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REVIEW

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Multimodality imaging approach of patent foramen ovale: Practical considerations for transient ischemic attack/stroke

Mariana Floria[1,2] | Elena Diana Năfureanu[1,3] | Diana-Elena Iov[1,2] | Mihaela Dranga[1,2] | Radu Florin Popa[2,4] | Livia Genoveva Baroi[2,4] | Radu Andy Sascău[1,5] | Cristian Stătescu[1,5] | Daniela Maria Tănase[1,2]

[1]Internal Medicine Department, "Grigore T. Popa" University of Medicine and Pharmacy of Iaşi, Iaşi, Romania

[2]"Sf. Spiridon" Emergency Clinical Hospital, Iaşi, Romania

[3]Military Emergency Clinical Hospital, Iaşi, Romania

[4]Surgery Department, "Grigore T. Popa" University of Medicine and Pharmacy of Iaşi, Iaşi, Romania

[5]Cardiovascular Disease Institute of Iaşi, Iaşi, Romania

Correspondence
Elena Diana Năfureanu, Internal Medicine Department, "Grigore T. Popa" University of Medicine and Pharmacy of Iaşi, Iasşi, Romania.
Email: diananafureanu@outlook.com

Abstract

A patent foramen ovale, which is present in up to 25% of the population, is a risk factor for cryptogenic stroke (which accounts for 15%–40% of strokes) and transient ischemic attack via paradoxical embolism. This narrative review focuses on the multimodality imaging approach of the diagnosis and periprocedural guidance of patent foramen ovale, with an emphasis on the use of agitated saline as contrast medium in echocardiography, starting from embryologic aspects. Therefore, we aimed to make a concise and complete presentation of the protocol used for this type of evaluation, along with multimodality imaging approach of the patent foramen ovale and practical considerations for transient ischemic attack/stroke.

KEYWORDS

agitated saline contrast, echocardiography, multimodality, patent foramen ovale

1 | INTRODUCTION

According to TOAST criteria,[1] patent foramen ovale (PFO) is a low risk potential source of cardioembolic stroke, together with other interatrial septum anomalies such as atrial septum aneurysm (ASA) and atrial septum defect (ASD).[1,2] A PFO is present in up to 25% of the adult population and results from the incomplete fusion of the septum primum and secundum after birth.[3] It causes paradoxical embolisms via a right-to-left shunting and it has an increased risk of stroke recurrence when associated with ASA, due to the nidus properties of the saccular like structure of the aneurysm.[2,4]

Likewise, the presence of Eustachian valve facilitates blood flow direction from the inferior vena cava toward the PFO, increasing the risk for stroke.[2,3] A tricuspid regurgitation flow directed to atrial septum may also result in a right-to-left shunt, favoring the passage of thrombi from the right to the left atrium. Besides stroke, the presence of PFO is associated with other clinical syndromes, the most known being migraine headaches and platypnea-orthodeoxia.[3,5]

There is no gold standard technique for assessing PFO and diagnosis is established based on multimodality imaging, with echocardiography being the most frequently used. The use of agitated saline as contrast when performing transthoracic (TTE) and transesophageal echocardiography (TTE) increases the sensitivity and sensibility of these methods by establishing right to left shunting.[3,6,7]

This paper aims to represent a practical guide for PFO multimodality imaging assessment in the setting of transient ischemic attack/stroke.

2 | THE EMBRYOLOGY OF PATENT FORAMEN OVALE

In order to achieve a better understanding of the difference between PFO and ASD, a few notions of the embryology of PFO should be understood.

During fetal evolution, septation is the process that defines the development of the single chamber cardiac tubule into the known form of the four-chamber heart (Figure 1). This process takes place between the fourth and seventh week of gestation[8] and is initiated by the development of septum primum from the roof of the primitive atrium.[8–10]

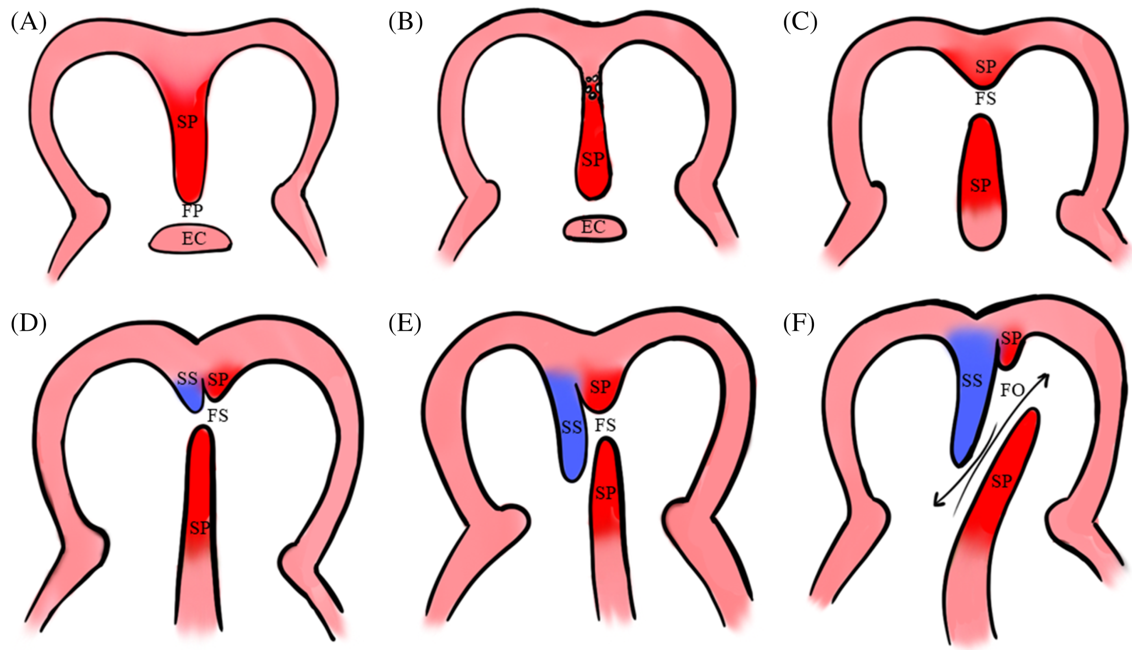

FIGURE 1 Atrial septation. (A) septum primum growth toward endocardial cushions with the foramen primum between them; (B) fenestrated septum primum in the upper part; (C) fusion of septum primum with the endocardial cushions, closure of foramen primum and ful development of the foramen secundum; (D) start of development of the septum secundum on the right of septum primum; (E) growth of septum secundum toward septum secundum; (F) lack of fusion between septum primum and septum secundum, with foramen ovale between them. EC, endocardial cushions; FO, foramen ovale; FP, foramen primum; FS, foramen secundum; SP, septum primum; SS, septum secundum

