


# Transcranial Doppler to Detect Right to Left Communication: Evaluation Versus Transesophageal Echocardiography in Real Life

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## Abstract

We compared transcranial Doppler (TCD) with transesophageal echocardiography (TEE) and transthoracic echocardiography (TTE) for the detection of right to left communication (RLC) in the heart. All patients explored from 2013 to 2016 in a vascular medicine unit to detect RLC by TCD were included. Right to left communication was detected by TCD monitoring for microembolic signals after intravenous injection of agitated 5% glucose and air. One hundred one patients were explored for RLC by TCD, 64 by TEE (not possible in 10, bubble injection in 51), and 93 by TTE because of unexplained stroke or arterial thrombosis (51 males, 50 females, age  $51.0 \pm 15.8$  years) (bubble injection in 35). Fifty-three patients were positive after TCD (TEE: 4 negative, TTE: 7 negative). Of the negative patients after TCD, none was positive for TEE and 1 was positive for TTE with no evidence of patent foramen ovale. Transcranial Doppler was sensitive to detect RLC, even in patients with negative TTE or TTE. A negative TEE did not exclude RLC demonstrated by TCD. Transcranial Doppler might be proposed as first line to detect RLC.

## Keywords

cardiovascular disease, peripheral arterial disease, stroke, thrombosis

Right to left communication (RLC) through a patent foramen ovale (PFO) is found in 25% of the general population.<sup>1-6</sup> However, a PFO is considered to be responsible by paradoxical embolism for cryptogenic strokes and unexplained peripheral arterial embolism in young patients without any cardiovascular risk factor.<sup>5</sup> Risk factors for paradoxical embolism have been reported such as large PFO or interauricular septum aneurysm (ISA).<sup>5-11</sup> The gold standard to detect PFO is considered to be transesophageal echocardiography (TEE), but transcranial Doppler (TCD) has been proposed for this indication.<sup>4</sup> Transcranial Doppler may be performed to monitor microembolic signals (MES) in the middle cerebral arteries (MCAs), and injection of agitated saline or glucose solution may result in the detection of MES in cases of RLC.<sup>4</sup> High sensitivity has been reported for TCD (89%-97%) and some authors found TCD to be even more sensitive than TEE to detect RLC, and false-negative TCDs have been demonstrated to be due to small-size PFO.<sup>12-19</sup> In the present study, we evaluated the use of TCD to detect RLC and we compared the results with those obtained by TTE and TEE.

## Patients and Methods

This study was conducted in a single vascular medicine unit from a University Hospital between November 1, 2013, and October 1, 2016. We started to use TCD to detect PFO in our institution in 2013. All patients referred for TCD for PFO detection were included. Those without any temporal window were excluded. The demographic and clinical data were recorded together with the results of TCD, TTE, and TEE.

Transcranial Doppler was performed by 2 experienced operators. A specific helmet was fitted on the patient's head. Two TCD probes were set in the helmet in order to detect the flow in both MCAs (Looki Device; Atys Medical, Soucieu-en-

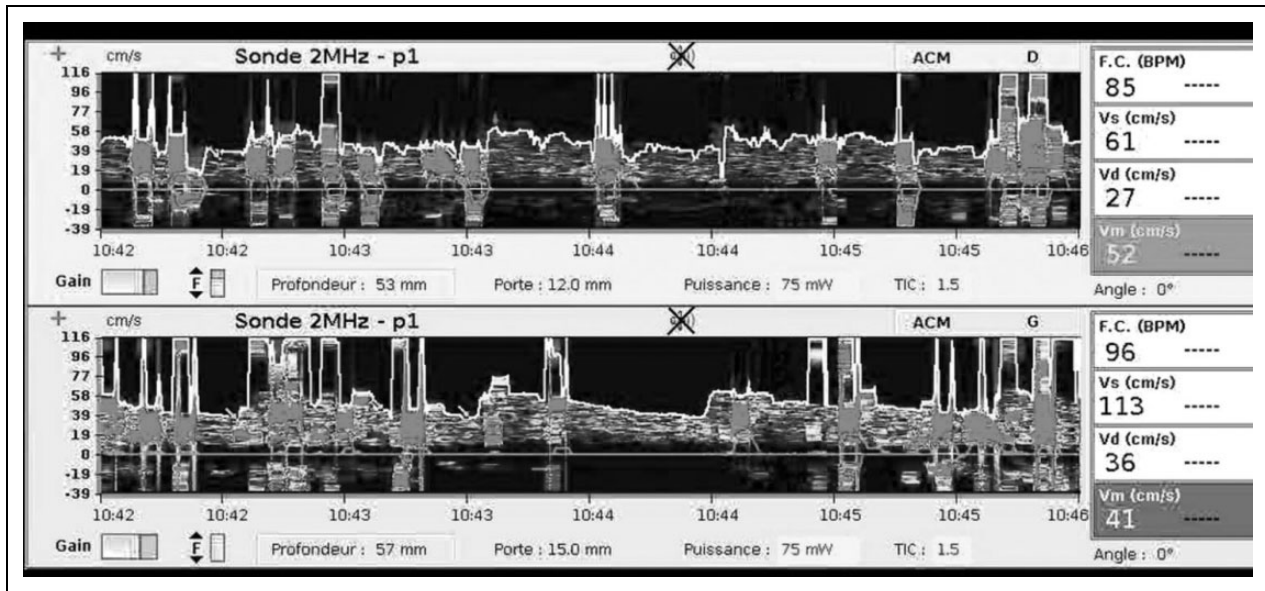
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**Figure 1.** Positive transcranial Doppler (TCD): microembolic signals (in light gray) after intravenous infusion of microbubbles.

