


REVIEW

Platypnoea–orthodeoxia syndrome as an uncommon cause of dyspnoea: a literature review

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Abstract

Platypnoea–orthodeoxia syndrome (POS) is an uncommon but challenging clinical condition characterised by positional dyspnoea (platypnoea) and arterial desaturation (orthodeoxia) in the upright position that improve in the supine position. Since its first description, many cases have been reported and many conditions have been associated with this syndrome. Herein, we review the clinical presentation, pathophysiology, diagnostic work-up and management of patients with POS, aiming to increase the awareness of this often misdiagnosed condition.

Introduction

Platypnoea–orthodeoxia syndrome (POS) is a clinical syndrome characterised by positional dyspnoea (platypnoea) and arterial desaturation (orthodeoxia) in the upright position.¹ This syndrome, first described in 1949 by Burchell *et al.*,² occurs predominantly in the elderly population and in women.³ The prevalence of POS is unknown; a literature review published in 2017 found only 150 articles, including a total of 239 patients,¹ with patent foramen ovale (PFO) being the most common underlying cause.⁴

Pathophysiology

The presence of a PFO represents the most common anatomical substrate associated with POS. However, POS requires a combination of an anatomical substrate and a functional cause to the reverse of a left-to-right shunt. In fact, more than 25% of all adults have a PFO⁵ and most of them do not have a right-to-left interatrial shunt due to a higher left-to-right atrial (RA) pressure gradient and a higher left-to-right ventricular compliance, ultimately closing the shunt.

When the RA pressure becomes higher than the left atrial (LA) pressure, a right-to-left shunt can occur through a PFO or an atrial septal defect (ASD). This may be acutely precipitated by pulmonary thromboembolism, cardiac tamponade, right ventricular myocardial infarction, pneumothorax and post pneumonectomy, or chronically caused by any of the conditions causing chronic pulmonary hypertension⁶ or severe tricuspid regurgitation.⁷ However, even in the absence of a fixed RA hypertension, deoxygenated blood may shunt from the right to left atrium across a PFO or ASD in the presence of a concomitant predisposing condition leading to right-to-left shunting.⁸ These conditions include the dilatation with or without dissection of the ascending aorta, alterations of the thoracic spine kyphoscoliosis or hemidiaphragmatic paralysis, persistent Eustachian valve or Chiari's network that can result in a horizontal distortion of the RA and the interatrial septum in the upright position.^{9,10} These cumulative changes influence vortex formation, filling pressures and cause flow redistribution that allows the stream of deoxygenated venous return from the inferior vena cava through the now orthostatically opened shunt into the systemic circulation with the ensuing POS.^{4,8} Moreover, ascending aortic dissection or dilatation can cause a reduction of the RA compliance and a

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narrowing of the angle between atrial septum and inferior vena cava, favouring the return of venous blood flow into the defect.¹¹ In Figure 1 and Supporting Information Videos S1–S5, a classic example of POS in a patient with a PFO and concomitant aortic dissection is shown.

POS has also been described in patients with intrapulmonary shunting, such as pulmonary arteriovenous malformations (AVM) or hepatopulmonary syndrome.¹ In patients with hepatopulmonary syndrome, the dilatation of the pulmonary capillary and precapillary vessels determines a ventilation–perfusion mismatch, an arteriovenous pulmonary shunt and decreased alveolar–arterial oxygen diffusion.^{1,12} The orthodeoxia in these cases is related to the preferential perfusion of intrapulmonary vascular dilatations when the patient is upright. The arteriovenous fistulae are usually located in the lung bases and cause a right-to-left shunt of deoxygenated blood from pulmonary arteries to pulmonary veins. In the upright position there is an increased flow in those areas and consequently an increased shunt.¹³

Table 1 summarises the most common causes of POS encountered in clinical practice.

