

## EDITORIAL COMMENT

# Diagnosing Patent Foramen Ovale

## Too Little or Too Much?\*

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It is estimated that 25% to 30% of the world's population, or 1.7 to 2.0 billion individuals, have patent foramen ovale (PFO). The vast majority of these people will have no problem associated with this condition. Very rarely, the pathogenesis of stroke or peripheral arterial embolization includes paradoxical embolization related to a thrombus formed in the systemic venous system or the right

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atrium and its crossing the interatrial septum via a PFO (1). In recent years, it has been suggested that patients with cryptogenic strokes or transient ischemic attacks (TIA) have a higher prevalence of PFO (2,3). Furthermore, the presence of PFO has been implicated in many other pathological entities, such as migraine headaches, orthodeoxia-platypnea syndrome, decompression illness, refractory hypoxemia, and sleep apnea syndrome (4,5).

The ingenuity and creativity of physicians, inventors, and the medical device industry have led to the design of systems capable of closing PFOs using a percutaneous transcatheter approach. Although there is still no clear-cut, evidence-based recommendation for the use of these closure devices for secondary prevention in individuals with stroke or TIA who also have

PFO, such closure is frequently performed by many practitioners in an attempt to prevent the catastrophe associated with a second embolic event (6,7). Although the best therapeutic approach is still debated, it is generally accepted that accurate diagnosis of PFO is a sine qua non in patients with embolic stroke or TIA.

Our diagnostic armamentarium includes cardiac catheterization, which can show the PFO by the path of the venous catheter from the right to the left atrium, and Doppler echocardiography, which can show the blood flow across the PFO. During echocardiography, intravenous injection of agitated saline (bubble injection) is used to document the transit of these bubbles from right to left across the PFO. Although transthoracic echocardiography can be diagnostic, its sensitivity is relatively low. Higher-resolution echocardiographic images, such as those obtained by transesophageal echocardiography (TEE) or intracardiac echocardiography (ICE), are possible using high-frequency transducers brought to closer proximity to the heart, thereby providing higher sensitivity and specificity for PFO detection. Finally, transcranial Doppler (TCD) studies can, after intravenous agitated saline injection, show the appearance of the bubbles in the middle cerebral artery, thereby suggesting the diagnosis of right-to-left shunt (RLS) via a PFO.

The RLS across the PFO depends on the pressure gradient between the right and left atria. Normally, the left atrial pressure is slightly higher than the right atrial pressure throughout the cardiac cycle, and thus a RLS is not possible. Interestingly, in many such cases, the PFO is not hermetically sealed, and a small left-to-right shunt is frequently detected by color flow Doppler.

To produce a RLS, the right atrial pressure must exceed the left atrial pressure. This occurs in conditions such as pulmonary embolism, right ventric-

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ular failure, and tricuspid insufficiency, or during the release stage of the Valsalva maneuver. The straining phase of the Valsalva maneuver raises the intrathoracic pressure, and thus both atrial pressures. It also compresses the intrathoracic pulmonary veins and the intrathoracic portion of the venae cavae (8,9). The extrathoracic portions of the venae cavae become engorged, as can be seen when observing a patient who performs the straining. With the release phase of the maneuver, the increased systemic venous return precedes the pulmonary venous return, thus creating a right-to-left atrial pressure gradient.

When clinically indicated, most practitioners attempt to visualize PFOs by echocardiography following the intravenous injection of agitated saline as the patient performs the Valsalva maneuver. The immediate appearance of 3 or more bubbles in the left atrium across the atrial septum is considered diagnostic. Unfortunately, even with the use of high-resolution TEE or ICE, this procedure may fail to diagnose PFO (10). This failure to diagnose may be related to an insufficient increase in the right atrial pressure above the left atrial pressure necessary to drive bubbles across the PFO. This may be the case especially in patients who have high left atrial pressure. The tomographic nature of the images obtained echocardiographically may be another reason why bubbles could be missed.

