

# Characteristics and analysis of right-to-left shunt-related dizziness in patients without hypoxemia

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## Abstract

**Objective:** This study aimed to analyze right-to-left shunt-related dizziness in three patients without hypoxemia.

**Methods:** Case 1 was a 47-year-old man with a history of cerebral infarction 8 years previously and recurrent dizziness for > 6 months. Patent foramen ovale (PFO) was found with a severe right-to-left shunt. Case 2 was a 50-year-old man with acute stroke. He had a history of repeated dizziness for > 4 years. He was diagnosed with PFO with a severe right-to-left shunt after admission. Case 3 was a 73-year-old woman with recurrent dizziness for > 10 months. Pulmonary arteriovenous fistula was diagnosed upon admission. No patients had hypoxemia.

**Results:** After percutaneous PFO occlusion in Cases 1 and 2, the patients were followed up for 6 months and 1 year, respectively. Two patients had relief of dizziness without recurrence. In Case 3, the pallor improved and the dizziness was relieved after pulmonary arteriovenous fistula embolization and did not recur over a 6-month follow-up.

**Conclusions:** There was a possible association between a severe right-to-left shunt and dizziness, although hypoxemia was absent in the cases. Intervention to eliminate a left-to-right shunt can improve dizziness in patients without hypoxemia with a severe right-to-left shunt.

## Keywords

Right-to-left shunt, dizziness, contrast-enhanced transcranial Doppler ultrasound, patent foramen ovale, pulmonary arteriovenous fistula, embolization, hypoxemia

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## Introduction

Central dizziness is a common clinical neurological symptom. Right-to-left shunt-related dizziness is rare. The position of the right-to-left shunt can be categorized into heart and lung levels, and the former is the most common in patent foramen ovale (PFO), followed by atrial septal defects. Approximately 20% to 25% of adults have PFO.<sup>1</sup> Pulmonary arteriovenous fistula (PAVF) is the main cause of a right-to-left shunt being present at the pulmonary level.<sup>2</sup> In this report, right-to-left shunt-related dizziness is characterized in patients without hypoxemia and insight is provided into the diagnosis and treatment of right-to-left shunt-related dizziness.

## Patients and methods

The clinical manifestations, treatment, and follow-up results of three patients with right-to-left shunt-related dizziness were analyzed. The Delicay TCD ultrasound diagnostic instrument (Delicay Company, Shenzhen, China) with a probe frequency of 1.6 MHz was used. The Philips 265-slice spiral computed tomographic instrument (Philips Company, Amsterdam, The Netherlands) was also used to assess the patients.

The study protocol was approved by The Third Affiliated Hospital of Shenzhen University Committee on Human Research. The patients provided written informed consent for publication of this study.

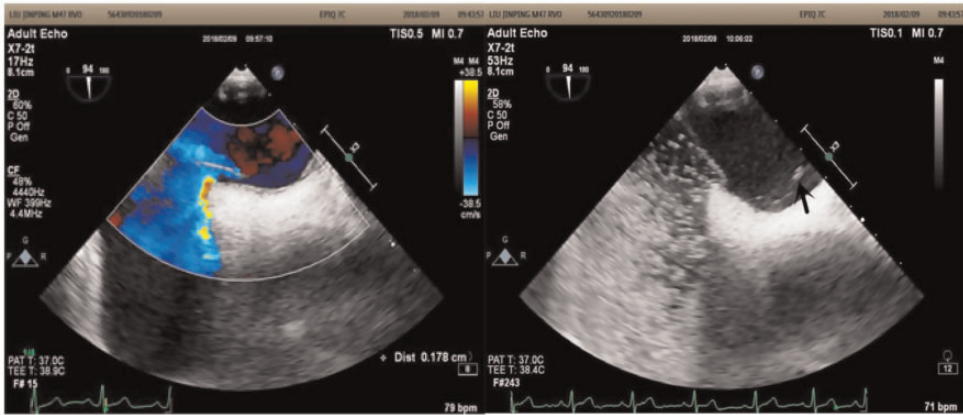
## Results

### Case 1

A 47-year-old man was hospitalized for recurrent dizziness for >6 months in January 2018. In addition to dizziness, he was prone to fatigue and dozing off.