Septum primum grows into a caudal manner toward the endocardial cushions. In the embryonic and fetal heart, a communication between the right and left part is necessary in order to allow blood coming from the placenta elude the pulmonary circulation of the fetus and enter into the systemic circulation.[8,11,12] This is the reason why initially a free space remains between the inferior edge of the septum primum and the endocardial cushions, known as foramen primum. Foramen primum closes by the end of the sixth week due to the full growth and fusion of septum primum with the endocardial cushions at the atrioventricular level, but this process happens simultaneously with the formation of a new opening, known as foramen secundum, in the superior part of the septum primum by its localized fragmentation.[8–10]

Throughout the seventh week, the septum secundum appears at the right of the septum primum from an invagination of the atrial roof toward the atrioventricular junction.[8] Septum secundum obliterates the foramen secundum, but due to the lack of fusion with the endocardial cushions at its inferior edge, an opening remains. This further forms an oblique orifice with the foramen secundum, which is known as the foramen ovale.[9] The inferior part of the septum primum now acts as a flap valve for the foramen ovale, allowing the blood to flow only from the right toward the left cavities.[9]

At birth and soon after, due to respiration which causes inflation of the lungs, allows the pulmonary circulation to become functional and the left side pressure to increase, the foramen ovale closes by the permanent contact of the septum primum and septum secundum. This transforms foramen ovale into the fossa ovalis.[10,12]

TABLE 1 Conditions associated with PFO and right to left shunting

Pulmonary hypertension (chronic or acute)
Sleep apnea syndrome
Right atrium dilation and remodeling
Valsalva maneuver
Interatrial septum aneurysm
Chiari network
Eustachian valve

3 | MULTIMODALITY IMAGING OF PATENT FORAMEN OVALE DIAGNOSIS

A PFO is not an ASD per se because it occurs as a consequence of the imperfect fusion of the septum primum and secundum and not due to loss of atrial septal tissue.[3] Normally, given the higher pressures on the left side, the shunting through PFO is left to right; however, in situations with increased pressures in the right atrium or when other associated conditions are present (Table 1), the foramen ovale opens in a transient or permanent manner, associating a right to left shunt.[3,13] Due to its particular position within the interatrial septum and given the fact that expert consensuses on the subject did not establish a gold standard imaging technique, the diagnosis and evaluation of consequences of PFO are made using a rather patient, skilled and availability-based approach in which multiple tools can be used.[6,7]

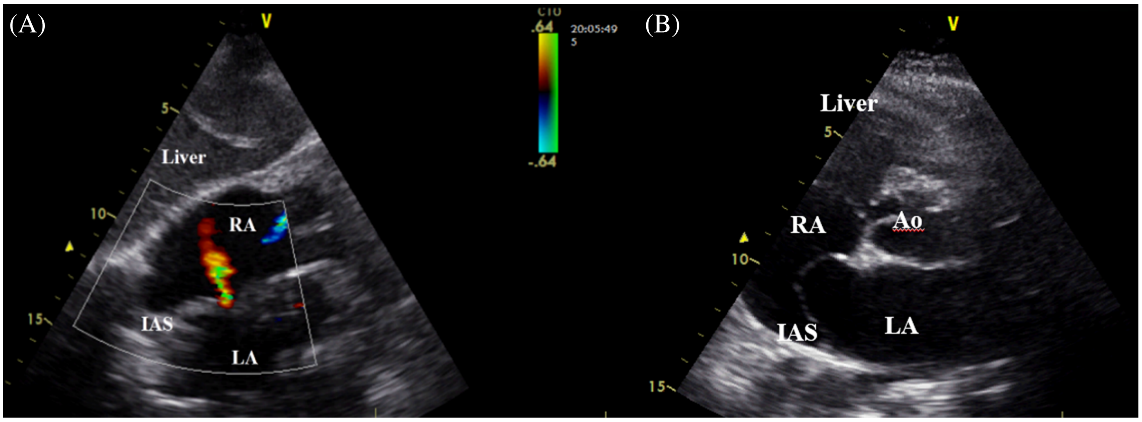

FIGURE 2 Transthoracic echocardiography: (A) subcostal four chamber view, showing left to right shunt in color Doppler through a patent foramen ovale; (B) parasternal short axis view showing atrial septum aneurysm. Ao, aorta; IAS, interatrial septum; LA, left atrium; RA, right atrium

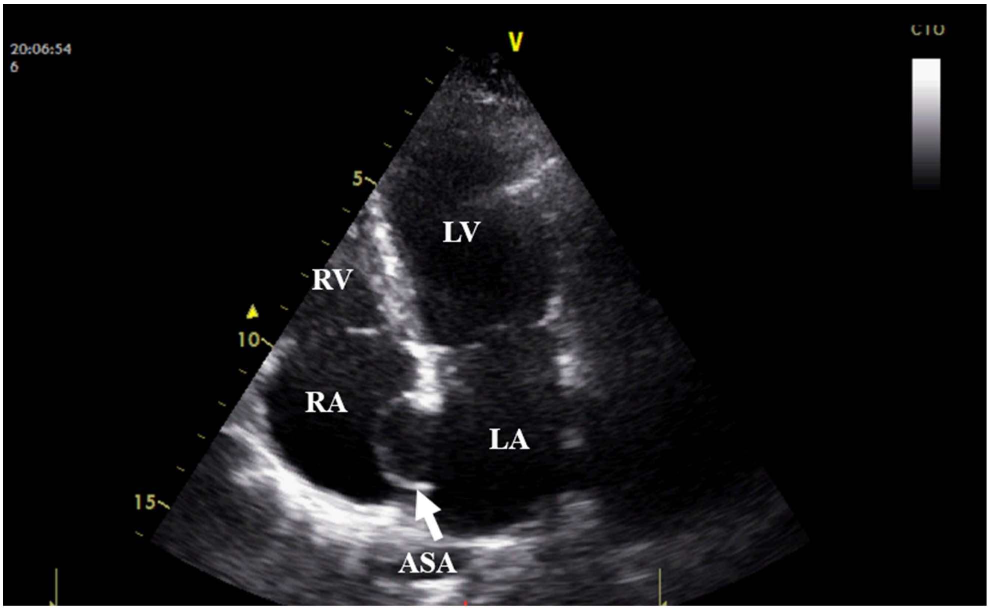

FIGURE 3 Transthoracic echocardiography in apical four chamber view showing atrial septal aneurysm with left to right displacement. ASA, atrial septum aneurysm; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle

