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Современные методы диагностики и подходы к лечению синдрома платипноэ–ортодеоксии у пациентов с открытым овальным окном

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АННОТАЦИЯ

Введение. Платипноэ определяется как возникновение или усиление одышки при переходе пациента из положения лежа в положение сидя или стоя. Такое состояние обычно сопровождается ортодеоксией — достаточно быстрым (2–3 мин.) возникновением гипоксемии при таком же изменении позы. В данном обзоре особое внимание уделяется патофизиологическим механизмам, диагностическому подходу и методам хирургического лечения синдрома платипноэ–ортодеоксии (ПОД) при такой сердечной патологии, как открытое овальное окно (ООО).

Цель. Провести анализ литературы, отражающей основные современные методы диагностики и подходы к лечению синдрома ПОД у пациентов с ООО.

Материалы и методы. Для написания обзорной статьи был выполнен поиск источников литературы по реферативным базам PubMed, Scopus и eLibrary за период по 2023 г. включительно. Поиск был произведен с использованием следующих ключевых слов: «синдром платипноэ–ортодеоксии», «открытое овальное окно», platypnea–orthodeoxia syndrome, patent foramen ovale.

Результаты. Синдром ПОД является довольно редким клиническим явлением, более чем в 80% случаев причиной развития синдрома ПОД является наличие внутрисердечного шунта, в частности ООО. При данной патологии происходит сброс дезоксигенированной крови в большой артериальный круг. Диагностика синдрома обычно заключается в проведении трансторакальной или чреспищеводной эхокардиографии с «пузырьковым» контрастированием. Наименее травматичным методом закрытия ООО является чрескожное вмешательство, эффективность которого достигает 99%. Данную операцию проводят пациентам с синдромом ПОД с целью купирования клинических симптомов.

Заключение. В ряде исследований и клинических случаев показано положительное влияние чрескожного закрытия ООО на уменьшение симптомов гипоксии у пациентов с ПОД.

Ключевые слова: *синдром платипноэ–ортодеоксии; открытое овальное окно; эндоваскулярное закрытие открытого овального окна*

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Modern Diagnostic Methods and Approaches to Treatment of Platypnea–Orthodeoxia Syndrome in Patients with Patent Foramen Ovale

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ABSTRACT

INTRODUCTION: Platypnea is defined as initiation or worsening of dyspnea when a patient moves from a supine to a sitting or standing position. This condition is usually accompanied by orthodeoxia, a rather rapidly (within 2–3 minutes) developing hypoxemia triggered by this change in posture. This review focuses on the pathophysiological mechanisms, diagnostic approaches and methods of surgical treatment of platypnea–orthodeoxia syndrome (POS) in such cardiac pathology as patent foramen ovale (PFO).

AIM: To conduct an analysis of the literature reflecting the main modern diagnostic methods and approaches to treatment of POS in patients with PFO.

MATERIALS AND METHODS: In writing the review article, a search for literature sources was conducted in the PubMed, Scopus and eLibrary abstract databases for the period up to 2023 inclusive using the following keywords: 'platypnea–orthodeoxia syndrome', 'patent foramen ovale'.

RESULTS: POS is a rather rare clinical phenomenon, caused in more than 80% of cases by the existence of the intracardiac shunt, in particular, PFO. In this pathology, deoxygenated blood is discharged into the systemic arterial circulation. The syndrome is usually diagnosed using bubble contrast transthoracic or transesophageal echocardiography. The least traumatic method of PFO closure is percutaneous intervention with the effectiveness reaching 99%. This operation is performed on patients with PFO syndrome to arrest clinical symptoms.

CONCLUSION: A number of studies and clinical cases have shown a positive effect of percutaneous closure of PFO in alleviating hypoxia symptoms in patients with POS.

Keywords: *platypnea–orthodeoxia syndrome; patent foramen ovale; endovascular closure of patent foramen ovale*

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ECO•VECTOR

LIST OF ABBREVIATIONS

EchoCG — echocardiogram
IAS — interatrial septum
ICS — intracardiac shunt
IVC — inferior vena cava
LA — left atrium
PaO_2 — partial oxygen tension
PFO — patent foramen ovale
POS — platypnea–orthodeoxia syndrome
RA — right atrium
RV — right ventricle
SVC — superior vena cava
SaO_2 — oxygen saturation

INTRODUCTION

The terms ‘platypnea’ and ‘orthodeoxia’ were first described in 1969 and 1976 [1, 2]. Platypnea is defined as onset or enhancement of dyspnea in a patient when changing from the lying to sitting or standing position with relief of symptoms on assuming the horizontal position. This condition is usually accompanied by orthodeoxia a rather rapidly (within 2–3 minutes) developing hypoxemia (a decrease in the partial tension of oxygen in blood (PaO_2)) in such change of posture.