The symptoms of dizziness were similar each time. After rest, his dizziness would improve, without hemiplegia, vagueness of speech, double vision, fever, or headache. The patient had a normal diet, slept for more than 10 hours a day, and had normal urine and stool. He had a history of cerebral infarction 8 years previously and facial neuritis 9 years previously, without obvious residual symptoms. The patient denied a history of exposure to toxic radioactive substances and a history of alcohol or drug addiction. He had smoked 20 cigarettes a day for more than 20 years. A physical examination showed that his blood pressure was 132/99 mmHg. He had a normal mental status, clear speech, no obvious abnormalities in cranial nerve function, and a soft neck. His muscle strength and tension and tendon reflexes were normal, and pyramidal signs were negative. No obvious abnormality was detected in a cardiopulmonary examination. The results of routine stool, blood, and urine tests after admission were normal. The results of liver function and renal function tests, and levels of iron, C-reactive protein, thyrotropin, blood glucose, D-dimer, glycosylated hemoglobin, and blood lipids were also normal. Results of tests for autoimmune vasculitis antibodies, antinuclear antibodies, and blood gas analysis were normal. The homocysteine level was 31  $\mu\text{mol/L}$  and the prothrombin activity was 77%. Thromboelastography, electrocardiography, chest radiography, color Doppler ultrasonography of the abdomen, and 24-hour ambulatory electrocardiography also showed no obvious abnormalities.

Color Doppler ultrasonography of the carotid artery showed bilateral carotid atherosclerosis and the right vertebral artery was thin. Brain magnetic resonance imaging and brain magnetic resonance angiography showed a small left thalamic infarction (obsolete lesion). Transesophageal echocardiography and contrast-enhanced



**Figure 1.** Transesophageal right ventricular echocardiograms of Case 1. After the Valsalva maneuver, many microbubbles were released from the left atrium at approximately 30 frames/section

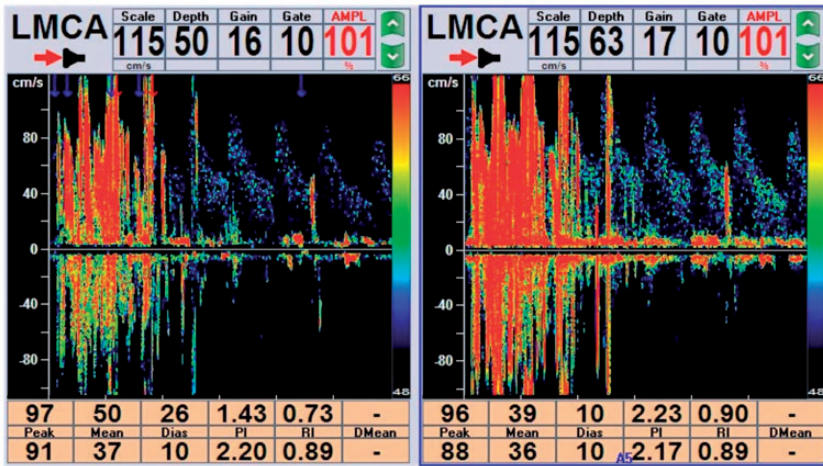
ultrasonography showed a moderate PFO with a severe right-to-left shunt (Figure 1).

After admission, the patient was treated with anti-platelet therapy and lipid-regulating, collateral circulation-improving, and blood pressure-lowering medications (as in previous hospitalizations). Although his dizziness was temporarily improved, it was expected to recur soon. Occlusion of the patient's PFO was performed at the end of February 2018. The patient's dizziness was relieved without recurrence during the 6-month postoperative follow-up period.