The three pillars of PFO imaging assessment of are the various types of echography using contrast agents: contrast transcranial Doppler (c-TCD), contrast transthoracic echocardiography (c-TTE) and contrast transesophageal echocardiography (c-TEE), each with its own advantages, drawbacks and various specificity and sensibility percentages reported in studies.[3,6]

3.1 | Transthoracic echocardiography

Transthoracic echocardiography is the first method which may rise clinical suspicion and could diagnose and evaluate the consequences of PFO; it also has the added benefit of being the most widely available imaging tool.[6,7,14] Diagnosis in TTE can be made based on imaging of the left to right or right to left shunting by using color Doppler or agitated saline contrast. The first view that allows to evaluate the integrity of the interatrial septum and PFO is the short parasternal axis, but without the possibility of correct assessment due to the parallel orientation of the ultrasound beam to the interatrial septum. In this regard, the preferred windows and views are those in which the ultrasound beam falls perpendicularly to the interatrial septum, such as the subcostal four-chamber view (Figure 2A, Video S1) and short axis view[3] (Figure 2B).

Bidimensional imaging in either window allows for an evaluation of the causes, consequences or anatomic variations associated with PFO. Apical four-chamber view should be used in order to measure an ASA (Figure 3), evaluate the presence of Chiari network or thrombi, estimate atrial enlargement by measuring atrial volumes and assess the tricuspid gradient and the shunt by using an agitated saline contrast. The presence of some anatomic variations (Chiari network, ASA, presence of Eustachian valve and a lipomatous interatrial septum) classifies PFO as complex and should be carefully searched, especially when a patient with PFO is addressed for closure, as it can interfere with the procedure.[2,15]

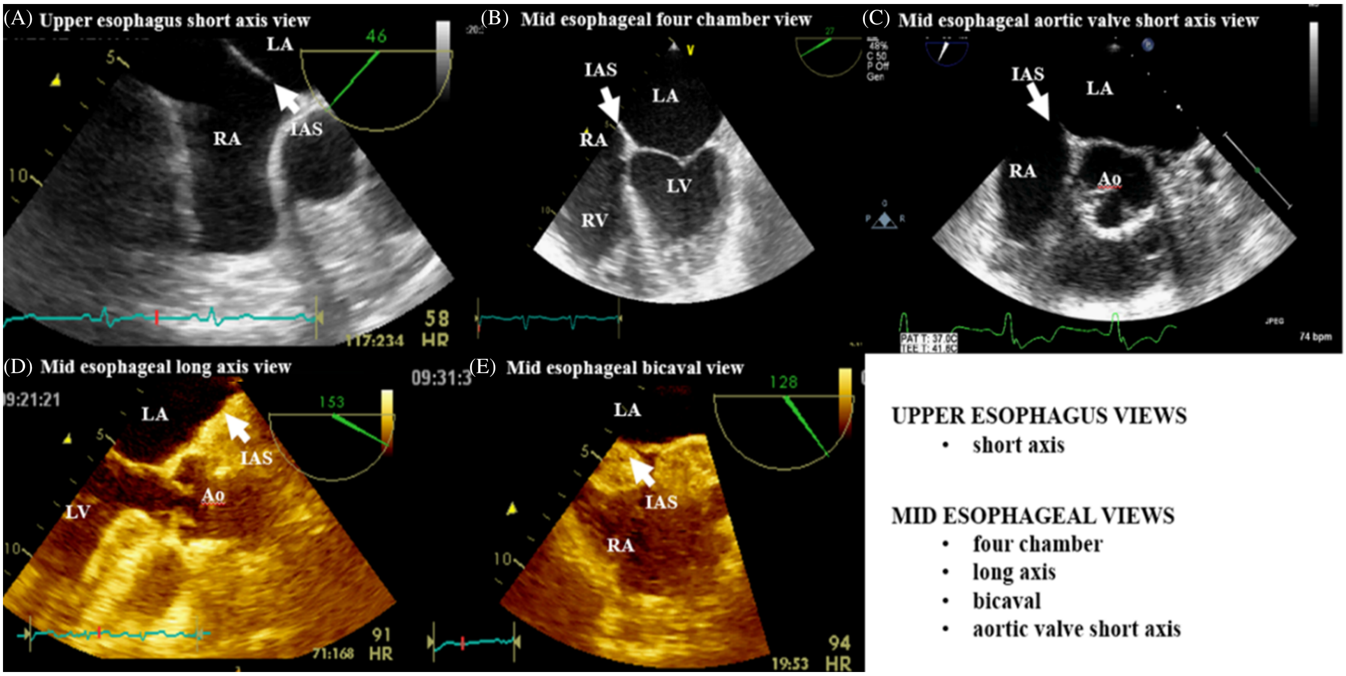

FIGURE 4 The views for interatrial septum evaluation in transesophageal echocardiography. (A) Upper esophagus short axis view; (B) Mid esophageal four chamber view; (C) Mid esophageal aortic valve short axis view; (D) Mid esophageal long axis view (lipomatous hypertrophy of the interatrial septum); (E) Mid esophageal bicaval view (lipomatous hypertrophy of the interatrial septum). Ao, aorta; IAS, interatrial septum; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle

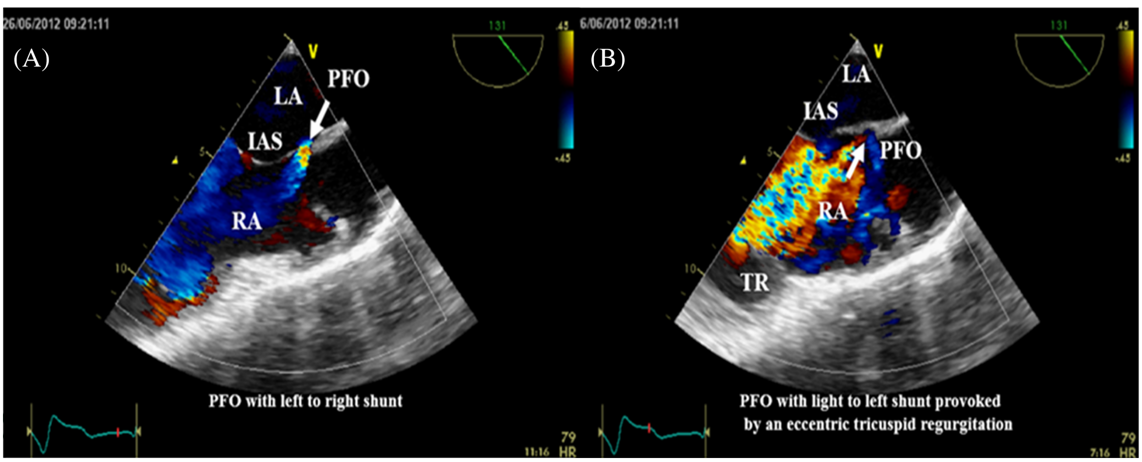

FIGURE 5 Transesophageal echocardiography mid esophageal long axis view with color Doppler showing a patent foramen ovale with left to right shunting (A) and right to left shunting (B) facilitated by a regurgitant tricuspid flow (favorized by a ventricular pacemaker lead) directed toward the IAS. IAS, interatrial septum; LA, left atrium; PFO, patent foramen ovale; RA, right atrium; TR, tricuspid regurgitation