In the 1970s, these terms began to be used to describe a platypnea–orthodeoxia syndrome (POS) [3]. POS was first described by J. B. Seward, et al. (1984) in a patient with a right-to-left intracardiac shunt (ICS) [4]. POS is relatively rare, with the true incidence in the population still unknown. Upon that, *in 13%–47% of cases, the etiology of the syndrome cannot be exactly defined*, i. e., orthodeoxia develops without an identifiable lung or heart disease [5].

Currently, POS is defined as postural dyspnea and desaturation of the arterial blood that occur in a patient in a sitting or standing position and are alleviated when assuming a horizontal position. Diagnostic criteria of the syndrome include more than 5% decrease in oxygen saturation (SaO_2) and more than 4 mm Hg decrease in PaO_2 [6].

Among the pathologies most often leading to the development of POS, the following are described [7]:

1) *cardiovascular pathologies*: ICS (patent foramen ovale (PFO), atrial septal defect and aneurysm, congenital cardiomyopathies)), tricuspid stenosis, transposition of great arteries, eosinophilic endomyocardial disease, constrictive pericarditis, atrial myxoma, aortic aneurysm, aortic elongation, right ventricle (RV) remodeling, elongated Eustachian valve, aortic dilation, aortic root dilation, pericardial effusion;

2) *pulmonary pathologies*: postpneumectomy, amiodarone pulmonary intoxication, recurrent pulmonary embolism, adult respiratory distress syndrome, pulmonary hypertension in obstructive sleep apnea syndrome, true pulmonary vascular shunts, bronchogenic carcinoma, interstitial fibrosis, pulmonary embolism, chronic obstructive pulmonary disease, emphysema, cryptogenic fibrosing alveolitis;

3) *hepatic pathologies*: hepatopulmonary syndrome, portopulmonary hypertension;

4) *infectious pathologies*: hydatid cyst, infection with cytomegalovirus, Infection with *pneumocystis jiroveci*;

5) n*eurological pathologies*: Parkinson's disease, diabetic autonomic neuropathy;

6) *others*: laryngeal cancer, unilateral phrenoplegia, blunt chest wall trauma, newly developed intestinal obstruction, radiation-induced bronchial stenosis, bronchopleural fistula, fat embolism, propafenone overdose in Epstein's anomaly, osteoporosis and severe kyphosis, progressive autonomic insufficiency, acute organophosphorus intoxication.

This review focuses on the pathophysiological mechanisms, diagnostic approach and surgical treatment modalities of PO syndrome in such cardiac pathology as patent foramen ovale.

The **aim** of this study to analyze the literature reflecting the main modern diagnostic methods and approaches to the treatment of platypnea–orthodeoxia syndrome in patients with patent foramen ovale.

MATERIALS AND METHODS

To write this review article, a literature search was conducted in the PubMed, Scopus, and eLibrary abstract databases using the following keywords: ‘platypnea–orthodeoxia syndrome’, ‘patent foramen ovale’ up to and including 2023.

The most common structural anomaly leading to ICS is the septal communication between the right and left atria (PFO), which occurs in 25%–30% of cases in the general population depending on age [3]. An isolated PFO does not usually cause significant right-to-left interatrial shunting because higher pressure in the left atrium (LA) allows for its functional closure. Upon that, PFO may remain asymptomatic for decades and may not require any intervention [8]. Indications

for its closure are decompensation of the condition, cryptogenic stroke, systemic embolization, migraine with aura and POS [9].

Causes and Pathogenetic Mechanisms of POS

The development of intracardiac POS requires the interaction of multiple complex structural and physiological alterations [3]. Normally, in adults, the pressure in the LA is approximately 5 mm Hg–8 mm Hg higher than in the right atrium (RA), which promotes functional closure of the defect [9]. The basic pathogenetic factor for development of POS in PFO is *shunting of deoxygenated blood* from the RA to the LA resulting in mixing of venous blood with arterial blood [10]. A patient with PFO manifested as PO syndrome was first reported by C. M. Roos, et al. (1981) [11].

