ORIGINAL ARTICLE

Platypnoea–orthodeoxia syndrome in a patient on haemodialysis: a case report and scoping review

A Asomaning[1], S Karamchand[2], MY Chothia[1]

[1]Division of Nephrology, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa; [2]Division of Cardiology, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa.

ABSTRACT

Introduction: Platypnoea–orthodeoxia syndrome (POS) is a rare condition caused most frequently by an intracardiac right-to-left shunt. Diagnosis requires a high index of suspicion. We report a case of a young man on chronic haemodialysis who developed POS because of superior vena cava obstruction. We also conducted a scoping review of the literature on POS in adult patients.

Methods: We followed the PRISMA–ScR guidelines. Studies were eligible for inclusion if they reported on patients with POS in hospitalised adults. We included case reports and case series from 1 January 1949 to 31 May 2023, sought from PubMed (Medline), Web of Science Core Collection, and the Cumulative Index of Nursing and Allied Health Literature.

Results: A 29-year-old man undergoing long-term haemodialysis experienced respiratory distress during his dialysis sessions, particularly when seated upright. His oxygen saturation improved to 100% when supine but dropped to 80% when he stood up. Blocking the arteriovenous fistula (AVF) while standing raised his oxygen saturation to 93%. Left heart catheterisation revealed extensive systemic venous collaterals draining into the left atrium via pulmonary veins. A diagnosis of POS from systemic venovenous collateral vessels due to superior vena cava obstruction was made. Because of the patient's comorbidities and the AVF being his last viable vascular access, no further interventions were pursued.

Three hundred and thirty-seven articles (662 patients) were identified in the search of the literature. Six of the patients were on kidney replacement therapy (KRT). The median age was 70 years (IQR 58–79 years). Overall, the most common cause (80%) of POS was an intracardiac right-to-left shunt and patent foramen ovale (PFO) was the most common (74%) primary cause. Hepatopulmonary syndrome (HPS) was the most common extracardiac cause (38%) of POS. Of the six patients on KRT, five had intracardiac causes of POS and one had an extracardiac cause. Most patients (67%) with PFO had percutaneous closure of the shunt. Four of the five patients on KRT with intracardiac shunt had percutaneous or open surgical closure whereas one was managed conservatively. Most of the patients were discharged and had a low mortality rate of only 5%.

Conclusions: This case report and literature review describes the causes, treatment, and outcome of POS. Since this is a rare condition, a high index of suspicion is needed for diagnosis. There is a limited number of documented cases in individuals receiving KRT. Although intracardiac shunts were still the most prevalent cause of POS in patients on KRT, SVC obstruction is another aetiology that should be considered. Overall, the prognosis for individuals with POS as reported in the literature was excellent, with a low mortality rate.

Keywords: dialysis; superior vena cava; obstruction; Africa.

Received 20 November 2023; accepted 27 March 2024; published 10 May 2024.
Correspondence: Yazied Chothia, yaziedc@sun.ac.za.

DOI: https://doi.org/10.21804/27-1-6223.

INTRODUCTION

Platypnoea–orthodeoxia syndrome (POS) is a rare clinical condition characterised by dyspnoea occurring in the upright posture and relieved by recumbency (platypnoea) as well as arterial oxygen desaturation accentuated by upright posture and relieved by recumbency (orthodeoxia) [1,2]. The original description of POS dates back to 1949 when Burchell et al. [3] reported a patient with a post-traumatic intrathoracic arteriovenous shunt who exhibited a threefold increase in ventilation and a 15% decrease in arterial oxygen saturation (SaO_2) whenever the patient assumed an upright posture. The terms platypnoea and orthodeoxia were first used in 1969 [4] and later in 1976 [5]. In 1981, Roos et al. [6] described the first case of POS associated with a patent foramen ovale (PFO). This was followed three years later by a description of POS due to a right-to-left intracardiac shunt in the absence of elevated intracardiac pressure or hepatopulmonary syndrome (HPS) [7]. The condition has rarely been described in patients receiving kidney replacement therapy (KRT) [8].