When it comes to hemodynamic consequences of PFO with left to right shunting, one must be aware that due to its dimensions, it does not cause significant overload of the right cavities and other septal defects must be searched. In this situation, pulmonary to systemic flow ratio (Q_p/Q_s) and right ventricular dimensions and function assessments are mandatory. Usually, a PFO does not modify the dimensions of the right atrium and ventricle by induced hemodynamic changes.

It is possible that in apical four chamber or subcostal view, the flow in color Doppler sometimes overlaps with that of the superior vena cava. Therefore, in this situation, the color Doppler sample should be greatly reduced to avoid overlapping.

3.2 | Transesophageal echocardiography

Although currently there is a lack of a gold standard technique for PFO diagnosis, some authors and practitioners consider TEE the optimal tool as it offers more detailed information regarding the integrity of the interatrial septum and nearby structures. It allows differentiation between PFO and other types of atrial septal defects, especially in situations in which TTE does not provide sufficient information. The current guidelines for assessment of ASD and PFO from the American Society of Echocardiography and the European position paper on the management of patients with PFO stipulate that TEE should be used in patients who have a poor acoustic window when evaluated through TTE and in selecting and guiding transcatheter occlusion.[3,6]

A specific protocol must be followed when evaluating a PFO in TEE.[16] Five views are ideal for evaluation of the interatrial septum (Figure 4): four midesophageal views (four chamber—Figure 4B, long axis—Figure 4D, aortic valve short axis—Figure 4C, and bicaval—Figure 4E) and one obtained from the upper esophagus (short axis—Figure 4A).[3,16,17] Because of the foramen ovale's particular tunnel-like form within the interatrial septum, measurements of its total length and maximal size at the left and right atrial ends should be made whenever possible. Due to the fact that TEE is used in selecting patients which are candidates for PFO closure, an evaluation of PFO's distance to venae cavae must be performed.[3,16]

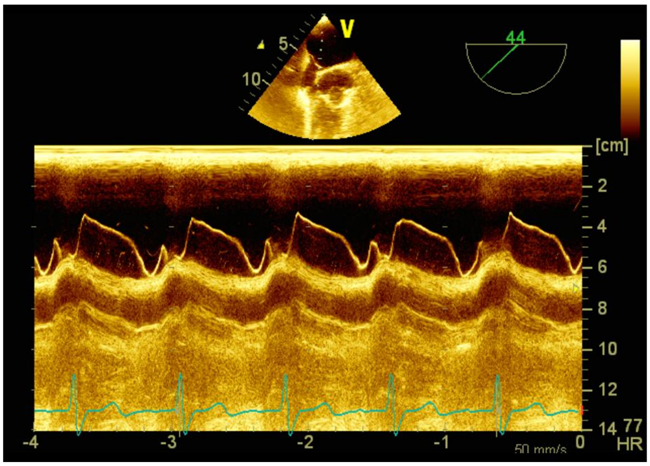

FIGURE 6 Transesophageal echocardiography: excursion of the interatrial septum in M mode

Left to right shunting (or right to left shunting under Valsalva maneuver or specific conditions) through a PFO is evaluated in the same manner as with TEE, using color Doppler (Figure 5 A, B) and agitated saline contrast.[3] Regarding the ASA, this anatomic anomaly is defined as the movement of the interatrial septum of at least 10 mm into the left or right atrium from the plane or a combined left and right movement of 15 mm^3 (Figure 6). The excursion of the interatrial septum in ASA could be assessed either in TTE or in TEE. ASA is present in about 4%[18] of cases of PFO and is associated with a high risk of paradoxical embolism due to the fact that the aneurysmal portion is a zone of capture for thrombi[2] (Video S2). Likewise, the presence of the Eustachian valve is associated with a higher risk of paradoxical embolism. This structure is a remnant of the inferior vena cava's valve present in the embryo and fetus, whose role is to direct blood flow from the inferior vena cava toward the foramen ovale. A prominent Eustachian valve can cause a PFO because it comes into contact with the septum primum and blocks the fusion to the septum secundum; in addition to that, it direct thrombi from inferior vena cava to the PFO[3] (Video S3).

Transesophageal echocardiography performed in experienced centers is a safe and easy procedure. However, overall complication rate during diagnostic and intraoperative TEE is 0.18%–2.8%. The absolute contraindications for TEE are perforated viscus, stricture, tumor, perforation, laceration or diverticulum of the esophagus and