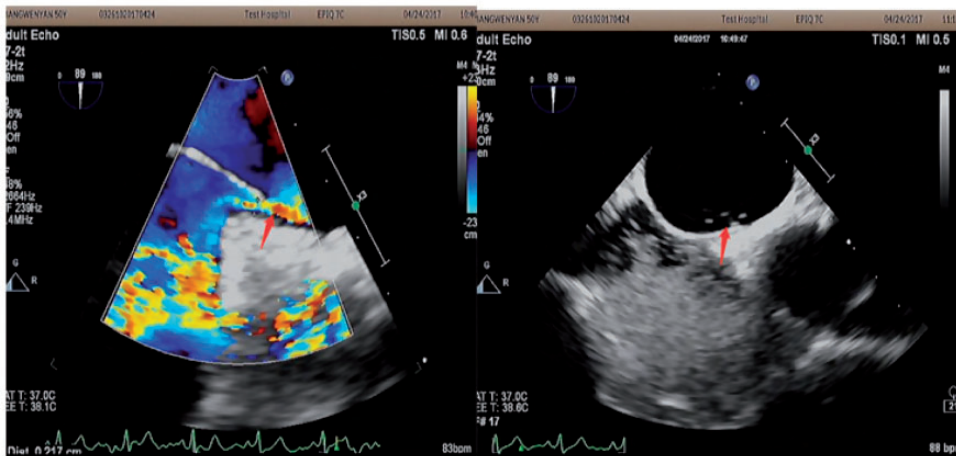
## Case 2

A 50-year-old man was admitted because of weakness of the right lower limb in April 2017. The patient had no obvious signs of vague speech. He did not have cough, fever, shortness of breath, consciousness disorder, or convulsions. Since the onset of right lower limb weakness, the patient had a normal diet, normal stool and urine, and no recent remarkable weight loss. He had experienced recurrent dizziness (especially during motion) for > 4 years and had a history of gastritis. He denied a history of

infectious diseases, surgery, major trauma, blood transfusion, allergy, or genetic disorders. After admission, routine blood, urine, blood lipid, and renal function tests were performed, which showed normal results. Tests for human immunodeficiency virus antibody and syphilis antibody were also negative. His D-dimer level was 0.58 mg/L FEU. His liver function test results, levels of iron, anti-nuclear antibody, immunoglobulin, and fasting blood glucose, and coagulation function were normal. His thromboelastography and blood gas analysis results, as well as glycated hemoglobin, vasculitis antibody, protein S, and protein C levels were also normal. Electrocardiography, 24-hour ambulatory electrocardiography, and chest computed tomography showed no obvious abnormalities. Color Doppler ultrasonography of the abdomen and urinary system and transthoracic echocardiography showed no remarkable abnormal findings. Carotid artery ultrasonography revealed uneven thickening of the intima-media of both vertebral arteries. Brain magnetic resonance imaging and brain magnetic resonance angiography showed multiple acute cerebral infarctions in the frontal and left temporal lobes.



**Figure 2.** Contrast-enhanced transcranial Doppler ultrasound showing a severe right-to-left shunt (intrinsic) in Case 2



**Figure 3.** Transesophageal echocardiograms showing a patent foramen ovale and right-to-left shunt in Case 2

Contrast-enhanced transcranial Doppler ultrasound showed a severe right-to-left shunt (Figure 2). Transesophageal echocardiography showed a PFO and bidirectional shunt (Figure 3). Percutaneous closure of the PFO was successfully performed in August 2017. At the follow-up 1 year after

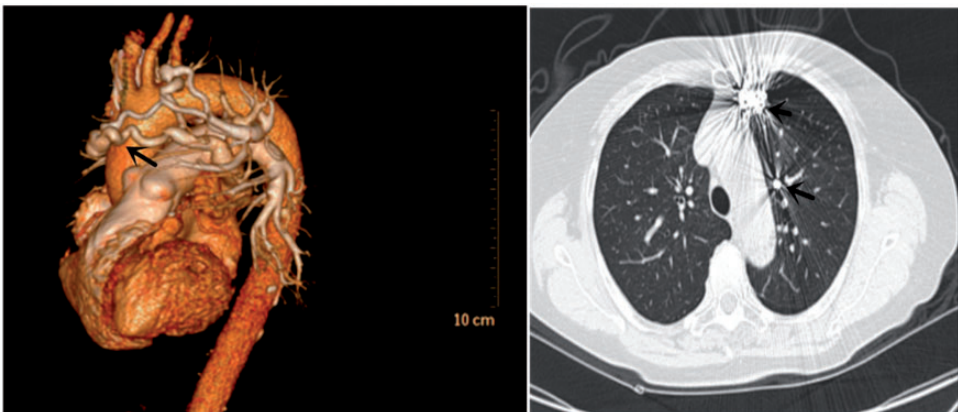
discharge, the patient’s dizziness was completely resolved.

**Case 3**

A 73-year-old woman was admitted for recurrent dizziness for > 10 months in July

2017. In June 2016 and February and March 2017, she experienced recurrent dizziness with fatigue, but no cough, hemiplegia, or altered consciousness. She was diagnosed with posterior circulation ischemia and treated with anti-platelet therapy and lipid-regulating and circulation-improving medication. She had a 7-year history of hypertension and had had three cerebral infarctions since 2012, with residual vague speech. She had a history of pneumonia, hyperlipidemia, dry eyes, depression, and long-term use of diazepam. She denied a history of major trauma, blood transfusion, allergy, and hereditary disorders. A physical examination at admission showed a blood pressure of 132/62 mmHg, and she was conscious, had vague speech, had a soft neck, had normal limb muscle strength and tension, had normal limb tendon reflexes, and had negative pyramidal sign. A functional examination of the cranial nerve showed normal results. Her blood cell count was normal at admission. Furthermore, urine analysis results, liver function, myocardial enzymes, electrolytes, levels of C-reactive protein, thyroid-stimulating hormone, blood

