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The Role of Transcranial Doppler in Detecting Patent Foramen Ovale

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Abstract

Air embolic signals detected in the intracranial arteries using transcranial Doppler after intravenous injection of agitated saline bubbles indicate right-to-left cardiac shunting. They prove that emboli from venous sites can bypass the lungs and flow to the intracranial arteries. The Valsalva maneuver immediately after an intravenous injection of agitated saline bubbles helps the air bubbles pass through the shunt. If the air embolic signal appears in the intracranial arteries without the Valsalva maneuver, the shunting is highly significant to the etiology of embolism. Transcranial Doppler to detect air embolic signals after intravenous injection of agitated saline bubbles may not be mandatory to diagnose and treat patent foramen ovale; however, as with echocardiography, transcranial Doppler is considered a noninvasive, convenient, and low-cost investigation. The test should be helpful to confirm the significance of the corresponding patent foramen ovale.

Keywords

transcranial Doppler, right-to-left shunting, patent foramen ovale, Valsalva maneuver, cryptogenic stroke, Muller maneuver

Introduction

Transcranial Doppler (TCD) ultrasound can be used to evaluate blood flow velocity in the intracranial arteries.[1] It is limited in clinical practice because the skull lacks large acoustic insonation windows,[2] but it remains popular among physicians because it is noninvasive and convenient. Modern TCD machines are increasingly compact and portable, so TCD is a convenient adjunctive test in the daily practice of most physicians.[3]

In addition to measuring blood flow velocity, TCD can be used to detect emboli because the parameters of the embolic signal are distinct from those of normal blood flow. Specifically, the high-intensity transient signal (HITS) is a significant characteristic of the embolic signal. In normal blood flow, the HITS deflects 180° from erythrocytes and lies on top of the Doppler signal. The most common signals mimicking the HITS are artifacts.[4] The HITS associated with air emboli are easily detected using TCD because the sound of air emboli is distinctive from that of normal blood flow. Air embolic signals within the intracranial arteries after intravenous injection of agitated saline bubbles imply right-to-left shunting, the most common example of which is a patent foramen ovale (PFO).

Cryptogenic Stroke With PFO

Cryptogenic stroke is defined as a cerebral infarct of uncertain or indeterminate cause, as initially defined in the Trial of Org 10172 in Acute Stroke Treatment (TOAST) stroke-subtype classification. The causes of cryptogenic stroke remain indeterminate, mainly because the episode itself is temporary or reversible, and the available forms of clinical investigation do not address all possible causes. Moreover, some etiologies may remain unrecognized.[5]

The prevalence of PFO in patients with cryptogenic stroke ranges from about 40% to almost 60%.[6] The diagnosis of PFO sometimes becomes incidental, not causative, of the concurrent stroke. When the characteristics of the concurrent stroke are nonembolic, PFO could be just incidental. Once cerebral infarction occurs with corresponding carotid hemodynamic stenosis that prevents the ascending emboli from the heart, the PFO should not become a causative agent. Embolic stroke of undetermined source (ESUS) is a likely embolic stroke mechanism, defined as a nonlacunar cerebral infarct without responsible arterial stenosis or major cardiogenic sources.[7] When PFO is present in patients with ESUS that could have no other cause, it is the most likely etiology. The risk of paradoxical embolism (RoPE) score was established to identify pathological PFO and select patients who should undergo PFO closure.[8]

Protocol for TCD With Agitated Saline Bubbles

The recommended injectate for intravenous injection of agitated saline bubbles is 1 mL of air mixed with 9 mL of normal saline. However, adding 1 mL of the patient's blood to 8 mL of

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normal saline and 1 mL of air may improve air embolic signal detection,[9] although this remains controversial.[10] Ultrasound contrast agents, which consist of a stabilized skin shell surrounding an air bubble, are commercially available.[11] These agents provide similar accuracy as agitated saline bubbles.[12,13] Ultrasound contrast agents should be distinguished from ultrasound enhancing agents, which can pass into the pulmonary circulation and are used in the left ventricle rather than to detect right-to-left shunting.[14] In transthoracic echocardiography (TTE), 50% glucose contrast medium may increase sensitivity to shunting, but no previous studies have used it in TCD.[15]