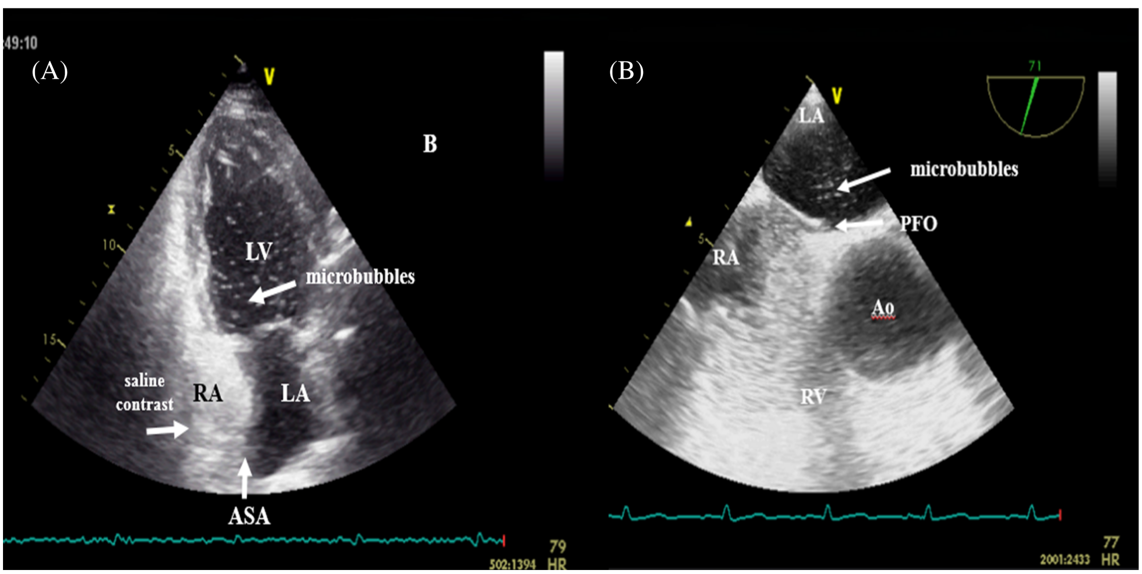

FIGURE 7 Contrast echocardiography with microbubbles shows the presence of patent foramen ovale. (A) transthoracic echocardiography in apical four chamber view, showing right to left shunting through a patent foramen ovale during Valsava maneuver. (B) transesophageal echocardiography in mid esophageal short axis aorta view. Ao, aorta; ASA, atrial septum aneurysm; LA, left atrium; LV, left ventricle; PFO, patent foramen ovale; RA, right atrium; RV, right ventricle

TABLE 2 Materials needed and the technique of making microbubbles in six steps

Materials needed	Microbubbles protocol with technique details
• 2 syringes of 10 ml • intravenous catheter • 3-way stopcock • 8 ml saline • 1 ml of patient's blood	1. Place an intravenous catheter into an antecubital vein • attach a 3-way stopcock to it • please take sure that stopcock is very well screwed (to avoid syringes detaching during test) 2. Agitated saline preparation • mix it in a 10 ml syringe with 8 ml saline and 1 ml air • take 1 ml of patient's blood 3. Place the two syringes (the empty and the filled one) in the free orifices of the stopcock • close de orifice that connects the stopcock to the catheter 4. Start making microbubbles • move very fast the plungers back and forth for 10 s so the mixture will pass from a syringe to another • microbubbles must be visible in the syringes 5. Push the mixture into the vein • in order to do that, close de orifice connecting to the empty syringe and open the ones connecting the intravenous catheter to the filled syringe • microbubbles must be injected in bolus (very rapidly) 6. Repeat twice agitated saline test • for better recognition of a positive test and for reproducibility

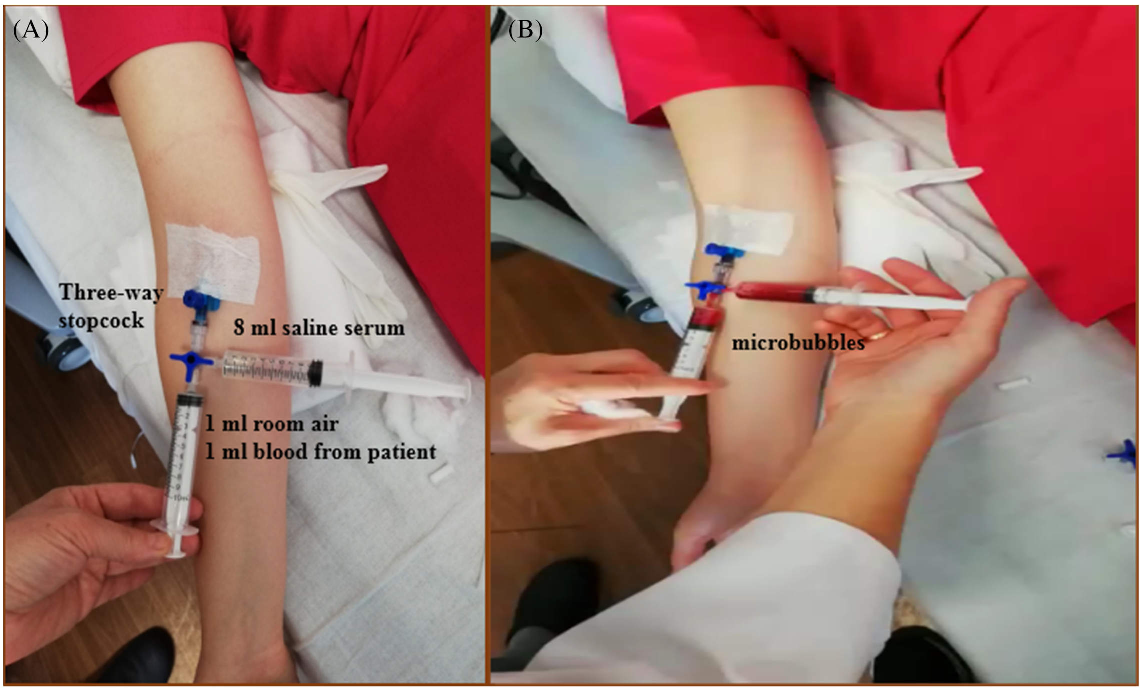

FIGURE 8 (A, B) Agitated saline contrast technique (please see Table 2 for details)

active upper gastrointestinal bleeding, while conditions such as a history of radiation to the neck and mediastinum, a history of gastrointestinal surgery, recent upper gastrointestinal bleed, Barrett's esophagus, a history of dysphagia, restriction of neck mobility (severe cervical arthritis, atlantoaxial joint disease), symptomatic hiatal hernia, esophageal varices, coagulopathy, thrombocytopenia, active esophagitis or active peptic ulcer disease constitute relative contraindications.[19]

3.3 | Agitated saline contrast echocardiography

Use of agitated saline while performing TTE (Figure 7A and Video S4) or TEE (Figure 7B and Video S5) is an inexpensive, ready to use method of assessing the right to left shunting in PFO. Agitated saline can also be used in assessing the right to left shunting when combined with transcranial Doppler (c-TCD).