A right-to-left shunt (hereafter simply referred to as a shunt) exists when blood passes from the right to the left side of the heart without being oxygenated. A shunt is an extreme example of ventilation-perfusion (V/Q) mismatch where there is no ventilation. Poor response to oxygen therapy is a feature that differentiates shunt from other mechanisms of hypoxaemia including V/Q mismatch [9]. Hypercapnia is also uncommon in a shunt unless the shunt fraction is ≥50% [10]. For a better understanding of the mechanism of hypoxaemia due to a shunt, see Figure S1 in the supplementary data [9].

The causes of POS include intracardiac and extracardiac shunts. Previous studies have reported that most cases of POS are caused by an intracardiac shunt (87%), whereas 9% are due to pulmonary arterio-venous shunts, and 4% attributed to pulmonary parenchymal diseases [1]. A study focusing on 141 patients with "platypnoea-orthopnoea disease", POS with intracardiac shunt without elevated right heart pressures or pulmonary hypertension, reported that all patients were over 50 years old. PFO accounted for 88% of the interatrial shunts, with atrial septal defect (ASD) accounting for 20% and atrial septal aneurysm (ASA) accounting for 14% [11].

In extracardiac-related POS, deoxygenated blood shunts from the venous to the arterial system outside the heart [1]. The lungs are the most common site for extracardiac shunting. Extracardiac causes of POS include: anatomic pulmonary shunts such as pulmonary arteriovenous communications [11], physiological pulmonary shunts from basal-predominant lung parenchymal diseases such as coronavirus-19 (COVID-19) pneumonia, interstitial lung disease and emphysema [1,12,13] and HPS [14]. Rarely, combined cardiac and pulmonary-related POS occurs following a pneumonectomy in a patient with an existing intracardiac shunt such as a PFO or ASD [2]. Miscellaneous causes of POS include amiodarone pulmonary toxicity [2], autonomic neuropathy from diabetes mellitus, and severe organophosphate poisoning [1,15].

Diagnosis of POS requires a high level of clinical suspicion and the first step involves the demonstration of a decrease in partial pressure of arterial oxygen (PaO_2) of >4 mmHg or arterial oxygen desaturation (SaO_2) of >5% from supine to an upright position [1]. The next step should involve the identification of the underlying cause starting with a bubble contrast-echocardiogram (using agitated saline) in both the supine and upright positions. The appearance of bubbles in the left atrium within three cardiac cycles suggests an intracardiac shunt and, after three cardiac cycles, suggests an extracardiac shunt [1,11,16].

Management of POS is directed at the underlying cause of vascular shunting. In interatrial shunting, repair of the defect is necessary [2]. Co-existing secondary anatomical defects also require surgical intervention. For extra-cardiac shunts such as pulmonary arteriovenous malformation (AVM), pulmonary artery embolisation is performed [1]. In primary pulmonary parenchymal disease, treatment of the underlying condition results in resolution of symptoms [17]. The definitive treatment for HPS is liver transplantation [18].

In this report, we describe a case involving a young male undergoing haemodialysis, who experienced POS because of superior vena cava obstruction resulting from prior dialysis catheter placements. The presence of an arteriovenous fistula (AVF) exacerbated this condition. Subsequently, we conducted a scoping review on the topic of POS.

CASE PRESENTATION

A 29-year-old male known with kidney failure secondary to crescentic glomerulonephritis on thrice weekly haemodialysis (HD) for the past five years, presented with progressive dyspnoea. A month prior to presentation, he developed mild dyspnoea on exertion, which progressively worsened to dyspnoea at rest. He denied having fever, orthopnoea, paroxysmal nocturnal dyspnoea, cough, chest pain, swelling of lower limbs or weight gain. Two months prior, pulmonary tuberculosis was diagnosed, and one month before his current presentation, he developed a provoked deep venous thrombosis (DVT) in his right lower limb, which was linked to a haemodialysis catheter. A pulmonary embolus was excluded on computed tomogram pulmonary angiography.

The history was notable for multiple procedures for haemodialysis vascular access. He had previous tunnelled catheters in both internal jugular veins (IJV) and femoral veins with a history of traumatic IJV catheterisation requiring right thoracotomy on account of a massive haemothorax. A venogram one year ago after a failed right AVF showed right brachiocephalic vein occlusion. His current haemodialysis access was a left brachio-basilic AVF.

Current medications included rifampicin, isoniazid and renally adjusted doses of pyrazinamide and ethambutol. He was also on warfarin, calcium carbonate, oral iron, and a recombinant erythropoiesis-stimulating agent.