The antecubital vein is the most popular injection site for agitated saline bubbles. Although injection through the femoral vein may yield a better rate of right-to-left shunting detection,[16,17] femoral puncture at the bedside is inconvenient. Moreover, femoral injections have a higher rate of spontaneous air bubble destruction because they involve a longer venous transit time. The supine position is standard during the procedure,[18] although alternative positions, such as right lateral decubitus, upright sitting, and sitting with right lateral leaning, may confer a better rate of shunting detection.[19,20] However, the routine use of positions other than supine is not recommended due to a lack of supporting evidence.[21]

The most popular location for air embolic signal detection is the middle cerebral artery on either side via the temporal acoustic insonation window. When the temporal window is poor, insonation of the basilar artery via a suboccipital window is an acceptable alternative location.[22] The power M-mode is preferred over the single-gate technique for monitoring.[23,24] The intracranial artery should be monitored for at least 25 s after the intravenous infusion of agitated saline bubbles.

The Valsalva maneuver is performed by having the patient fully inspire before forcing expiration against a closed glottis. The intrathoracic pressure should be elevated by about 35 mm Hg for 10 s after the maneuver.[25] This elevated intrathoracic pressure compresses the right atrium and augments flow through the PFO into the left atrium.[26] In patients with normal cerebral autoregulatory responses, the mean flow velocity in the middle cerebral artery should be decreased by 20% to 35% during the Valsalva maneuver.[27,28] To ensure correct technique, patients must fully understand and co-operate during the procedure. Therefore, the process must be clearly explained, and patients must practice the maneuver several times before performing the test. It is recommended that physicians put their hand on the patient's belly and have them perform the maneuver against that hand.[25] The mean flow velocity in the middle cerebral artery must be reduced by at least 20% after the maneuver to ensure adequate effect.[29] Abdominal compression during the strain phase of the Valsalva maneuver may augment paradoxical right-to-left shunting.[30] Adverse events from air embolization after an intense Valsalva maneuver remain uncommon, although the curtain feature of HITS can be detected.[31] The Valsalva maneuver should be started 5 s after the injection of agitated saline bubbles and performed for 10 s.[18,21] In patients who show poor compliance with the Valsalva maneuver, a simple cough maneuver may provide similar right-to-left shunting enhancement.[32]

The Muller maneuver is performed by having the patient force inspiration against a closed glottis to simulate the physiological effects of obstructive sleep apnea.[33,34] It is an alternative maneuver that enhances right-to-left shunting.[35] The modified Muller maneuver is forced inspiration against pinched nostrils, which should deliver a similar physiological effect as the original maneuver.[36] Obstructive sleep apnea syndrome is a common disease that induces right-to-left shunting in patients with PFO.[37] Performing TCD with agitated saline bubbles after the original or modified Muller maneuver may demonstrate the mechanism of cryptogenic stroke in individuals with PFO when stroke onset occurs during sleep.[38] The protocol for TCD in diagnosing right-to-left shunting is shown in Figure 1.

Two methods are commonly applied to grade right-to-left shunting: the International Consensus Criteria (ICC) and the Spencer Logarithmic Scale (SLS), as shown in Table 1.[18,23] In the ICC grading method, the degree of embolic signal detection, which reflects the significance of shunting, is divided into 4 categories: no HITS or negative shunt (category 1), 1 to 10 HITS or small shunt (category 2) (Figure 2A), 11 to 25 HITS or medium shunt (category 3) (Figure 2B and 2C), and >25 HITS, including the curtain feature or large shunt (category 4) (Figure 2D).[12,18,29] The number of HITS is related to the size of the PFO and represents the clinical significance of right-to-left shunting.[39] In the SLS grading method, the degree of embolic signal detection is divided into 6 grades: no HITS or negative (grade 0), 1 to 10 HITS (grade I), 11 to 30 HITS (grade II), 31 to 100 HITS (grade III), 101 to 300 HITS (grade IV), and >300 HITS (grade V). The SLS grades III or higher are the most predictive of large right-to-left shunting.[40]