Right-sided shunting may occur with both normal and elevated pressure in the RA. Pressure increases primarily in acute conditions: pulmonary thromboembolism, RV myocardial infarction, pneumothorax, hydrothorax, pericardial effusion, pneumectomy. Chronic conditions associated with elevated pressure in the RA, include pulmonary hypertension, severe tricuspid regurgitation, pulmonic valve stenosis [12].

In the absence of right atrial hypertension, pathological shunting may occur due to a transient change in the pressure gradient between the RA and LA in each cardiac cycle due to premature depolarization of the RA associated with the location of the sinoatrial node or displacement of the IAS in breathing [13, 14]. Respiratory movements can cause the IAS to be displaced to the left, resulting in a pronounced right-to-left shunt, or in the opposite direction from the limbus of the fossa ovalis, preventing right-to-left shunt [13].

In healthy individuals, blood from the superior vena cava (SVC) flows down to the anterior RA, and from the inferior vena cava (IVC) flows up to the posterior RA. Alterations in cardiac anatomy may redirect blood flow from the IVC to the left atrium via a defect in the IAS, such as PFO [6].

Patients with POS with normal RA pressure usually demonstrate concomitant anatomical changes in the ascending aorta (dilation or aneurysm), spine (thoracic kyphosis), diaphragm (paralysis) or an elongated Eustachian valve [6, 15, 16]. Twenty five percent of patients with PFO with the diagnosis of POS, have *associated aortic anomalies leading to RA compression* [17, 18]. Enlargement of the aortic root leads to a decrease in the distance between the aorta and posterior wall of the LA, causing deformation of the RA and decreased tension of the IAS. This distortion contributed to the fossa ovalis valve moving freely, keeping the foramen ovale wide open and providing a constant right-to-left shunt of blood. Upon that, in the standing position, due to the effect of gravity, the size of the PFO increases and shunting to the right from the IVC enhances [19–21].

In POS deoxygenated blood enters the systemic arterial circulation directly. Further severity of symptoms and hypoxemia in POS are proportionally related to the amount of the shunted blood. In the presence of the ICS, a part of blood returning from the lungs does not participate in gas exchange, since the concentration of O_2 in it equals that in the venous blood. The concentration of O_2 in the arterial blood is described by the formula:

$$CaO_2 = Qs/Qt \times CvO_2 + (1 - Qs/Qt) \times CcO_2,$$

where Qs and Qt are blood flow through the shut and pulmonary circuit, respectively; Qs/Qt is the proportion of shunted blood flow compared to the total blood flow; CcO_2 is the content of oxygen in the pulmonary terminal blood capillaries; CvO_2 is the concentration of oxygen in venous blood.

This equation can be rearranged to give the formula for calculating the fraction of shunted blood flow as follows:

$$Qs/Qt = (CcO_2 - CaO_2)/(CcO_2 - CvO_2).$$

The shunted fraction required to maintain PaO_2 at about 70 mm Hg, is 20%–25%, in severe hypoxemia (PaO_2 < 40 mm Hg), the shunted fraction of about 50% is required [3].

Diagnosis and Diagnostic Criteria of POS

The diagnosis of POS is initially established clinically. The first step is clinical examination of the patient. SaO_2 should be analyzed in the horizontal and vertical positions. *If in the standing position SaO_2 decreases by more than 5% and increases in the supine position, the diagnosis of POS can be made* [6]. With a large right-to-left shunt of blood, there may be no significant improvement in hypoxemia even when the patient is treated with 100% oxygen.

The next step is determining the underlying mechanism of desaturation. Despite the fact that POS is considered to be rare, *it may be misdiagnosed by using only routine electrocardiogram and chest X-ray*. ICS can be examined by several methods, the *most preferable being echocardiography* (EchoCG). This method permits to examine the interatrial and interventricular septa for defects, aneurysms and other anomalies. To identify right-to-left cardiac shunts, bubble-contrast EchoCG is used. It is performed in both supine and vertical positions. This test permits differentiation between intracardiac and extracardiac shunts. *In ICS, bubbles are determined in the LA within three cardiac cycles* [22]. *Delayed appearance of bubbles in the LA*

(after 3–6 cardiac cycles) indicates extracardiac shunt, which most often occurs in the pulmonary vascular network [23].