On examination, his temperature was 36.5°C, pulse rate of 100 beats per minute and blood pressure 109/60 mmHg. He had tachypnoea with a respiratory rate of 24 breaths per minute and oxygen saturation of 82% while breathing ambient air in a semi-recumbent position. His weight was 62 kg with a dry weight of 61 kg. He had distended neck and upper chest veins. The conjunctivae were pale and pedal oedema was absent. Lung auscultation was normal. Cardiovascular examination revealed normal heart sounds with no murmurs. The abdominal and neurologic examinations were unremarkable.

During routine attendance for haemodialysis treatment, it was noted that the patient had respiratory distress while he was seated in an upright position. Arterial blood gas analysis was performed, while he was breathing ambient air, and revealed a pH of 7.47, partial pressure of oxygen (PaO_2) of 4.2 kPa (31.5 mmHg), partial pressure of carbon dioxide ($PaCO_2$) of 5.1 kPa (38 mmHg) and haemoglobin concentration was 10.9 g/dL. The calculated alveolar-arterial gradient was 9.5 kPa (71 mmHg) [expected value for age: 1.5 kPa (10 mmHg)]. Although the patient was not clinically fluid overloaded, there was a concern for pulmonary oedema. Following a session of haemodialysis, the patient remained hypoxaemic despite supplemental oxygen via face mask. It was noted that the patient's pulse oximetry oxygen saturation (SpO_2) improved to 100% when the bed was supine but he quickly experienced dyspnoea and a drop in SpO_2 to 80% upon standing. His SpO_2 improved to 93% on occlusion of the AVF when standing.

A transthoracic echocardiogram was performed due to suspicion of an intracardiac shunt, but no shunt was detected. Instead, a substantial pericardial effusion with an effusive-constrictive pattern and without signs of tamponade were observed. The left ventricular ejection fraction was 30%. A pericardiocentesis was performed which drained 200 mL of serosanguinous fluid. Although the patient remained hypoxaemic, there was a moderate improvement of SpO_2 to 92% while breathing ambient air in the upright position. GeneXpert for tuberculosis and culture of pericardial fluid were negative.

Because our suspicion of an intracardiac shunt remained high, we conducted a follow-up transoesophageal echocardiogram (TOE) with agitated saline, also known as a bubble study. This examination was conducted with the patient in both the supine and upright positions. The results revealed the early appearance of microbubbles from the pulmonary vein into the left atrium, occurring within three cardiac beats, indicating the presence of an intracardiac shunt; however, no shunt was identified.

A computed tomographic (CT) angiogram showed complete occlusion of the superior vena cava (SVC) with extensive venous collaterals (Figure 1). The CT scan also revealed the presence of a persistent left-sided superior vena cava (PLSVC). Cardiac magnetic resonance imaging (MRI) showed PLSVC with apparent drainage into the coronary sinus, and intact interatrial and interventricular septa. The right SVC was obstructed with the presence of extensive venous collateral vessels.

As a result of the absence of an intracardiac shunt on the TOE with agitated saline as well as the cardiac MRI, a left and right heart catheterisation with venography was performed. The right heart could not be catheterised due to severe stenosis of the right IJV and of both femoral veins caused by previous haemodialysis catheters. During the left heart study, we did not detect any atrial septal defect (ASD) equivalents, including the absence of an unroofed coronary sinus in association with the PLSVC or sinus venosus defect. However, we observed extensive systemic venous collaterals that drained into the left atrium via the pulmonary veins. This was accompanied by left ventricular oxygen desaturation, which reached 85%. The left ventricle (LV) pressure was only 6 mmHg, which favoured intracardiac shunting from right to left. There were no discernible changes in oxygen saturation levels from the LV to the ascending aorta and descending aorta, suggesting the absence of a patent ductus arteriosus.

We diagnosed POS from extensive systemic venovenous collateral blood vessels caused by the SVC obstruction, which behaved functionally as an ASD equivalent. Because of the patient's comorbidities and the fact that the current AVF was his last vascular access, and following consultation with the patient, we decided against any further interventions.

Ethical considerations

The patient gave written, informed consent and the Health Research Ethics Committee of Stellenbosch University granted approval for publication (reference number C23/08/019; project identification number 28855).