Safety of TCD With Agitated Saline Bubbles

Adverse events associated with the procedure are rare.[41] One-fifth of patients may experience transient neurological symptoms, including headache, dizziness, and visual aura. Patients with a large shunt have a higher prevalence of postprocedural symptoms than those with a small or no shunt. Patients who experience these symptoms show no permanent deficits.[42] The procedure is also safe to perform in patients with cardiac structural abnormalities such as tetralogy of Fallot, intracardiac thrombus, ventricular septal defect, and atrial myxoma.[31] One case report found a hemodynamic abnormality associated with massive air embolism due to large shunting in a patient with a ventricular septal defect. The curtain pattern of air emboli was reported for more than 100 s in that case. However, the protocol of TCD with agitated saline bubbles was not described.[31]

Accuracy of Testing for PFO With Agitated Saline Bubbles

Transthoracic echocardiography is the most common initial screening method for PFO in patients with cryptogenic stroke because it is convenient and noninvasive.[43] However, a

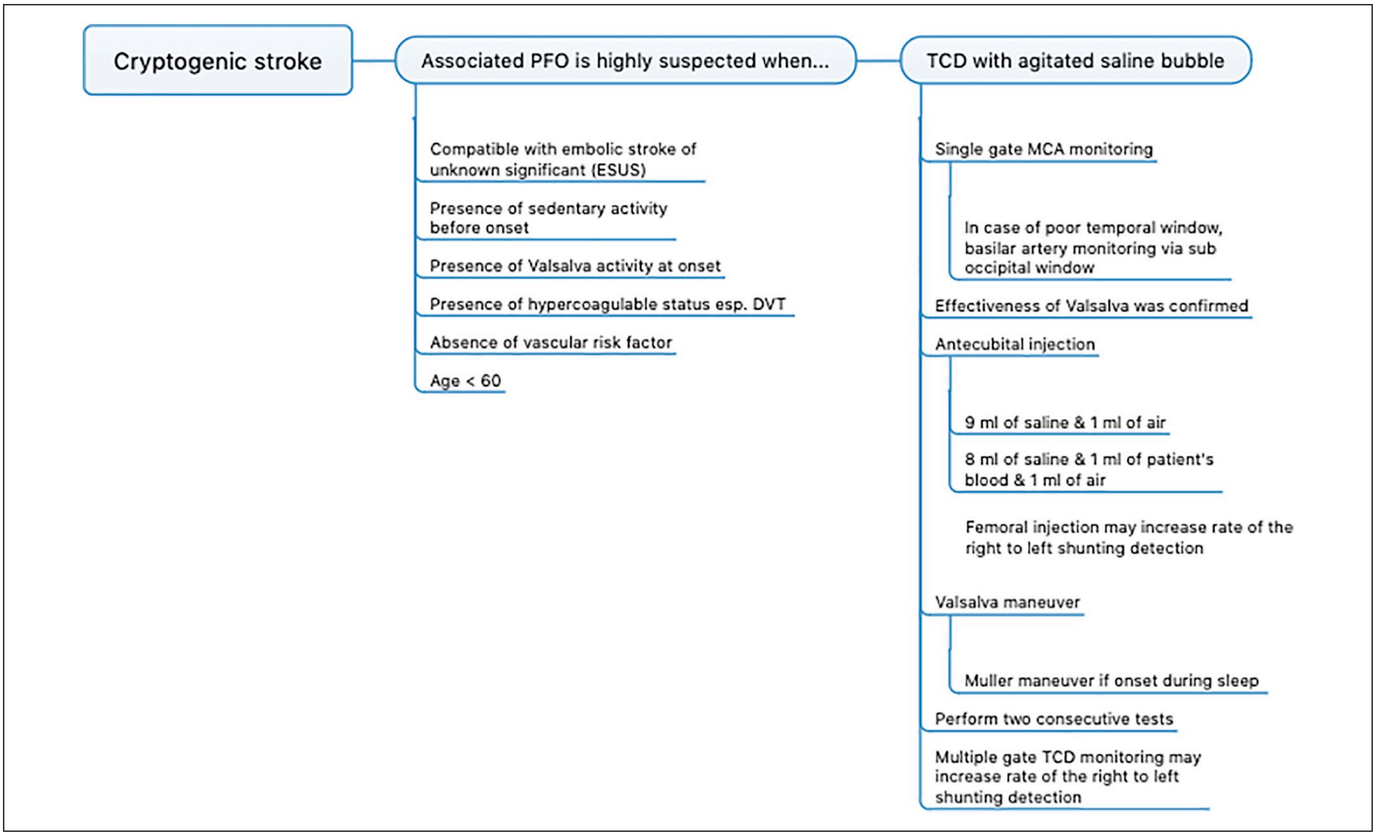

Figure 1. Protocol for using TCD in the diagnosis PFO with right-to-left shunting.
Note. TCD = transcranial Doppler; PFO = patent foramen ovale; MCA = middle cerebral artery; DVT = deep vein thrombosis.

Table 1. Two Methods of Grading Right-to-Left Shunting.

International consensus criteria		Spencer logarithmic scale	
Category	High-intensity transient signal appearance	Grade	Quantity of high-intensity transient signal
1	No occurrence	0	0
2	1-10	I	1-10
3	11-25 but no curtain	II	11-30
4	>25 or curtain	III	31-100
