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Analysis of Sensitivity and Accuracy of Transthoracic Echocardiography Right Heart Contrast Combined with Transcranial Doppler Bubble Test in the Diagnosis of Patent Foramen Ovale

Jianmei Chen, Dai Zhang, Dongdong Ji, Shuhua Wang, Qiushuang Wang*

The Fourth Medical Center of the PLA General Hospital, Beijing 100048, China

**Author to whom correspondence should be addressed.*

Abstract: *Objective*: To analyze the diagnostic value of transthoracic right heart contrast echocardiography (c-TTE) combined with transcranial color-coded Doppler (c-TCCD) in patent foramen ovale (PFO). *Methods*: A total of 180 suspected PFO patients admitted from October 2023 to October 2025 were selected and evenly divided using a random number table. The observation group underwent c-TTE combined with c-TCCD for diagnosis, while the reference group underwent c-TTE alone. The diagnostic effects of the two groups were compared. *Results*: The detection rates of PFO in the observation group under both resting state and Valsalva maneuver were higher than those in the reference group ($p < 0.05$). Apart from the aperture size and thickness of the secondary septum, there were differences in other anatomical indicators between the two groups ($p < 0.05$). The detection rate of grade III shunt in the observation group was higher than that in the reference group ($p < 0.05$). Using the diagnostic results of transesophageal echocardiography (TEE) as the gold standard, the sensitivity and accuracy of the observation group were higher than those of the reference group, while the missed diagnosis rate was lower than that of the reference group ($p < 0.05$). *Conclusion*: The diagnosis of c-TTE combined with c-TCCD can effectively detect PFO, fully assess changes in the cardiac anatomical structure of patients, and determine shunt conditions, demonstrating high diagnostic efficacy.

Keywords: Contrast transthoracic echocardiography; Transcranial doppler cerebral bubble study; Patent foramen ovale; Sensitivity; Accuracy

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1. Introduction

Patent foramen ovale (PFO) is a relatively common congenital heart disease, characterized by a structural abnormality in which the physiological channel (foramen ovale) that exists during fetal development fails to close completely by the age of three after birth. The underlying cause of this condition is developmental abnormalities [1].

The gold standard for diagnosing this disease is transesophageal echocardiography (TEE), which can accurately assess the closure status of the foramen ovale in patients and thereby comprehensively evaluate the condition. However, this diagnostic procedure is invasive, causing significant discomfort to patients and resulting in poor compliance, thus presenting certain limitations. Contrast transthoracic echocardiography (c-TTE) is a non-invasive and safe diagnostic technique that can be performed repeatedly and demonstrates high diagnostic sensitivity. When combined with contrast transcranial Doppler cerebral bubble study (c-TCCD), it can qualitatively diagnose the disease and utilize the grading of right-to-left shunt (RLS) to semi-quantitatively assess the severity of the disease [2].

Furthermore, the operational method of c-TCCD is simple, non-invasive, and highly accurate, enabling it to achieve a high level of patient cooperation and thus demonstrating excellent diagnostic efficiency. Based on this, this study selected 180 suspected PFO patients to evaluate the diagnostic role of c-TTE combined with c-TCCD.

2. Materials and methods

2.1. General information

A total of 180 patients suspected of having patent foramen ovale (PFO) who were admitted and diagnosed between October 2023 and October 2025 were selected. These patients were evenly divided into two groups using a random number table: the observation group (90 cases), comprising 49 males and 41 females, aged between 19 and 57 years with a mean age of (36.52 ± 2.74) years; and the reference group (90 cases), comprising 48 males and 42 females, aged between 20 and 59 years with a mean age of (36.73 ± 2.65) years. Comparisons of the data between the two groups yielded a p-value greater than 0.05.

2.1.1. Inclusion criteria

Preliminary diagnosis of PFO; meeting the indications for examination; able to fully tolerate the examination procedure; normal liver and kidney function; complete basic information; informed consent and agreement to participate in the study.