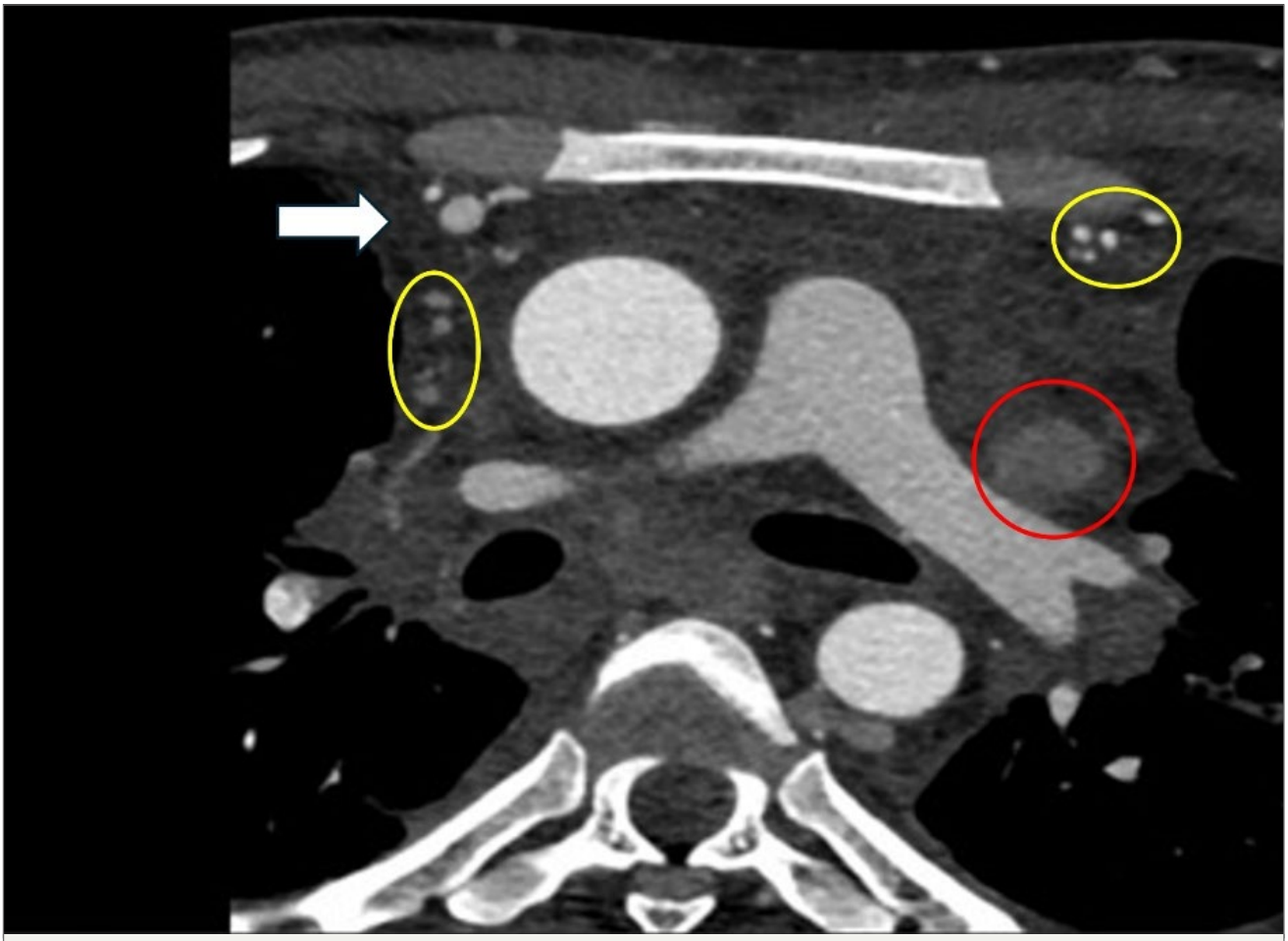

Figure 1. Contrast-enhanced computed tomography scan of the superior mediastinum.
Persistent left-sided superior vena cava (red circle). Extensive mediastinal (yellow ovals) and chest wall venous collateral blood vessels (not indicated). Right superior vena cava not visible (white arrow).

