clinically are completely different structures.



Mateusz K. Hołda, MD, PhD

Jagiellonian University Medical College  
Heart Stroke Association | Association Cracow, Poland

### Disclosures

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