Diagnostic work-up

The first step in the diagnosis of POS is the clinical assessment of the patient. Oxygen (O₂) saturation and arteriosus O₂ levels need to be analysed in the lying and upright position. POS can occur insidiously, often as progressive positional unexplained dyspnoea and oxygen desaturation for months or years, or less often as an acute life-threatening unexplained hypoxaemia, especially if an acute trigger occurs (i.e. aortic dissection). A drop of partial pressure of O₂ >4 mmHg (often to values lower than 60 mmHg) and/or a drop of O₂ arterial saturation >5% from baseline (often to values lower than 90%), from supine to an upright position, have been considered diagnostic of POS.^{1,14} Patients presenting late after symptom onset, may have cyanosis and erythrocytosis with a resultant increase in haematocrit

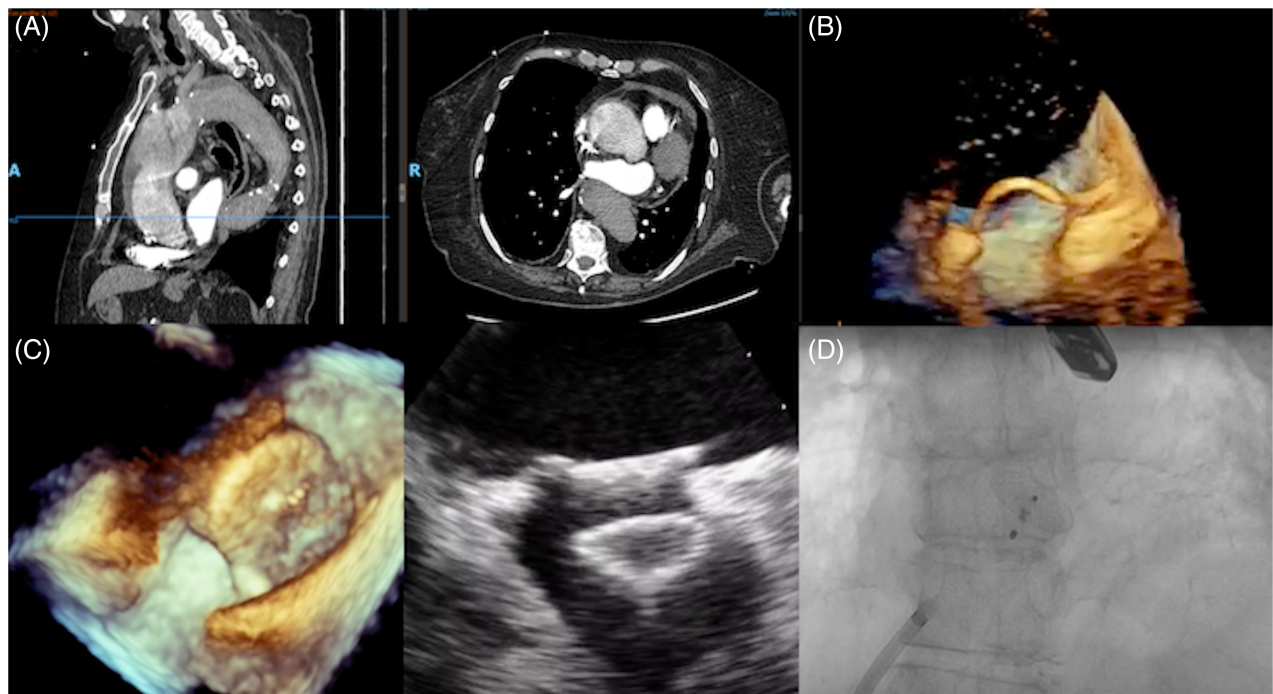


Figure 1 Clinical case of platypnoea–orthodeoxia syndrome (POS). An 89-year-old woman, with a known history of ascending aortic aneurysm, was admitted to our emergency department with a complaint of intermittent chest pain and dyspnoea over a few days. Peripheral oxygen saturation was 85% in ambient air. Chest computed tomography scan showed an ascending aortic aneurysm with a type A dissection according to Stanford classification (A). Because of the patient's advanced age, she was considered not suitable for surgical intervention. Physical examination revealed orthostatic dyspnoea (platypnoea) associated with significant deoxygenation in the sitting position (orthodeoxia). Agitated saline contrast transthoracic echocardiography identified an early opacification of the right chambers in clinostatism with a marked increase in orthostatism (Video S1). Agitated saline contrast transesophageal echocardiography confirmed a 'tunnel-like' patent foramen ovale with a significant early right-to-left shunt at rest (B; Videos S2, S3). POS was then diagnosed. She underwent a successful percutaneous closure with an Amplatzer device (25/25 mm) with minimal residual right-to-left shunt (C,D; Videos S4,S5) leading to a significant relief of the dyspnoea and improvement of arterial saturation.