LITERATURE REVIEW

We conducted a scoping review of POS in the literature and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis-Scoping Reviews (PRISMA-ScR) guidelines. The following questions were addressed:

1. What are the common primary intracardiac causes of POS?
2. What are the common extracardiac causes of POS?
3. Are there any causes of POS in patients on KRT?
4. What is the optimum management and expected outcome of patients with POS?

REVIEW METHODS

Eligibility criteria

Research articles were eligible for inclusion if they reported on patients with POS in adults at least 18 years old. We included case reports and case series, but excluded systematic reviews, cohort studies, patients not treated in hospital and animal studies.

Information sources

To identify relevant research, we searched the following bibliographic databases: Medline (PubMed), Web of Science Core Collection, and the Cumulative Index of Nursing and Allied Health Literature (CINAHL) (EBSCOhost).

The search strategy was tailored to each database, which is available in the supplementary data (Table S1). All eligible research reports from 1 January 1949 to 31 May 2023 were included, regardless of language.

Selection of eligible research

The search yield was imported into Rayyan screening software (https://rayyan.ai/) and duplicate articles were removed. Titles and abstracts were screened. Uncertainties were resolved by consensus between the authors (AA and MYC). Full-text articles were obtained for the potentially eligible articles, and these were subsequently screened. Reasons for exclusion of articles are provided in the supplementary data (Table S2).

Data extraction tool and data items

The data extracted included the year of publication, name of author, patient's age, sex, primary cause of POS (intracardiac vs. extracardiac), functional component of POS and any other contributing factors, oxygen saturation and or partial pressure of oxygen of patient when supine and upright, presence of normal or elevated right atrial pressures, presence or absence of pulmonary hypertension, management of the patient, and outcome.

RESULTS

The results of the search strategy and study selection are shown in Figure 2. A total of 337 research articles were included in the scoping review (List S1 in the supplementary data).

Characteristics of included research

The most common study design was case reports (302 studies). About 70% of reported cases were from the years 2013 to 2023. A summary of the individual study characteristics is provided in Table S3 of the supplementary data.

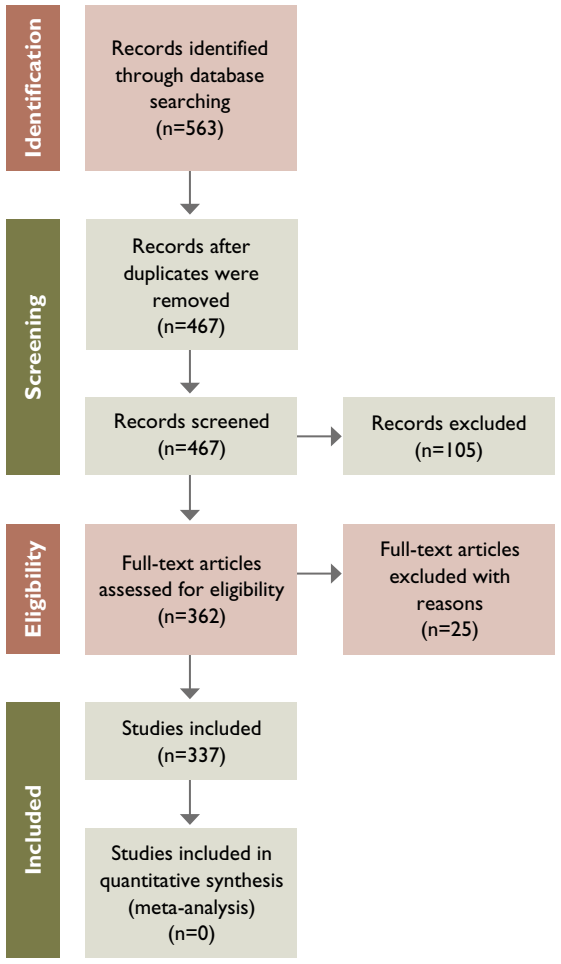

Figure 2. Consort diagram.