glucose, glycosylated hemoglobin, and finger pulse oxygen were normal at admission. Renal and coagulation function were also normal at admission. Measurement of her blood lipid levels showed a total cholesterol level of 5.74 mmol/L and low-density lipoprotein level of 3.62 mmol/L. No obvious abnormalities were found on echocardiography or electrocardiography. Chest radiography showed enlargement of the heart and atherosclerotic changes along the thoracic aorta. Carotid artery color Doppler ultrasonography showed bilateral carotid plaque formation. Pulmonary artery computed tomography angiography showed an arteriovenous fistula in the left upper lobe (Figure 4). Contrast-enhanced transcranial Doppler ultrasonography showed a severe right-to-left shunt. After admission, the patient was administered anti-platelet therapy. She was also administered cerebral circulation-improving, blood pressure-lowering, sleep-improving, and nutritional nerve medications, as well as anti-depressants. However, after temporary improvement, the patient's dizziness recurred. In November 2017, PAVF embolization was performed. The patient's pallor



**Figure 4.** Pulmonary artery computed tomography angiogram showing an arteriovenous fistula of the left superior lobe (black arrow) with no considerable drainage on enhanced computed tomography after embolization of the pulmonary arteriovenous fistula in Case 3

improved postoperatively. The dizziness was relieved, with no recurrence observed for > 12 months of follow-up.

## **Discussion**

The first and third patients in this study did not have acute cerebral infarction or anterior circulation transient ischemic attack on admission. Therefore, their dizziness was not related to acute stroke. After intervention to eliminate the left-to-right shunt, the patients' dizziness was relieved immediately without recurrence. Therefore, the possibility of the dizziness being caused by the right-to-left shunt was considered. The second patient had recurrent dizziness for 4 years, and this was not due to acute stroke. After percutaneous PFO occlusion, the dizziness was relieved and did not recur. Therefore, the possibility that the dizziness was caused by the right-to-left shunt was also considered. All three patients had a severe right-to-left shunt with dizziness and stroke (two cases of old stroke, one case of new stroke). Further, none of the patients had recurrence of dizziness after intervention to eliminate the left-to-right shunt. Therefore, the dizziness might have been caused by a large number of right-to-left shunts.

PFO can cause cryptogenic stroke,<sup>3</sup> diving decompression sickness, migraine with aura,<sup>1</sup> platypnea–orthodeoxia syndrome (POS), and cryptogenic brain abscess.<sup>4</sup> Only two cases of PFO with hypoxemia and dizziness have been reported to date.<sup>5,6</sup> Few cases of PFO-related right-to-left shunt with dizziness as the main symptom have been reported.<sup>5,6</sup> Dizziness as the main symptom of PAVF is easily overlooked. To the best of the author's knowledge, no case of dizziness caused by a right-to-left shunt in PAVF has been reported. No symptoms of hypoxemia, such as dyspnea or shortness of breath, were found in any of the three patients in

this study. After percutaneous closure of PFO and percutaneous PAVF embolization, the patients' dizziness was relieved, without recurrence. This study suggests that there may be an association between a severe right-to-left shunt and dizziness. POS is a rare syndrome of postural hypoxemia accompanied by dyspnea. Dyspnea and hypoxemia occur in the upright position and improve in the supine position. POS is often caused by serious heart, lung, and liver diseases. PFO is an important and common cause of POS. PFO is associated with unexplained hypoxemia. Patients with PFO have mixing of venous blood with arterial blood (without pulmonary circulation), reduced oxygen saturation, and secondary dizziness. Most cases of hypoxemia without pulmonary hypertension are caused by PFO. There was no obvious hypoxemia or dyspnea in the patients in the current study, unlike previous reports<sup>5,6</sup> of POS-related dizziness. Therefore, these patients failed to meet the diagnostic criteria for POS and were possibly in the pre-clinical stage of POS.