Table 1 Most common causes of platypnoea–orthodeoxia syndrome (POS)

Intracardiac shunt
Patent foramen ovale (PFO)
Atrial septal defect (ASD)
Associated conditions:
• Aortic dilation/aneurysm/dissection
• Pericardial effusion/constrictive pericarditis
• Tricuspid regurgitation
• Pulmonary hypertension
• Pneumothorax
• Post-pneumectomy
• Hemi diaphragmatic paralysis
• Blunt chest trauma
• Abnormally long Eustachian valve/Chiari Network
• Kyphosis/kyphoscoliosis
• RA lipomatous hypertrophy/RA myxoma
Intrapulmonary shunt
Hepatopulmonary syndrome (chronic liver disease, portal hypertension)
Lower lobe arterial–venous malformation
Osler–Weber–Rendu syndrome
Ventilation–perfusion mismatch
Interstitial lung disease
Infections
Pulmonary embolism

ASA, atrial septal aneurysm; ASD, atrial septal defect; PFO, patent foramen ovale; RA, right atrial.

as a physiological response to chronic hypoxia.¹⁵ In the presence of a significant right-to-left shunt, usually there is no significant improvement in hypoxaemia when the patient is treated with O₂ supplement.

A transthoracic bubble contrast echocardiogram with intravenous agitated saline is the first examination in the diagnostic algorithm and it should be performed in both lying and upright positions and with provocative manoeuvres (Fig. 2). The appearance of agitated saline contrast in left-sided heart structures is consistent with either an intracardiac or an intrapulmonary shunt. The appearance of microbubbles within three cardiac cycles after RA opacification and the leftward bulging of the interatrial septum is considered suggestive of the presence of an intracardiac shunt, such as a PFO.¹⁶ Direct visualisation of bubbles crossing the interatrial septum increases the specificity of the bubble study to identify an intracardiac shunt. If the bubbles are seen in the right chambers after more than three cycles from the shifting of the interatrial septum, an intrapulmonary shunt has to be suspected, especially if the bubbles are coming from the pulmonary veins.¹⁶ If the transthoracic echocardiogram is inconclusive or an interatrial communication is suspect, a transesophageal echocardiography

can be performed for a better visualisation of the cardiac defect^{16,17} (Fig. 2).

In case of high clinical suspicion with an indeterminate echocardiography study, cardiac magnetic resonance imaging may be used for a detailed assessment of the cardiac anatomy and function.¹⁸

Furthermore, a ventilation–perfusion scan can be performed to assess changes in pulmonary perfusion with positional changes as well as to detect extrapulmonary uptake.

Ventilation–perfusion pulmonary scintigraphy using technetium-99 m-labelled macro-aggregated albumin may in fact reveal multiple focus of albumin macroaggregates outside the lungs compatible for veno-arterial shunt (in absence of shunt, all the albumin aggregates are hampered in the lungs' field). However, unlike contrast echocardiography, distinguishing intracardiac versus intrapulmonary shunts is not possible with ventilation–perfusion pulmonary scintigraphy.^{19,20} In the case of absence of intracardiac findings, other causes of POS due to intrapulmonary shunting should be investigated.

A computed tomography coronary angiogram can be performed to assess the presence of pulmonary AVM or parenchymal lung diseases. Pulmonary arteriography can be considered if the aetiology remains unknown despite other diagnostic tests having been performed.¹

Treatment

Treatment varies according to the aetiology of POS. Nowadays, percutaneous intervention represents the first choice for patients with PFO and ASD due to the low procedural risks and the low costs.^{21–23} Percutaneous closure of PFO or ASD can be performed with specific devices, such as the Amplatzer Septal Occluder or Amplatzer PFO Occluder (Abbott).^{21,22} In a large multicentre French retrospective study, Guérin *et al.*²⁴ reported a success rate for percutaneous closure of PFO of 97%, with improvement in the O₂ saturation in all cases, a normalisation in 78% of patients and a symptomatic improvement in 84% of patients. Dual antiplatelet therapy is recommended for 1–6 months after percutaneous closure, followed by a single antiplatelet therapy thereafter.^{21,22,25} Antibiotic prophylaxis against endocarditis before an invasive procedure or surgical intervention should also be considered routinely in all cases within the first 6 months after the implantation and beyond 6 months in patients with a residual shunt.^{21,22}

Regarding the extracardiac causes of POS, the treatment of choice is the correction of the underlying cause. In case of intrapulmonary shunts, the treatment is represented by pulmonary artery embolisation, whereas lung surgery is performed in patients with rupture of the AVM or in those cases not amenable to embolotherapy.^{26,27} Lung transplant should be considered in