The method suggested by Van et al. (11) in this issue of *ijACC* may overcome these shortfalls and may be more sensitive for the detection of PFO. These investigators studied patients with known PFO before and after transcatheter device closure. They showed that blowing into a manometer at a pressure of 40 mm Hg resulted in higher right atrial pressure as compared with that attained with the Valsalva maneuver. This was associated with significantly more bubbles detected in the middle cerebral artery by TCD. Furthermore, with the use of the manometer, they detected bubbles by TCD in cases in which ICE results were negative. This technique of combining blowing into a manometer with use of TCD may be not only more sensitive, but also more cost effective. It is almost completely noninvasive (except for the venipuncture and injection of the

agitated saline). Unlike TEE, there is no need for esophageal intubation, and unlike ICE, there is no need to use expensive, disposable invasive imaging catheters.

The Valsalva maneuver is not quantitative, and the degree of straining is variable. Patients studied using TEE are frequently sedated and therefore are less cooperative; they do not follow orders and often do not perform the maneuver effectively. The new technique is easily performed, and the patient can readily adjust the intensity of exhalation to obtain the target pressure indicated on the manometer.

The exact specificity of the technique suggested by Van et al. (11) is unknown. All of their studies were performed in patients with known PFOs, and there was no control group to evaluate the technique in patients without PFOs. It is therefore unclear whether transient nonphysiologic elevation of intrathoracic pressure may be by itself responsible for the appearance of the bubbles in the left heart by mechanisms other than interatrial shunting, such as changes in gas solubility in the blood or opening of new arteriovenous channels in the lungs.

The gold standard for detecting the presence of PFO has traditionally been the demonstration of a probe-patent PFO on a surgical or a pathological specimen. Obviously, 10- $\mu$ m bubbles can travel from left to right across a microscopic hole or a pore in the atrial septum or the device that closed it. Such defects may not be visualized by any macroscopic observation.

Van et al. (11) should be commended for their attempt to produce a standardized, possibly more sensitive test to define the RLS across a PFO. However, the clinical implications and the added value of shunt detection only by TCD and not by TEE or ICE are yet to be defined and will require further clarification.

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## REFERENCES

1. Conheim J. Thrombose und Embolie: Vorlesungen Uber Allgemeine Pathologie. Berlin, Germany: Hirschwald, 1877:134.
2. Lechat P, Mas JL, Lascault G, et al. Patent foramen ovale in patients with strokes. *N Engl J Med* 1988;318:1148-52.
3. Kronzon I. Patent foramen ovale: echocardiographic evaluation and clinical implications. *Isr Med Assoc J* 2006;8:793-7.
4. Kedia JB, Tobis J, Lee MS. Patent foramen ovale: clinical manifestations and treatment. *Rev Cardiovasc Med* 2008;9:168-73.

5. Azarbal B, Tobis J, Suh W, Chan V, Dao C, Gaster R. Association of interatrial shunts and migraine headaches: impact of transcatheter closure. *J Am Coll Cardiol* 2005;45:489-92.
6. Messe SR, Silverman JE, Kitzner JR, et al. Recurrent stroke in patent foramen ovale and atrial septal aneurysm. Report of the quality standard committee of the American Academy of Neurology. *Neurology* 2004;62:1042-50.
7. Hung J, Landzberg MJ, Jenkins KJ, et al. Closure of patent foramen ovale for paradoxical emboli: intermediate risk of recurrent neurological events following transcatheter device placement: *J Am Coll Cardiol* 2000;35:1311-6.
8. Gindea AJ, Slater J, Kronzon I. Doppler echocardiographic flow velocity measurements in the superior vena cava during the Valsalva maneuver in normal subjects. *Am J Cardiol* 1990;65:387-91.
9. Attubato MJ, Katz ES, Feit F, Bernstein N, Schwartzman D, Kronzon I. Venous changes occurring during the Valsalva maneuver: evaluation by intravascular ultrasound. *Am J Cardiol* 1994;74:408-10.
10. Woods TD, Patel A. A critical review of patent foramen ovale detection using saline contrast echocardiography: when bubbles lie. *J Am Soc Echocardiogr* 2006;19:215-22.
11. Van H, Poommipanit P, Shalaby M, Gevorgyan R, Tseng C-H, Tobis J. Sensitivity of transcranial Doppler versus intracardiac echocardiography in the detection of right-to-left shunt. *J Am Coll Cardiol Img* 2010;3:343-8.

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