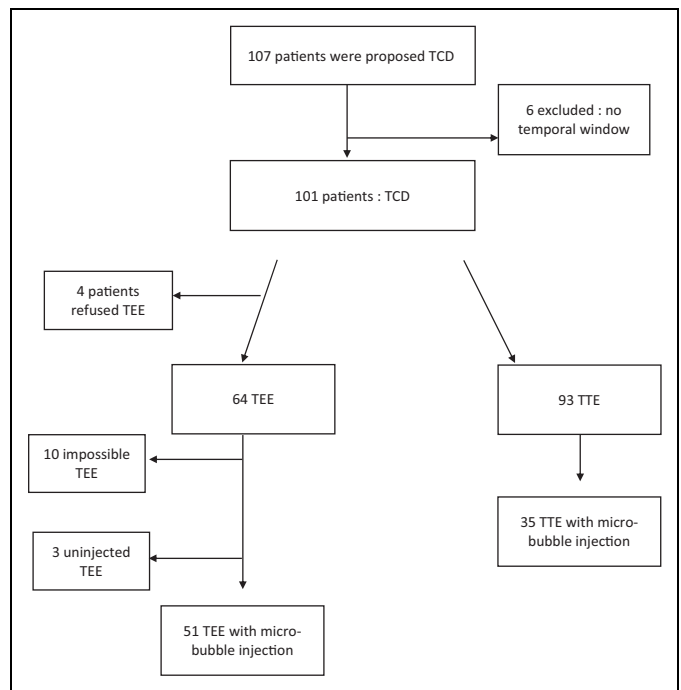
Jarret, France). Continuous monitoring was performed for both MCAs. Nine milliliters of 5% glucose solution were mixed with 1 mL air, shaken together and then injected into a forearm vein. The test was performed first spontaneously, then after the Valsalva maneuver. The test was considered as mildly positive if <3 microbubbles were recorded, moderately positive if the number of microbubbles was between 3 and 10, strongly positive if >10 bubbles were recorded, and curtain-like if the bubbles were so many that we were unable to count them (Figure 1). We compared the results of TCD with those of TTE and TEE to detect RLC for all the patients.

**Results**

From November 2013 to October 2016, 107 patients were referred to the vascular medicine unit to detect RLC. Six patients (all above 65 years old) had no temporal window and were not analyzed so that the study sample was 101 patients. From these 101 patients, 93 had TTE, of whom 35 had a microbubble injection, and 68 were proposed for TEE, of whom 4 refused and 64 finally had this test (51 with microbubble injection, 3 uninjected TEE, and TEE was not possible for 10; Figure 2).

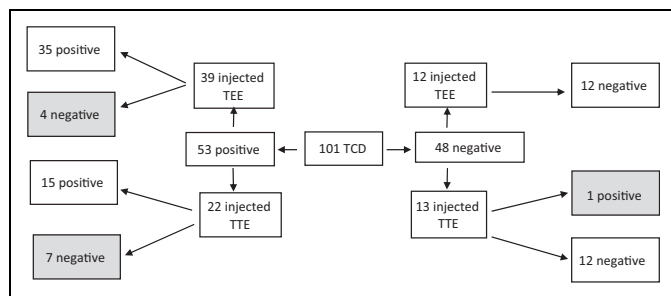
The study sample was made up of 51 male and 50 female patients. Mean age was  $51.0 \pm 15.8$  years; 27 patients had hypertension, 7 had diabetes, 20 were overweight, 49 were active smokers, and 19 had hyperlipidemia. Seven patients had migraine, 41 had a previous thromboembolic event, and 20 had a family history of arterial thrombotic events. The reason for RLC investigation was cryptogenic stroke in 58%, stroke with known etiology in 11%, limb artery thrombosis in 20%, visceral artery thrombosis in 9%, and unknown reason in 2%.