If transthoracic echocardiography shows ambiguous results, transesophageal echocardiography should be performed for direct visualization of the heart defect [24]. It has a higher spatial resolution in detecting ICS and is considered the *reference standard for diagnosing PFO* [25]. Transesophageal echocardiography also permits detection of other shunts (e. g., sinus venosus defect), which are difficult to be visualized with the transthoracic method [26]. The combination of transesophageal echocardiography with contrast permits characterization of the IAS motion depending on the time of contrast transit [27].

In cases the final diagnosis cannot be established using EcoCG, the interatrial septum defects can be identified using magnetic resonance of the heart [28].

When differentiating the probable cardiologic causes of PO, some moments should be should be kept in mind [8].

Firstly, it is necessary to exclude concomitant pulmonary pathology.

Secondly, PO syndrome is sometimes associated with a combination of several cardiac diseases. For example, kyphotic posture and dilation of the thoracic aorta can change the intrathoracic relationships, with the result of increased shunting through an open IAS defect in the upright position [29]. When describing a clinical case M. Faller, et al. (2000) suggested that the patent foramen ovale may result from mechanical deformation of the IAS aneurysm in combination with the aneurysm of the thoracic aorta [30]. Another case of PO development was associated with the fact of pressure on the RA exerted by the elongated thoracic aorta, causing deformation of the IAS, which could lead to the opening of the foramen ovale in the upright position of the patient [31].

Thirdly, it can be diagnostically difficult to distinguish between intrapulmonary and intracardiac shunts, since in both cases, in echocardiography, the contrast passes from the right to the left chambers of the heart. This question is especially important when there is a high suspicion of intrapulmonary shunting, as in patients with hepatic cirrhosis. The appearance of contrast cross-over within four cardiac cycles after RA emptying speaks in favor of intracardiac shunting, whereas late appearance of contrast cross-over (later than after four cardiac cycles) is indicative of intrapulmonary shunting.

Treatment of POS

After confirmation of the cause of PO syndrome being the presence of ICS, a question of surgical or percutaneous closure of the shunt may be considered. IAS defects less than 5 mm in diameter without signs of RV dilation or pulmonary hypertension do not require closure unless they are associated with POS or paradoxical embolism [32].

Although the surgical intervention was the main method of PFO closure for a number of years, it has recently been replaced by percutaneous intervention from considerations of a decreased frequency of complications and lower cost [33–35]. The main disadvantages of the open-heart surgery are the need for anesthesia and artificial circulation, and arrhythmogenic effects of atrial and ventricular scars (although they are rare causes of arrhythmia in themselves), a long recovery period, and cosmetic defects of postoperative skin scars [36].

Percutaneous PFO closure is conducted under local anesthesia. The intraoperative IAS condition is assessed using an intracardiac ultrasound sensor or transesophageal EchoCG. A diagnostic multiposition catheter is introduced through the femoral vein using a guidewire with a J-shaped tip. Then the catheter on a long guidewire is changed for the delivery system that is inserted into the LA cavity. After washing, the folded occluder is also fed into the LA to the edge of the delivery system under obligatory fluoroscopic control. The first disk located in the LA, is liberated, and them the whole complex is pulled up to the IAS. After the first disk is completely adjacent to the septum, the second disk opens in the RA cavity. A control EchoCG shows the correct anatomical and functional installation of the device, after which the delivery system is removed through the femoral vein [37].

According to a number of authors, *complete PFO closure with this procedure is achieved in 99% of cases* [38, 39]. Improvement of PO symptoms with percutaneous closure of PFO is observed in more than 95% of patients. The operation often leads to immediate improvement of SaO_2 level in the vertical position by 10%–20% [20, 40]. A study by R. J. Snijder, et al. (2015) showed good long-term safety and efficacy profiles after percutaneous closure of the IAS defect with more than five-year follow-up period [41].