Patient characteristics

A total of 662 patients featured in the 337 articles reviewed. Three hundred and thirty-nine patients were female (51%); their median age was 70 years (inter-quartile range (IQR) 58–79 years). There were six patients on KRT: two patients with a kidney transplant and four patients on haemodialysis. One patient had continuous venovenous haemodialysis on account of acute kidney injury. The median oxygen saturation (pulse oximeter oxygen saturation [SpO_2] or arterial oxygen saturation [SaO_2]) in the supine position was 95% (IQR 92–97%) and in the upright position 82% (IQR 76–87%). The median partial pressure of oxygen (PaO_2) in the supine position was 74 mmHg (IQR 63–83.5 mmHg) and when upright 51 mmHg (IQR 43–59 mmHg). Pulmonary pressure was normal (<25 mmHg) in 149 out of 163 patients (91%). Right atrial pressure was normal in 48 out of 59 patients (81%). Figure 3 and Figure 4 show the oxygen saturation and PaO_2 values in the supine and upright positions. Table 1 summarises patient characteristics.

Causes of platypnoea-orthodeoxia syndrome

The most common cause of POS was intracardiac shunts, which accounted for 80% of cases (Table 2). Extracardiac

Table 1. Patient characteristics.

Demographic data	
Age in years, median (IQR)	70 (58–79)
Female, n (%)	339/662 (51)
Kidney replacement therapy	
Kidney transplant, n (%)	2/662 (0.3)
Haemodialysis, n (%)	4/662 (0.6)
Peritoneal dialysis, n (%)	0 (0)
Oxygen saturation	
Supine (%), median (IQR)	95 (92–97)
Upright (%), median (IQR)	82 (76–87)
Partial pressure of oxygen	
Supine (mmHg), median (IQR)	74 (63–84)
Upright (mmHg), median (IQR)	51 (43–59)
Pulmonary arterial pressure	
Normal (<25 mmHg), n (%)	149/162 (92)
High, n (%)	14/162 (8)
Right atrial pressure	
Normal, n (%)	48/59 (81)
High, n (%)	11/59 (19)

Abbreviation: IQR, interquartile range.

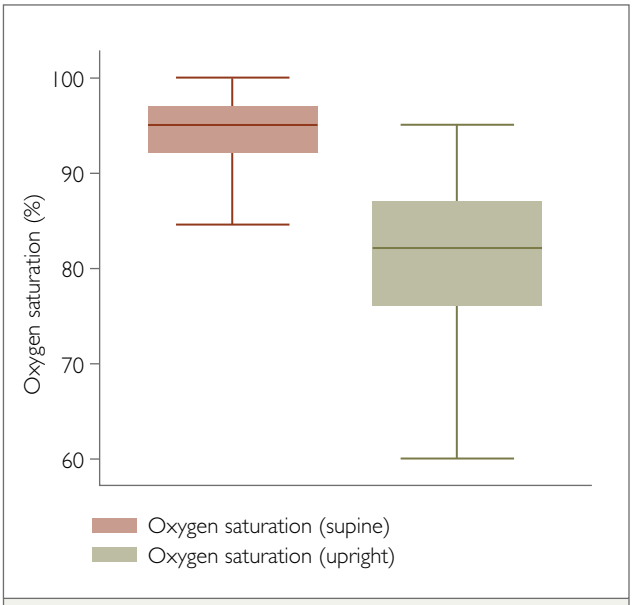

Figure 3. Oxygen saturation in the supine and upright positions.

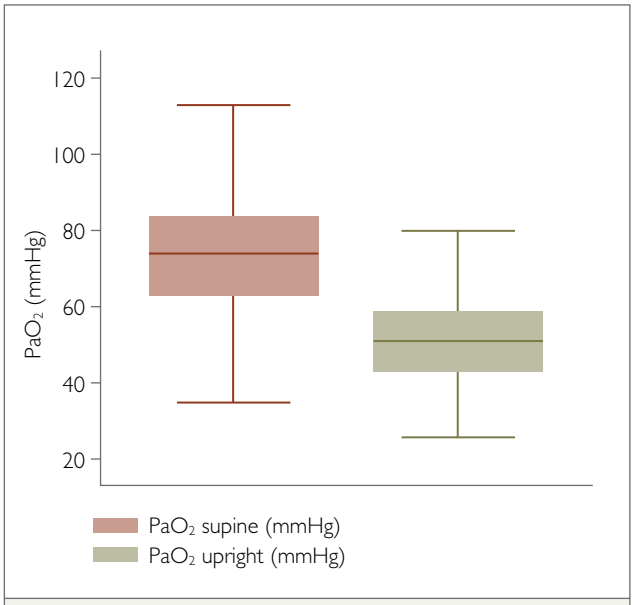

Figure 4. Partial pressure of arterial oxygen (PaO_2) in the supine and upright positions.