The main results of the study are shown in Figure 3. Transcranial Doppler found RLC in 53 of the 101 patients.



**Figure 2.** Flowchart of the study. TCD indicates transcranial Doppler; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography.

Transthoracic echocardiography with injection was performed in 22 of these 53 patients and was negative in 7. Transesophageal echocardiography with injection was performed in 39 patients and negative in 4. Transcranial Doppler was negative in 48 patients, among whom 13 had TTE (positive in 1) and 12 had TEE (negative in all cases). Finally, the number of patients positive for TCD was 53 for RLC, 35 for TEE, and 16 for TTE. Transesophageal echocardiography was negative in 10% of



**Figure 3.** Results of right to left communication (RLC) detection by TTE and TEE according to the results of transcranial Doppler. TCD indicates transcranial Doppler; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography.

patients positive by TCD, and TTE was negative in 32% of patients positive by TCD. Only 1 patient, negative by TCD, was positive by TTE. This patient had no morphological evidence of PFO by TTE but mildly positive bubble test. Of the 54 patients positive for RLC, 33 had PFO on echocardiography (associated with ISA in 21) and 1 patient positive by TCD but not by TTE or TEE was found to have intrapulmonary shunt. Of the 53 positive TCD, 19 were only positive after the Valsalva maneuver; as in 11 other, Valsalva maneuver increased the level of positivity.

In the population of 53 patients with positive TCD, 62% of patients had strong or curtain-like positivity. The size of PFO was measured in 16 patients. Patent foramen ovale above 10 mm was associated with moderate positivity in TCD in 1 case and curtain-like positivity in 1. Patent foramen ovale between 3 and 10 mm was associated with mild positivity in 1, strong positivity in 1, and curtain-like positivity in 7. Therefore, among the 11 patients with PFO above 3 mm, strong or curtain-like positivity was observed in 9.

## Discussion

This retrospective study in current practice found a good performance of TCD that detected more numerous RLC than the other methods. In our population, 53% of patients had PFO, twice as many as in the general population, but our population was selected as young patients with arterial thrombosis of unknown origin. A limitation of the present study is its retrospective design so that TCD, TTE, and TEE with bubble injection were not performed in all patients. However, TCD was sensitive to detect RLC. The rate of false negatives compared with TEE was reported to be 0% to 32%.<sup>19-23</sup> Recently, a meta-analysis showed TCD to be more sensitive than TTE compared with TEE to detect PFO (96% vs 45%).<sup>19</sup> We confirm a good sensitivity of TCD since only 1 patient had positive TTE and negative TCD.

Our study has limitations such as a retrospective design or performing some of the tests in many, but not all, patients. However, TCD provided good practical results and has some advantages compared with other methods. Positivity was strong or curtain-like for all the large PFO that are more likely

to be related to paradoxical embolism.<sup>24</sup> Transthoracic echocardiography is less sensitive than TEE to detect RLC, but the Valsalva maneuver is useful but difficult to perform in TEE and impossible if TEE is performed under general anesthesia.<sup>23-25</sup> Moreover, TEE is an unpleasant method and 4 patients did not agree to have TEE. In 10 other patients, TEE was not possible. We notice that TCD also had limitations, the main one was absent temporal window in 6 patients who were all above 65 years. A temporal window is often absent in women older than 65 years, while in young patients, this problem is rare. The detection of RLC is considered to be useful in young patients so that the temporal window in TCD is probably a rare limitation in practice.

The good sensitivity of TCD to detect RLC may modify the strategy to detect PFO. The main advantage of TEE over TCD is to show cardiac abnormalities such as ISA or other cardiac causes of arterial embolism (endocarditis, cardiac tumors). Transcranial Doppler seems to be at least as sensitive as TEE to detect RLC and proved to detect positive patients negative on TEE. Then TEE might be performed in patients positive for RLC in TCD in the case of high suspicion of paradoxical embolism or in the patients with abnormal TTE. Transesophageal echocardiography may show aorta atheroma that may also be found by computed tomography scan, and the proposed strategy may perhaps decrease the need for TEE in young patients with stroke or arterial embolism of unknown origin (with CHADS<sub>2</sub>-VASC = 0).<sup>7</sup> In older patients at risk of left atrial thrombus, TEE still has to be done. If TEE is performed first, we think that TCD is necessary in the case of still unknown etiology in order to detect a false-negative TEE for RLC.

## Author Contribution

All authors substantially contributed to (1) conception and design, acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, and (3) final approval of the version to be published.

## Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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