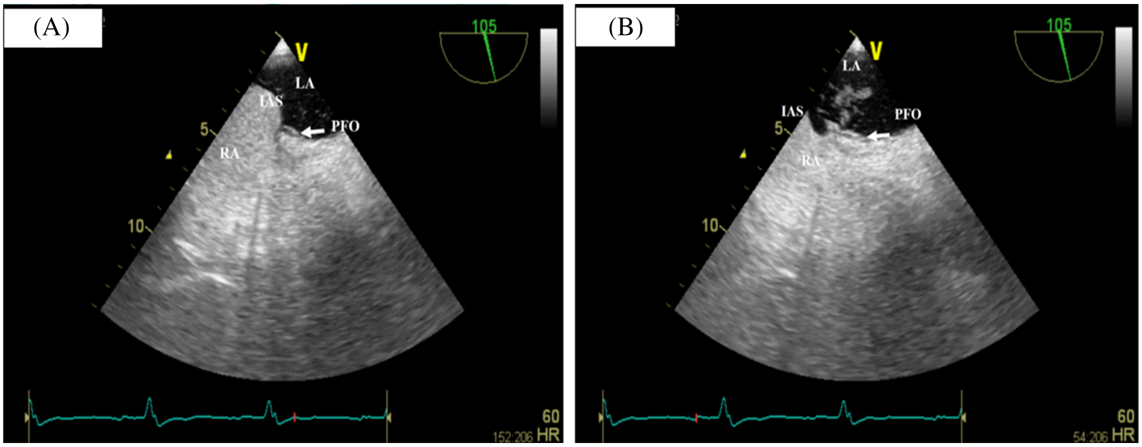

FIGURE 9 Agitated saline contrast when performing c-TEE. (A) before Valsalva (no microbubbles seen in the LA). (B) after Valsalva (microbubbles seen in LA). IAS, interatrial septum; LA, left atrium; PFO, patent foramen ovale; RA, right atrium

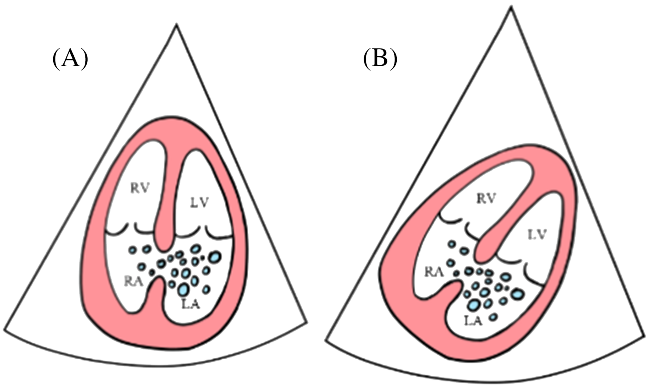

FIGURE 10 Agitated saline TTE with microbubbles passing from right to left atrium in (A) apical four chamber view, (B) subcostal four chamber view. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle

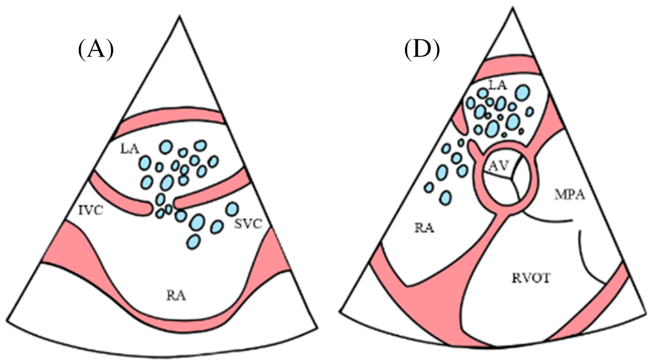

FIGURE 11 Agitated saline TEE with microbubbles passing from right to left atrium in (A) midesophageal bicaval view and (B) midesophageal short axis aortic valve level view. AV, aortic valve; IVC, inferior vena cava; LA, left atrium; LV, left ventricle; MPA, main pulmonary artery; RA, right atrium; RV, right ventricle; RVOT, right ventricle outflow tract; SVC, superior vena cava

Older studies comparing contrast transthoracic echocardiography using agitated saline to the other two contrast enhanced techniques concluded that c-TTE is the least useful diagnostic tool[6,20]; however, more recent studies gave c-TTE the credibility of being a specific and sensitive mean for PFO diagnosis. This is probably mostly due to the fact that it is the first method used in the diagnostic algorithm for causes of stroke and its wide availability. Another reason could reside in the fact that performing a Valsalva maneuver during transesophageal echocardiography is more difficult.[6,21,22]

The technique (Table 2, Figure 8, and Video S6) which uses 80% saline, 10% air, and 10% patient's blood as the solution to be injected is preferred because studies have shown better contrast intensity due to higher concentrations of microbubbles with added blood.[23,24] After injection of the solution in an arm vein, it is expected to see microbubbles in the right atrium. When performing this test, the inclusion of a well-trained nurse in the team is mandatory, in order to allow the imagist to correctly assess the presence of the PFO and the shunt.

When a right to left shunt is present, microbubbles will be seen entering the left atrium through the interatrial septum when performing a Valsalva maneuver (Figure 9). As a rule of thumb, in order to establish a diagnosis of right to left shunting caused by a PFO, microbubbles should appear in the left atrium within three cardiac cycles. If microbubbles appear in the left atrium after more than three cardiac cycles, then the shunt is located intrapulmonary, with microbubbles entering the left atrium via the pulmonary veins.[25] This is why when performing this test using transthoracic echocardiography, a subcostal four chamber view should be used in order to observe the passage of microbubbles from the right to left atrium via the interatrial septum. When the subcostal window does not offer a clear image, an apical four chamber view must be used[3,25] (Figure 10). If this test is performed by TEE, the best views for the assessment of the right to left shunting are mid-esophageal bicaval and aortic short axis view (Figure 11).

Agitated saline contrast echocardiography can allow a semi-quantitative assessment of the right to left shunting based on the

TABLE 3 Severity grades of right to left shunt when assessed with agitated saline contrast

Author	Grade	Severity
Gonzalez-Alujas et al.[21]	3 grades	Mild: < 10 microbubbles Moderate: 10–20 microbubbles Severe: > 20 microbubbles
Vitarelli et al.[26]	4 grades	0: no microbubbles seen 1: < 10 bubble 2: ≥ 10 microbubbles 3: 25% opacification of left atrium
Rana et al.[27]	4 grades	1: < 5 microbubbles 2: 5–25 microbubbles 3: > 25 microbubbles 4: chamber opacification
Lee et al.[28]	5 grades	0: no microbubbles 1: 1–5 microbubbles 2: 6–20 microbubbles 3: 21–50 microbubbles 4: > 50 microbubbles

number of microbubbles seen in the left atrium. There is no standard classification of grades of right to left shunting, but most practitioners classify right to left shunting in three to five grades (Table 3).[21,26–28]

An agitated saline contrast echocardiography does not lack false positive or false negative results. Various situations (Table 4) can erroneously establish a diagnosis of PFO or, in contrast, may lead to missing it.[3,21,28]

Sometimes inferior vena cava flow is directed toward the interatrial septum (Figure 12), in some cases favored by the presence of Eustachian valve, thus leading to the opening of the foramen ovale. When the procedure is performed by injecting agitated saline into an arm vein, this may cause a subsequent "wash-out" effect of the contrast coming from the superior vena cava.