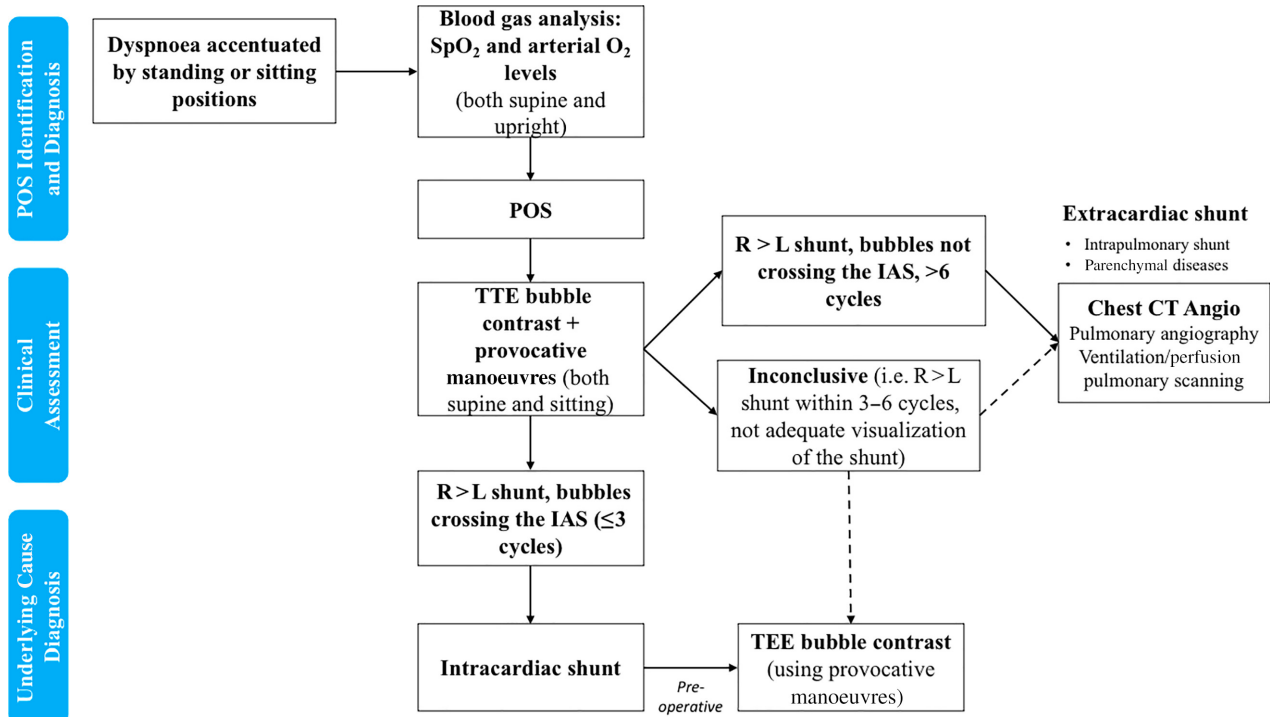


Figure 2 Diagnostic work-up for establishing a diagnosis and aetiology in patients presenting with POS. CT, computed tomography; IAS, interatrial septum; L, left; PO₂, partial pressure of O₂; POS, platypnoea-orthodeoxia syndrome; R, right; SpO₂, saturation O₂; TEE, transesophageal echocardiography; TTE, transthoracic echocardiogram.

non-responder patients or in those with diffuse bilateral pulmonary AVM.²⁸ In patients with hepatopulmonary syndrome, patients should be evaluated and receive priority for liver transplantation¹² as it is the only effective treatment.

Conclusion

POS is a challenging clinical syndrome requiring high clinical suspicion and multimodality evaluation to

outline the underlying cause. Therapeutic interventions directed towards correction of the cause of POS are fundamental for improving symptoms and can potentially be curative.

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Supporting Information

Additional supporting information may be found in the online version of this article at the publisher’s web-site:

Video S1. Agitated saline contrast transthoracic echocardiography in clinostatism and orthostatism.

Video S2. Agitated saline contrast transesophageal echocardiography confirming a ‘tunnel-like’ PFO.

Video S3. Agitated saline contrast transesophageal echocardiography confirming a ‘tunnel-like’ PFO.

Video S4. Successful percutaneous closure with an Amplatzer device (25/25 mm) with minimal residual right-to-left shunt.

Video S5. Successful percutaneous closure with an Amplatzer device (25/25 mm) with minimal residual right-to-left shunt.