In the study by C. Blanche, et al. (2013), a database of patients who were submitted to percutaneous closure of PFO was analyzed [42]. *In 5 (2.2%) cases* of 224 patients, the *POS was identified in the setting of PFO*. The diagnosis was confirmed by measuring oxygen saturation in the blood of pulmonary veins in the horizontal and vertical positions. In 3 patients, PFO was combined with arterial septal aneurysm and elongated Eustachian valve. In all patients, the operation for PFO closure was successful. Immediately after the procedure, SaO_2 increased from 83.0 ± 3.0% to 93.0 ± 2.0% in the vertical position, POS symptoms regressed.

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In another study, M. K. Mojadidi, et al. (2015) examined patients with PFO referred for diagnostics to the University of California between 2001 and 2012 [21]. Of the 683 patients with PFO-associated diseases, *POS was detected in 17 cases (2.5%)*. In this sample, the severity of symptoms and SaO_2 were compared in the horizontal and vertical positions before and after closure. All patients underwent percutaneous PFO closure and according to the results were divided into two groups with 'improved SaO_2' and 'no change in SaO_2'. In 11 patients (64.8%), improvement of SaO_2 was noted. In this group, there was a decrease or a complete elimination of dyspnea and hypoxemia, as well as an increase in SaO_2 by 5.2 ± 4.7% in the supine position and by 15.6 ± 3.0% in the standing position ($p = 0.03$ and $p < 0.0001$ respectively) compared to baseline. Patients who showed no changes after PFO closure (35.2%) predominantly had pulmonary etiology of hypoxia with elevated mean pulmonary pressure before closure of the defect (51.4 ± 16.8 mm Hg, $p = 0.06$).

A. Hayek, et al. (2021) retrospectively studied the data of 54 patients with POS in the period from 2007 to 2020 who were recommended percutaneous closure of PFO [43]. The mean age of patients was 79 years, 37.0% (20 patients) were men. Nineteen (35.2%) patients were diagnosed with a chronic lung disease (obstructive apnea syndrome, restrictive or obstructive lung disease), 9 patients (16.7%) with a cardiac anomaly (pulmonary embolism or tricuspid insufficiency), 9 patients (16.7%) with an orthopedic triggering factor (fall, fracture). Twelve patients (22.2%) were hospitalized in the intensive care unit for hypoxia with the underlying POS. Atrial septal aneurysm was observed in 31 patients (70.0%). The median systolic pulmonary arterial pressure was 28 mm Hg, and the diameter of ascending aorta 39.0 mm.

The closure of the PFO was performed in 12 patients (21.8%), in 1 patient, the defect could not be closed because of thickened IAS. After the intervention, oxygen saturation in the vertical position significantly increased. The PFO closure permitted a complete cessation of oxygen therapy in 17 patients (76.5%), in 50 patients (94.3%), functional improvement was observed. However, 7 patients (12.9%) developed residual blood flow after implantation of the occluder.

In their study F. Othman, et al. (2022) sought to characterize patients with PFO-associated POS without pulmonary hypertension [44]. The authors respectively analyzed the databases of three hospitals in Australia between 2000 and 2019. In the sample, 14 patients with a mean age of 69.0 ± 14.0 were diagnosed with PFO, in 7 cases patients were bed-ridden with severe postural symptoms. Baseline oxygen saturation was 93.0 ± 5.0% supine, and 84.0 ± 6.0% upright. Two patients had a congenital heart defect, 4 had parenchymal lung disease with preserved lung function. The mean diameter of the aortic root was 37.0 ± 6.0 mm. In 11 patients (78.6%), the PFO was successfully closed using *Amplatzer* occluder, after which they showed a reliable improvement of the condition ($p < 0.003$), and SaO_2 in the semi-supine position increased by 13.0 ± 8.0% ($p < 0.001$).

Effectiveness of PFO Closure in Patients with POS

Below, clinical cases of patients with POS in the setting of PFO who underwent percutaneous closure of the defect are presented.

In a clinical case described by A. Rostamian, et al. (2013), a 75-year-old man was admitted to hospital after three weeks of dyspnea, which enhanced in the standing and resolved in the supine position [45]. Symptoms gradually increased and over time developed into a mild dyspnea in the supine position and severe dyspnea in the sitting position. With oxygen insufflation (15 l/min), SaO_2 was 97% when lying, 75% when sitting and 70% when standing. Partial tension of oxygen in the supine position was 88 mm Hg, and decreased to 35 mm Hg in the sitting position.