3.4 | Other imaging modalities

Several other techniques can be used in order to assess PFO, its associated anatomic variations and the resulting shunting, but some of them are less frequently used due to lower availability, high cost or lack of experience in performing and using them.

Contrast enhanced transcranial Doppler (c-TCD) uses the same principle as contrast echocardiography. It is performed by neurologists or radiologists following an established protocol[29] that uses agitated saline as contrast and evaluates the appearance of microbubbles in the middle cerebral artery. Thus, it establishes the presence of right to left shunting and rises a clinical suspicion of PFO in patients with paradoxical embolism. Results of studies comparing c-TCD to c-TTE and c-TEE are very non-homogeneous in terms of sensitivity and specificity, with older studies noting higher values in assessing right to left shunting. In spite of these findings, the major drawback of this method is its inability to establish the intra- or extracardiac nature of the shunt.[2]

Intracardiac echocardiography (ICE) and 3D echocardiography (3D-E) are two newer techniques used in guiding PFO closure because

TABLE 4 Situations that can result in a false negative or false positive agitated saline contrast echocardiography

False positive	False negative
Intrapulmonary shunts	Inadequate Valsalva maneuver
Unidentified ASDs	IVC flow creating a" wash out" effect
Sinus venosus septal defects	LV diastolic dysfunction
Poor acoustic image	Poor acoustic image

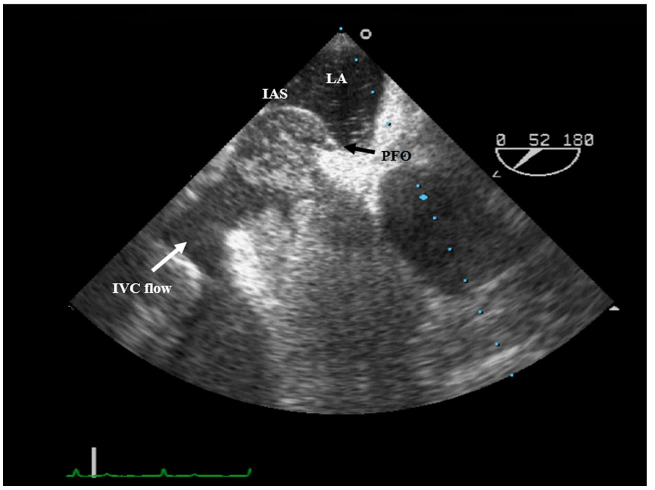

FIGURE 12 Transesophageal echocardiography in mid-esophageal short axis view showing flow from IVC creating a "wash-out" effect of the saline contrast. IAS, interatrial septum; IVC, inferior vena cava; LA, left atrium; PFO, patent foramen ovale

of their ability to assess the anatomy of the PFO and surrounding structures in great detail (Video S7).[3,27,30,31]

Cardiac computed tomography (CCT) is less frequently used because of its inferiority to echocardiography. It can be performed with or without electrocardiography gating. It provides accurate anatomic descriptions of the interatrial septum and can raise suspicion of a PFO, but cannot clearly diagnose it. One major disadvantage is the fact that even in cases in which contrast agents are used, Valsalva maneuvers cannot be performed during image acquisition.[18,32]

Cardiac magnetic resonance (CMR) has the advantage of a better estimation of right and left ventricular function by calculating volumes,[18] but it is inferior to TEE when it comes to assessing shunting through a PFO, therefore its clinical use is limited.[33]

Each imaging method has its advantages and disadvantages (Table 5) and, in order to use the most suitable technique, a clinical rationale must be followed.

Therefore, to summarize the multimodality imaging techniques for PFO diagnosis and management we propose the following flowchart (Figure 13). As c-TCD is performed by neurologists and, moreover, it cannot indicate the origin of shunt (intracardiac or extracardiac) we therefore propose this flowchart from the cardiologist point of view.

TABLE 5 Advantages and disadvantages of multimodality imaging methods for diagnosis of PFO

Imaging modality	Advantages	Disadvantages
TTE/c-TTE	• Accessible • Repeatable • Non-invasive • Low costs	• Poor image quality in some cases • Need for an accredited cardiologist/imagist
TEE/c-TEE	• Better image quality • Low costs	• Semi-invasive (a small risk of esophageal injury) • Need for a specialized cardiologist/imagist • Might require sedation
c-TCD	• Accessible • Repeatable • Non-invasive • Low costs	• Cannot establish the origin of shunt: intracardiac versus extracardiac
ICE	• Good image quality due to proximity to the interatrial septum • Limited personnel (can be performed by the interventionist) • Limits exposure to radiation	• Invasive: risk of arrhythmia and vascular injury • Expensive when performed with single use catheter • Needs a specialized practitioner
CCT	• Assessment of other associated cardiac/vascular disorders	• Impossibility to perform Valsalva maneuver due to image acquisition protocol • Radiation and contrast agent exposure • Expensive • Less accessible
CMR	• Assessment of other associated cardiac/vascular disorders	• Inferior to echocardiography in shunt assessment • Expensive • Less accessible

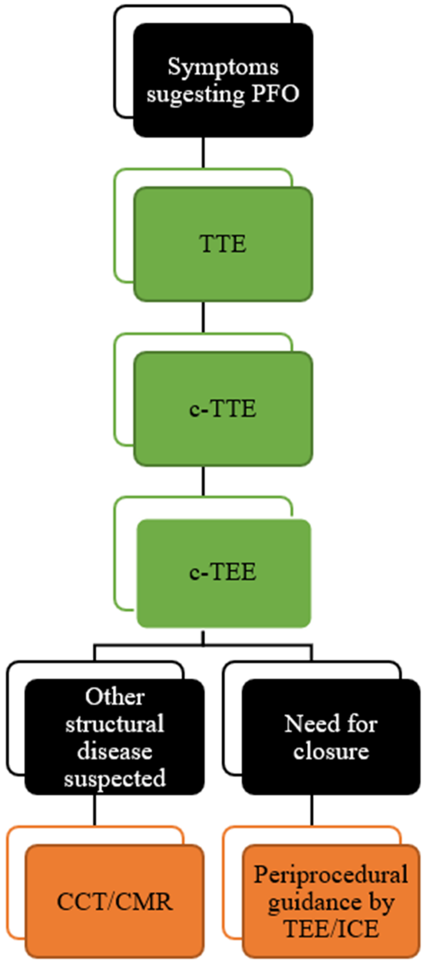

FIGURE 13 Multimodality imaging techniques flowchart for PFO diagnosis and management