2.1.2. Exclusion criteria

Presence of severe somatic diseases; concurrent cardiomyopathy; presence of psychiatric disorders; moderate to severe pulmonary hypertension; presence of cerebrovascular malformations; concurrent severe arrhythmia or valvular heart disease; inability to perform the Valsalva maneuver; withdrawal from the study midway.

2.2. Methods

The reference group underwent c-TTE diagnosis: Color Doppler ultrasound was used, with the S5-1 probe selected, and the specific frequency range was between 2 and 5 MHz. The patient was positioned in the left lateral decubitus position. First, two-dimensional ultrasound scanning was performed to comprehensively observe the cardiac chambers and assess the specific sizes of each chamber as well as the intracardiac structures. Determine whether there is shunting between the ventricles and between the atria, and check for any gaps between the foramen ovale valve and the observed secondary septum.

Then, perform color Doppler flow imaging to evaluate the trans-septal shunting flow. After puncturing the left upper extremity vein, inject a certain amount of normal saline. The patient is required to perform the Valsalva maneuver, after which right heart opacification will be observed. Three cardiac cycles are monitored to identify the characteristics of the shunting.

The observation group underwent diagnosis using c-TTE combined with c-TCCD. The diagnostic method for c-TTE is the same as described above. The operational procedure for c-TCCD is as follows: Select transcranial Doppler ultrasound and set the probe frequency at 2 MHz. Instruct the patient to maintain a supine position. Establish a venous access in one elbow vein, connect a three-way stopcock, with one end connected to a syringe containing 10 ml of normal saline. Install embolus detection equipment and monitor the middle cerebral artery using dual-depth and single-channel mode, with a depth of 50–60 mm. In the patient's resting state, inject an appropriate amount of normal saline through the elbow vein and observe the microbubble signals that appear within 10 seconds.

The diagnostic method for TEE is as follows: Select color Doppler ultrasound with a probe model of X7-2t and set its frequency at 2–7 MHz. Instruct the patient to take dyclonine hydrochloride capsules orally, followed by local anesthesia. The patient should lie in a left lateral position. Place the probe in the middle to lower segment of the esophagus, with the section at the level of the double atria, and scan for any obvious gaps between the secondary and primary septa.

2.3. Observation indicators

(1) Detection rate of PFO

Observe the detection rate of PFO under resting state and Valsalva maneuver.

(2) Anatomical indicators

Observe indicators such as aperture size, thickness of the secondary septum, length of the Eustachian valve, tunnel length, shunt angle, and mobility of the primary septum.

(3) Shunt grading

Refer to the "Chinese Expert Consensus on Prophylactic Closure of Patent Foramen Ovale". The specific grading is defined as follows: No right-to-left shunt (RLS) is observed, and no microbubbles/frame images are detected in the left cardiac chamber, recorded as Grade 0; A small amount of RLS is observed, with 1–10 microbubbles/frame images detected in the left cardiac chamber, recorded as Grade I; A moderate amount of RLS is observed, with 11–30 microbubbles/frame images recorded as Grade II; A large amount of RLS is observed, with more than 30 microbubbles/frame images recorded as Grade III.

(4) Diagnostic efficacy positive c-TTE

The presence of three or more microbubbles in the left atrium; Positive c-TCCD: Refer to the "Venice Conference Recommended Criteria (1999)" to evaluate specific data on microembolic signals. If no microembolic signals are detected, it is recorded as Grade I; If microembolic signals are present, with a quantity of 1–10, it is recorded as Grade II; If microembolic signals are visible, with a specific quantity of 11–25, it is recorded as Grade III; If the number of microembolic signals detected exceeds 25 and appears as a curtain-like pattern, it is recorded as Grade IV. A grade of ≥ II is considered positive. A positive TEE result indicates the presence of RLS or right-to-left shunt (LRS) in the primary and secondary septum. Using TEE diagnostic results as the gold standard, sensitivity = number of true positives / (number of true positives + number of false negatives); accuracy = (number of true positives + number of true negatives) / total number of cases in this group; specificity = number of true negatives / (number of true negatives + number of false positives); missed diagnosis rate = number of false negatives / (number of true positives + number of false negatives); misdiagnosis rate = number of false positives / (number of false positives + number of true negatives).