		IV	101-300
		V	>300

definitive diagnosis is made when PFO is directly visualized, and TTE is not appropriate for direct visualization of PFO because it has low resolution at the interatrial septum.[44] One study recommended using a subxiphoid 4-chamber view to best visualize PFO.[43] Combining color flow, Doppler with TTE does not improve shunting detection.[45] Instead, injection of intravenous ultrasonic contrast media, especially agitated saline bubbles, can improve shunting detection during TTE.[44,46] Intracardiac shunting is usually diagnosed in TTE when bubbles are visualized in the left atrium within 5 cardiac cycles of their appearance in the right atrium. In one meta-analysis, the sensitivity of TTE for right-to-left shunting detection was only 46%; however, its specificity for PFO detection was 98%.[47] Transthoracic echocardiography is less sensitive than TCD for detecting right-to-left shunting but more specific than TCD for detecting intracardiac shunting.[48]

Transesophageal echocardiography (TEE) remains the gold standard for detecting right-to-left shunting and visualizing a PFO.[49] Once a PFO is suspected, color flow Doppler and intravenous injection of contrast media are the routine procedures performed during TEE.[46] When compared with autopsy findings, TEE with color flow Doppler and agitated saline bubble injection has a sensitivity and specificity of 100% for PFO diagnosis.[50] The sedation given during TEE affects patients' ability to perform the Valsalva maneuver.[46] Most studies have found that TCD is at least not inferior to TEE for detecting right-to-left shunting.[51,52] In one study, TCD was marginally superior to TEE (by almost 5%).[53]