In this study, right-to-left shunt-related dizziness in patients without hypoxemia did not lead to significant hypoxemia, (i.e., a decrease in partial pressure of arterial oxygen by > 4 mmHg or a decrease in saturated oxygen levels by > 5%). However, the patients experienced dizziness, which could be attributed to cerebral hypoxia. The mechanism of dizziness caused by a PAVF-induced right-to-left shunt is the same as that of dizziness caused by a PFO-induced right-to-left shunt, both of which lead to brain hypoxia. Right-to-left shunt aggravation when performing actions that lead to increased thoracic pressure (including the Valsalva maneuver, screaming, coughing, and defecating) makes the dizziness more obvious. In this study, the patients were prone to dizziness during activity or in the upright position for a long time, and the dizziness was alleviated

in the supine position. A right-to-left shunt through the PFO/PAVF during vigorous activity or in the upright position is larger than that during recumbency or at rest. The length and diameter of the PFO increase with age,<sup>7</sup> and as the shunt volume increases gradually, dizziness becomes increasingly obvious. A large number of right-to-left shunts cause serious complications (e.g., stroke) and should be treated (percutaneous closure of PFO and percutaneous PAVF embolization) immediately. Percutaneous PFO occlusion can significantly improve PFO-related dyspnea and hypoxemia. The results of percutaneous PFO occlusion in 97 patients with hypoxemia and dyspnea<sup>8</sup> showed that this treatment was effective.<sup>7</sup> The combination of antiplatelet therapy with PFO occlusion significantly reduces the recurrence of cryptogenic ischemic stroke compared with antiplatelet therapy alone.<sup>9,10</sup> Forest et al.<sup>5</sup> reported an older patient with recurrent hypoxemia and dizziness (associated with PFO), who was followed up for 9 months after PFO occlusion, and showed no recurrence of hypoxemia and dizziness. Percutaneous closure of a PFO can resolve postural dyspnea and hypoxemia.<sup>6</sup> However, when the main cause of hypoxemia is pulmonary disease, percutaneous closure of a PFO is ineffective.<sup>11</sup> If dizziness is caused by PAVF, percutaneous PAVF embolization is necessary.

All of the patients had atherosclerosis in vessels to their brains. Therefore, PFO and pulmonary fistula may not have been involved in the dizziness. Additionally, atherosclerosis may induce dizziness in patients with large right-to-left shunts.

In conclusion, there is a possible association between a severe right-to-left shunt and dizziness, even in the absence of hypoxemia. Contrast-enhanced transcranial Doppler ultrasound is a convenient and sensitive method for diagnosing right-to-left shunts. Percutaneous closure of

PFO and percutaneous PAVF embolization can improve right-to-left shunt-related dizziness and prevent serious complications. Attention should be paid to the possibility of occurrence of right-to-left shunt-related dizziness. Further in-depth studies need to be performed on this condition.

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### Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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### References

1. Mojadidi MK, Ruiz JC, Chertoff J, et al. Patent foramen ovale and hypoxemia. *Cardiol Rev* 2019; 27: 34–40.
2. Ahn S, Han J, Kim HK, et al. Pulmonary arteriovenous fistula: clinical and histologic spectrum of four cases. *J Pathol Transl Med* 2016; 50: 390–393.
3. Saver JL. Cryptogenic stroke in patients with patent foramen ovale. *Curr Atheroscler Rep* 2007; 9: 319–325.
4. Chen FC, Tseng YZ, Wu SP, et al. Vegetation on patent foramen ovale presenting as a cryptogenic brain abscess. *Int J Cardiol* 2008; 124: e49–e50.
5. Forest A, Le Petitcorps H, Hammoudi N, et al. Recurrent hypoxemia and dizziness in an elderly adult associated with a patent foramen ovale. *J Am Geriatr Soc* 2012; 60: 2377–2378.

6. Zardi EM, Spoto S, Locorriere L, et al. Platypnoea-orthodeoxia syndrome in the elderly: a difficult-to-make diagnosis of intracardiac right-to-left shunt. *Scott Med J* 2017; 62: 122–125.
7. McKenzie JA, Edwards WD and Hagler DJ. Anatomy of the patent foramen ovale for the interventionalist. *Catheter Cardiovasc Interv* 2009; 73: 821–826.
8. Fenster BE, Nguyen BH, Buckner JK, et al. Effectiveness of percutaneous closure of patent foramen ovale for hypoxemia. *Am J Cardiol* 2013; 112: 1258–1262.
9. Søndergaard L, Kasner SE, Rhodes JF, et al. Patent foramen ovale closure or antiplatelet therapy for cryptogenic stroke. *N Engl J Med* 2017; 377: 1033–1042.
10. Saver JL. Trials of patent foramen ovale closure. *N Engl J Med* 2017; 377: 1022–1032.
11. Mojadidi MK, Gevorgyan R, Nouredin N, et al. The effect of patent foramen ovale closure in patients with platypnea-orthodeoxia syndrome. *Catheter Cardiovasc Interv* 2015; 86: 701–707.