Transthoracic EchoCG revealed normal left and right ventricular function, thin and hypermobile interatrial septum with a 2.1 cm aneurysm. Bubble test showed the presence of a right-to-left shunt, which allowed diagnosing PFO. Oxygen saturation was: RA — 71%, RV — 69%, pulmonary artery — 67%, LA — 90%, LV — 92%. The patient underwent successful percutaneous closure of PFO using a 20-mm *Amplatzer* occluder. *After the procedure, the patient's dyspnea regressed, and oxygenation normalized in all positions*.

In the same year L. H. Molina, et al. presented a clinical case of a 68-year-old woman with POS and dyspnea present for two months [46]. On physical examination, SaO_2 was 96% in the horizontal position and 86% in the vertical position. Gas analysis of arterial blood with 21% fractional oxygen concentration (FiO_2) showed: pH — 7.43, $PaCO_2$ — 31.3 mmHg, PaO_2 — 78.3 mm Hg with a subsequent decrease to 49.5 mmHg.

Transthoracic and transesophageal EchoCG showed the presence of a wide PFO (8 × 11 mm) with difficult passage of saline, as well as a ruptured interatrial septal aneurysm with moderate dilation of the aortic root, which contributed to right-left ICS. The PFO closure was performed percutaneously using a 25-mm *Amplatzer* occluder with access through the femoral vein. Control EchoCG after endovascular intervention showed the absence of ICS, the patient had positive clinical dynamics with the disappearance of PFO symptoms.

Another patient in the work of A. C. Agdamag, et al. (2019) was diagnosed with an ascending aortic aneurysm measuring 4.3 cm, as well as hypertension and obstructive sleep apnea [14]. SaO_2 parameter in the supine position was 86%. Transthoracic EchoCG with a bubble test revealed an aneurysm of the interatrial septum and a right-to-left shunt, indicating the presence of a non-closed foramen ovale. Intracardiac echocardiography using color Doppler confirmed the presence of PFO with a large right-to-left shunt. The patient was diagnosed with POS, and percutaneous closure of the PFO was conducted implantation of a 30-mm *Gore Cardioform* septal occluder. Postoperative transthoracic EchoCG revealed no residual shunt, SaO_2 increased to 92% (supine), after a month to 99%.

S. Mirwais, et al. (2020) in their work described a clinical case of an 87-year-old man with chronic obstructive pulmonary disease, myelodysplastic syndrome, chronic anemia, obstructive sleep apnea, coronary bypass grafting and percutaneous coronary intervention for coronary heart disease in history [47]. The coronary artery bypass grafting surgery was complicated with injury to the left phrenic nerve and left-sided paralysis of the diaphragm, which led to chronic dyspnea. The patient's complaints at presentation included a one-year history of exertional dyspnea. A few weeks before presentation, dyspnea began to buildup in the upright position and in movement. Oxygen saturation was in the range of 92%–96% when sitting and sharply dropped to 86% when standing.

Transesophageal EchoCG with contrast revealed the presence of PFO with a significant right-to-left shunt and hypermobile IAS. The patient underwent endovascular closure of the defect by implantation of a 25-mm *Amplatzer* occluder. Within two weeks after discharge, positional symptoms significantly decreased, SaO_2 was not lower than 96%.

A clinical case described by J. Pelayo, et al. was a 76-year-old woman who was admitted to the emergency department with periodical episodes of hypoxia [48]. The patient noted dyspnea, palpitations, chest pain, cough, fever, orthopnea, paroxysmal nocturnal dyspnea, edema and fatigue in the lower extremities. It is known from the history that she had been suffering from arterial hypertension and hyperlipidemia for a long time. It is also known that at the age of 55 she suffered a stroke. To maintain peripheral blood oxygen saturation above 90%, she required oxygen therapy via nasal cannula at 2 l/min at rest and 5 l/min under load.

Transesophageal EchoCG revealed a PFO measuring 0.3 cm–0.4 cm with right-sided blood shunting. Given the presence of positional hypoxia and PFO in the absence of right atrial hypertension, the patient was diagnosed with POS in the setting of PFO. The authors suggested the underlying mechanism of hypoxia be positional blood flow from the inferior vena cava to the LA due to displacement of the interatrial septum. PFO closure was performed using a 25 mm *Amplatzer* occluder, which resulted in significant improvement in oxygenation.