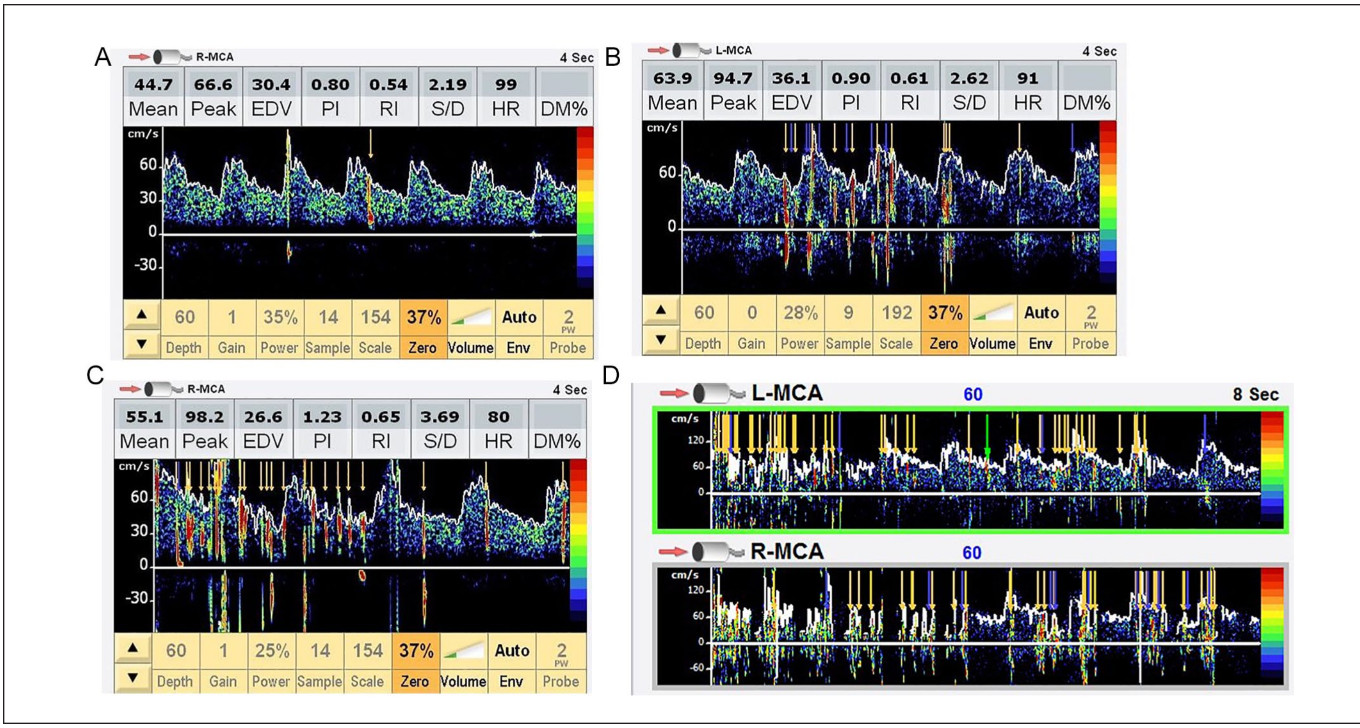

Figure 2. (A) A single HITS (arrow) in a right MCA. (B) Eleven HITS (yellow arrows) in a left MCA. (C) Twenty-three HITS (yellow arrows) in a right MCA. (D) More than 25 HITS (yellow arrows) in the left and right MCA.
Note. HITS = high-intensity transient signal; MCA = middle cerebral artery; EVD = end diastolic velocity.

Monitoring of PFO Closure

The percutaneous transcatheter technique is the most popular method of PFO closure. Intracardiac echocardiography (ICE) can guide percutaneous PFO closure.[54] Specifically, the absence of right-to-left shunting on ICE immediately after the deployment of the closure device confirms that the procedure was successful.[55] Transcranial Doppler is up to 30% more sensitive than ICE for detecting right-to-left shunting during surgery after deployment of the device.[56] Transcranial Doppler is useful for demonstrating residual and recurrent shunting in the short and long terms after percutaneous PFO closure. The severity of the right-to-left shunting detected by TCD reduces over time after closure.[57,58] Almost 20% of patients continue to have residual shunting for up to 5 years after the closure, whereas nearly 30% of patients develop recurrent shunting, whereby they show no shunting at the 6-month follow-up but recurrence at the 5-year follow-up.[59] Shunting detection after PFO closure may not always imply operative failure. It may indicate coexisting extracardiac or intracardiac shunting rather than PFO or incomplete PFO closure.

Transcranial Doppler with agitated saline bubbles cannot identify whether the right-to-left shunting is of the intracardiac or extracardiac subtype. In this regard, cardiac-based investigations, such as TTE, TEE, and ICE, show additional details about concomitant cardiac and great vessel abnormalities, which can affect decision making regarding PFO treatment. Patients with both atrial septal aneurysm and PFO show a higher prevalence of embolism.[60-62] The persistent eustachian valve, a remnant of the inferior vena cava valve, interferes with PFO closure and may promote the development of paradoxical embolism.[63] A Chiari network, which is a remnant of the sinus venosus, is also associated with PFO and atrial septal aneurysm, although the risk of embolism associated with a Chiari network is controversial.[64-66]

Conclusion

Transcranial Doppler with agitated saline bubbles plays a significant role in diagnosing right-to-left shunting in patients with cryptogenic stroke. Because it is noninvasive, low cost, accurate, and feasible for bedside use, TCD is popular in PFO management. Transcranial Doppler should be used to supplement cardiac-based imaging and provide more information in the management of PFO.

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Author Contributions

PH and SM equally contributed to conception and design of the work, data collection, drafting the article, critical revision of the article, final approval.

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