4 | INDICATIONS FOR PATENT FORAMEN OVALE CLOSURE AND PERIPROCEDURAL GUIDANCE

4.1 | Current indications for patent foramen ovale closure

At the present moment, PFO closure is not standardized and the assembling of a multidisciplinary team is encouraged in order to make a therapeutic decision.[34] What is clearly stated in current guidelines[35] is the contraindication of performing closure as a primary prophylaxis method for stroke in patients with PFO. Based on current literature data, PFO closure for the secondary prevention of stroke is made by a multidisciplinary team based on a multiple variable-based approach, including type of PFO (simple, complex) and age (usually between 18 and 60 years old), in patients with cryptogenic stroke, transient ischemic attack or other type of systemic embolism in whom the PFO is the certain the cause.[6,35] In this regard, the RoPE score (risk of paradoxical embolism) has been proposed for estimating the probability that PFO is the causal agent of the stroke and guiding further therapy.[36]

4.2 | Periprocedural guidance

In patients who are candidates for PFO closure, a double-disc device could be implanted percutaneously, under TEE and/or fluoroscopic guidance (Video S8). It is recommended that TEE be used to guide the closure because of better assessment of correct position and residual shunts by color Doppler (Video S9) and contrast (Video S10). In addition to that, it has the added benefit of minimizing the radiation that is normally used when guidance is obtained based on fluoroscopy only.[37]

It is essential that the device position is verified, focusing on a few key aspects: (1) the discs should be parallel to each other on each

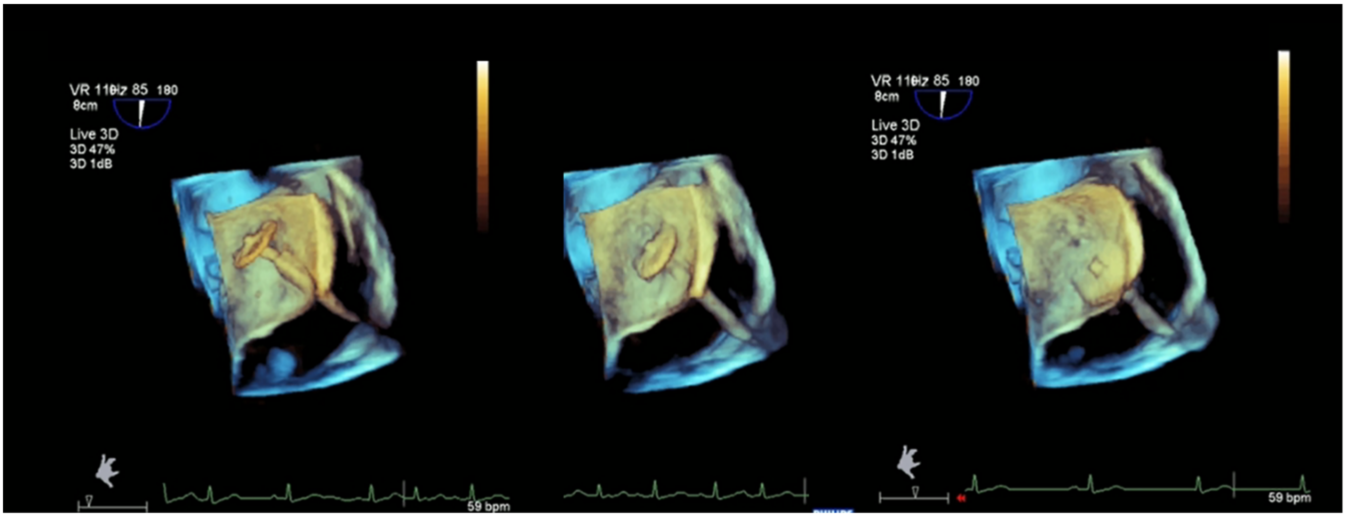

FIGURE 14 3D Transesophageal echocardiography images from PFO device closure guidance during positioning step

side of the interatrial septum; (2) the rims and edges of the device should be securely fixed; (3) the occluder should not come in contact with other structures (such as the aorta, for example). For better image acquisition and guidance, 3D-TEE can be used (Figure 14).

In spite of the fact that it is more invasive, as the probe is inserted via the right femoral vein into the right atrium under fluoroscopic guidance, intracardiac echocardiography is an excellent tool due to the proximity of the probe to the IAS and lower radiation exposure. In addition to that, it has the added advantage of requiring less personnel, because it can be performed by the same person who performs the closure and does not require an anesthesiologist due to lack of sedation.[38] Moreover, only two views are necessary for PFO closure (long and short atrial septal axis).[30,31,37] ICE with agitated saline contrast can also be used in order to evaluate the presence of right to left shunting, either for first assessment or in evaluating a residual shunt. However, ICE probes are expensive and therefore less accessible.[31]

Another possibility for PFO closure is using a suture-mediated device. During this procedure, two sutures are done—the first on septum secundum and the subsequent one on septum primum—which are then tightened together by a small plastic knot.[37]

After closure, follow-up is carried out by TTE in apical and subcostal four chamber views.[3,37]

5 | SPECIFIC CONSIDERATIONS FOR CLINICAL PRACTICE

Based on the aforementioned facts, in clinical practice a few checkpoints should be followed in order to improve diagnosis and management of PFO closure.

- In order to correctly assess anatomic structures and shunts, evaluation of PFO should be centered on contrast enhanced echocardiography, either transthoracic or transesophageal, completed in selected cases by other multimodality imaging techniques.
- Based on the principle of the "heart team," the decision for PFO closure should be made by a multidisciplinary cardio-neurology team; in order to accurately select cases that should be undergo this procedure, other specialists may be consulted depending on case complexity.
- Follow-up should be made by TTE.
- After closure, life-long antiplatelet therapy is mandatory in patients with a history of cryptogenic stroke or TIA, except for cases where anticoagulation must be used.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings will be available in JCU-22-471 at https://mc.manuscriptcentral.com/jcu?URL_MASK=83fce735835847a48ee3cc88fd5b9171 following an embargo from the date of publication to allow for commercialization of research findings.

ORCID

Mariana Floria https://orcid.org/0000-0002-9465-1503
Elena Diana Năfureanu https://orcid.org/0000-0002-5308-7176
Diana-Elena Iov https://orcid.org/0000-0003-2727-9913
Mihaela Dranga https://orcid.org/0000-0001-7750-6278
Radu Florin Popa https://orcid.org/0000-0001-5073-7463
Livia Genoveva Baroi https://orcid.org/0000-0002-0855-8063
Radu Andy Sascău https://orcid.org/0000-0002-5260-7520
Cristian Stătescu https://orcid.org/0000-0001-6439-4561
Daniela Maria Tănase https://orcid.org/0000-0002-7144-2506

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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