2.4. Statistical analysis

Data were processed using SPSS 28.0 software. Measurement values were compared using *t*-tests, and count values were compared using chi-square (c^2) tests. Statistical significance was defined as $p < 0.05$.

3. Results

3.1. Comparison of PFO detection rates between the two groups

The detection rates of PFO in the observation group were higher than those in the reference group under both resting state and Valsalva maneuver conditions ($p < 0.05$) (refer **Table 1**).

Table 1. Comparison of PFO detection rates between the two groups [n/%]

Group	n	Resting state	Valsalva maneuver
Observation group	90	59 (65.56)	71 (78.89)
Reference group	90	45 (50.00)	59 (65.56)
χ^2		4.464	3.988
p		0.035	0.046

3.2. Comparison of anatomical indicators between the two groups

Apart from aperture size and secondary septal thickness, there were differences in other anatomical indicators between the two groups ($p < 0.05$) (refer **Table 2**).

Table 2. Comparison of anatomical indicators between the two groups ($\bar{x} \pm s$)

Group	n	Defect size (mm)	Septum secundum thickness (mm)	Eustachian valve length (mm)	Tunnel length (mm)	Shunt angle (°)	Septum primum mobility (mm)
Observation group	90	2.75 ± 0.49	6.69 ± 1.78	7.66 ± 1.59	9.75 ± 1.64	6.98 ± 1.77	11.72 ± 2.59
Reference group	90	2.81 ± 0.52	6.58 ± 1.80	5.92 ± 1.43	4.98 ± 1.98	15.53 ± 2.64	6.87 ± 1.57
t		0.797	0.412	7.719	17.601	25.520	15.192
p		0.427	0.681	0.000	0.000	0.000	0.000

3.3. Comparison of shunt grades between the two groups

The detection rate of Grade III shunts in the observation group was higher than that in the reference group ($p < 0.05$) (refer **Table 3**).

Table 3. Comparison of shunt grades between the two groups [n/%]

Group	n	Grade 0	Grade I	Grade II	Grade III
Observation group	90	4 (4.44)	8 (8.89)	13 (14.44)	65 (72.22)
Reference group	90	11 (12.22)	17 (18.89)	22 (24.44)	40 (44.44)
χ^2		3.564	3.763	2.873	14.286
p		0.059	0.052	0.090	0.000

3.4. Comparison of diagnostic efficacy between the two groups

Using the diagnostic results from TEE as the gold standard, the diagnostic outcomes of the two groups are presented in **Table 4**. The observation group demonstrated higher sensitivity and accuracy, along with a lower missed diagnosis rate compared to the reference group ($p < 0.05$), as shown in **Table 5**.

Table 4. Analysis of diagnostic results in the two groups

Diagnostic method		Gold standard		Total
		Positive	Negative	
Observation group	Positive	68	3	71
	Negative	2	17	19
Reference group	Positive	55	4	59
	Negative	15	16	31

Table 5. Comparison of diagnostic efficacy between the two groups [n/%]

Group	Sensitivity	Accuracy	Specificity	Missed diagnosis rate	False positive rate
Observation group	97.14 (68/70)	94.44 (85/90)	85.00 (17/20)	2.86 (2/70)	15.00 (3/20)
Reference group	78.57 (55/70)	78.89 (71/90)	80.00 (16/20)	21.43 (15/70)	20.00 (4/20)
χ^2	11.315	9.423	0.173	11.315	0.173
p	0.001	0.002	0.677	0.001	0.677

4. Discussion

PFO is a primary type of congenital heart disease that does not cause biventricular shunting and does not affect the hemodynamics of myocardial tissue, resulting in a relatively high rate of missed or incorrect diagnoses [3]. The long-term presence of this condition increases the risk of stroke and is considered a risk factor for various cardiovascular and cerebrovascular diseases. It is also associated with symptoms such as migraines and angina pectoris. Therefore, early diagnosis of the disease is essential to fully assess its severity and to implement appropriate treatment measures.