Another case is presented by M. Matsuzawa, et al. (2021). An 83-year-old man was described who was scheduled for partial removal of the lower lobe of the left lung in connection with an oncological process [49]. On the day of the planned intervention, the patient developed difficulty breathing at the rate of > 20 breaths/min, SpO_2 86%–88%, with oxygen therapy (2 l/min) — 95%. Hypoxia was temporary. Then, during the installation of an epidural catheter, hypoxemia reappeared, and the patient was transferred to the supine position with additional oxygen therapy. However, SpO_2 remained below 95%. In view of all the above, the operation was postponed.

The man was suspected of having ICS, transesophageal echocardiography with contrast showed an intermittent right-to-left shunt through the PFO only on abdominal compression, which indicated the degree of right-to-left shunt depending on the interatrial pressure gradient. The patient was diagnosed with POS in the setting of PFO, and percutaneous PFO closure was successfully performed. With a significant improvement in the patient's condition and a decrease in hypoxia symptoms, six months later, the lower lobe of the left lung was removed.

In the same year F. Dipasquale, et al. described another clinical case: a 70-year-old man was admitted to the emergency department with neurological symptoms [50]. CT scan of the brain showed a subdural hematoma, for which the patient was operated on. In a few days he developed acute pulmonary failure due to pneumonia, SpO_2 decreased to 63%. Two weeks later, despite the resolution of pneumonia, dyspnea worsened and profound hypoxia appeared in the sitting position.

Transesophageal EchoCG with bubble contrast showed a lipomatous interatrial septum with a tunnel-like PFO resulting in a large right-to-left shunting of blood. The authors hypothesized the POS be secondary to PFO due to concomitant anatomical factors (atrial septal aneurysm and aortic root dilation) that was aggravated by previous pneumonia. The patient underwent percutaneous endovascular closure of the PFO. In a few days, no signs of hypoxia were observed after discontinuing oxygen insufflation. Echocardiography two weeks later showed the correct functional and anatomical implantation of the occluder that completely covered the PFO without any residual ICS. The patient reported improved exercise tolerance without any limitations in daily physical activity.

F. F. Alotaibi, et al. (2022) described a 54-year-old man who presented to the emergency department with complaints of subjective fever, cough, and dyspnea

in an upright position present for one day [51]. Oxygen saturation was 95% in the supine position and 85% in sitting position. The patient also had tingling of the fingers and central cyanosis.

Chest radiography revealed bilateral infiltrates, high-resolution CT showed a small consolidated area in the right upper lobe, sputum culture was positive for *Pseudomonas aeruginosa*.

Transesophageal EchoCG [52] with color Doppler and bubble test showed right-to-left shunting. After treatment of community-acquired pneumonia, the patient was referred to a specialized center, where percutaneous closure of PFO was performed using a 25-mm *Amplatzer* occluder. Postoperatively, SpO_2 increased to 97% upright and 98% supine, hypoxia symptoms were completely eliminated.

CONCLUSION

Platypnea–orthodeoxia syndrome is a rare, but important condition with various clinical manifestations. There are several mechanisms for development of platypnea in the setting of orthodeoxia. These are mainly intracardiac and intrapulmonary shunts, as well as mismatch between venous circulation and blood perfusion. The main cause of intracardiac shunting in platypnea–orthodeoxia syndrome is the presence of a defect in the interatrial septum, in particular, patent foramen ovale.

Differential diagnostics in patients with platypnea–orthodeoxia should exclude pulmonary hypertension. However, in cases with alterations in the intrathoracic anatomy and physiology, symptoms may as well occur with normal right atrium pressure. In patients with platypnea–orthodeoxia with secondary intracardiac pathology, a combination of anatomical defects is often observed, the most common ones being patent foramen ovale, atrial septum aneurysm, aortic root aneurysm, aortic dilation, elongated Eustachian valve. Diagnosis of the syndrome usually involves transthoracic or transesophageal echocardiography with bubble contrast.

In platypnea–orthodeoxia syndrome associated with patent foramen ovale, percutaneous endovascular closure of the atrial septal defect is a safe and effective treatment option that alleviates symptoms of orthodeoxia and other symptoms. The decision on the intervention is based on the severity of symptoms and potential complications associated with the defect.

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