Transesophageal echocardiography (TEE) serves as the gold standard for diagnosing this disease, capable of assessing atrial size and structural changes, reflecting the pathological conditions of cardiac valves, and observing the blood flow status in cardiac arteries and veins to facilitate differential diagnosis [4]. However, due to its invasive nature and the generally moderate tolerance of patients during the examination, TEE is difficult to be widely applied. Transthoracic echocardiography (TTE) is a commonly used diagnostic method for this disease.

However, it is susceptible to interference from gas factors and excessive obesity, making it difficult to clearly display the images of the atrial septal biatrial section. To enhance disease differentiation ability, it is necessary to increase the probe pressure during enhanced scanning and adjust the color gain mode [5]. Nevertheless, its detection effectiveness for lesions with small internal diameters and low-velocity blood flow remains limited. In comparison, contrast-enhanced transthoracic echocardiography (c-TTE) offers a more scientifically robust diagnosis. It utilizes microbubble signals to evaluate right-to-left shunt (RLS) conditions, boasting the advantages of being non-invasive and convenient. On the basis of evaluating cardiac function and structure, it can assess the flow state of microbubbles using right heart contrast echocardiography, thereby determining the severity of the disease [6]. Contrast-enhanced transcranial color-coded duplex sonography (c-TCCD) can place microspheres into the right atrium under the guidance of an esophageal ultrasound catheter. After injecting a contrast agent, it evaluates the distribution trajectory of microbubbles during cardiac pulsation to assess the shunt between the left and right atria. As microspheres pass through the left atrium, blood flow velocity increases; conversely, when they do not pass through, blood flow velocity slows down. Based on this, the presence or absence of a patent foramen ovale (PFO) can be determined.

The combined diagnosis of these two methods can leverage their respective strengths, thus offering high diagnostic feasibility [7]. The results showed that the detection rate of PFO in the observation group was higher than that in the reference group during both resting state and Valsalva maneuver; the length of the Eustachian valve, tunnel length, and mobility of the primary septum in the observation group were greater than those in the reference group, while the shunt angle was smaller in the observation group; the detection rate of grade III shunt in the observation group was higher than that in the reference group; taking the diagnostic results of TEE as the gold standard, the sensitivity and accuracy of the observation group were higher than those of the reference group, while the missed diagnosis rate was lower in the observation group ($p < 0.05$). The reasons for the analysis are as follows: c-TTE can utilize acoustic contrast agents to evaluate the number of microbubbles in the left and right atria, allowing for a comprehensive observation of shunt volume. However, it has limited temporal windows for a single diagnosis, only observing the blood flow status of the middle cerebral artery, making it difficult to accurately detect microbubble signals, which may lead to missed diagnoses [8,9].

Additionally, due to its average image quality, it is challenging to clearly visualize subtle emboli, resulting in a relatively high false-positive rate. Combining c-TCCD can enhance quantitative resolution and provide dual detection of the middle cerebral artery to observe the distribution of tiny bubbles. During the Valsalva maneuver, this diagnostic approach can bring microbubbles to their peak, enabling clear observation of disease conditions and improving diagnostic accuracy [10]. The combination of the two can effectively evaluate changes in cardiac anatomical structures, accurately measure the mobility and size of cardiac structures, and semi-quantitatively grade the number of microbubbles to accurately assess disease severity, thus demonstrating excellent diagnostic efficacy.

5. Conclusion

In conclusion, the combination of c-TTE and c-TCCD demonstrates superior diagnostic performance for PFO, enabling a comprehensive assessment of disease conditions and providing scientific guidance for subsequent treatment.

Disclosure statement

The author declares no conflict of interest.

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