causes constituted 20%. The most common primary cause of POS was PFO, which accounted for 74% and 92% of overall causes and intracardiac causes, respectively. Hepatopulmonary syndrome (HPS) was the second-most common primary cause of POS (8%) and the most common extracardiac cause of POS (38%). The most common secondary contributing factor was atrial septal aneurysm, which accounted for 21% of cases (Table 3). This was followed by right pneumonectomy (12%) and aortic root dilatation (9%). About 126 cases (19%) had two or more secondary contributing factors. Of the six patients on KRT, five had an intracardiac shunt (PFO in four patients and ASD in one patient) as the primary cause of POS with high output heart failure from an AVF contributing to the shunt in one patient. The secondary contributing factors in the remaining patients were atrial septal aneurysm, aortic root dilatation, prominent Eustachian valve, post-abdominal surgery and COVID-19 pneumonia. One patient on KRT had COVID-19 as the primary cause of POS.

Table 2. Primary causes of platypnoea-orthodeoxia syndrome.

	Frequency	Overall %	Intracardiac or extracardiac %
Total	662	100	–
Intracardiac causes	529	80	100
PFO	487	74	92
ASD	42	6	8
Extracardiac causes	133	20	100
HPS	51	8	38
COVID-19 pneumonia	34	5	26
Chronic pulmonary disease	12	2	9
Other*	36	5	27

Abbreviations: PFO, patent foramen ovale; ASD, atrial septal defect; HPS, hepatopulmonary syndrome.
*Other includes organophosphate poisoning, pulmonary arteriovenous malformations, pulmonary embolism, non-COVID-19 pneumonia, persistent left-sided superior vena cava, autonomic neuropathy, acute respiratory distress syndrome, Parkinson's disease, fat embolism, Chilaiditi syndrome, inferior vena cava obstruction and Fontan circulation.

Management and outcomes

Percutaneous closure of PFO was performed for 395 patients (67%), whereas 38 patients (6%) had open surgical closure. Percutaneous closure of ASD was performed for 23 patients (4%), whereas 16 patients (3%) had open closure. Liver transplantation was performed on three patients (0.5%) with HPS. Other surgical repairs such as surgical reconstruction of venous drainage and ligation of PLSVC was performed on three patients (0.5%). Fifty-two patients (9%) were managed conservatively, and they included patients who refused either percutaneous or open closure of PFO or ASD, patients managed at facilities with no definitive treatment modalities such as liver transplantation, and those awaiting liver transplantation for HPS.

Twenty-nine patients with COVID-19 pneumonia (5%) were managed with oxygen and physiotherapy, and five (1%) were treated with steroids. Other treatment modalities tailored towards the underlying cause of the POS included percutaneous occlusion of pulmonary AVMs, anticoagulation for pulmonary embolism, and atropine in conjunction with pralidoxime for organophosphate poisoning.

Table 3. Secondary contributing factors.

Contributing factors	n (%)
Atrial septal aneurysm	97 (21.0)
Right pneumonectomy	55 (12.0)
Aortic root dilatation	40 (9.0)
Chronic lung disease	33 (7.2)
Ascending aortic aneurysm	20 (4.3)
Right elevated hemidiaphragm	18 (3.9)
Aortic elongation	13 (2.8)
Valvular heart disease†	12 (2.6)
Post abdominal surgery	11 (2.4)
Left pneumonectomy	10 (2.2)
Right heart disease	9 (2.0)
Fracture	9 (2.0)
Prominent Eustachian valve	8 (1.7)
Pulmonary embolism	8 (1.7)
Atrial septal defect	7 (1.5)
Pneumonia (COVID-19 and others)	7 (1.5)
Spinal deformities (kyphosis, scoliosis, kyphoscoliosis)	6 (1.3)
Hypermobile atrial septum	5 (1.1)
Lipomatous atrial septum	5 (1.1)
Epstein anomaly	5 (1.1)
Hereditary haemorrhagic telangiectasia	2 (0.4)
Other*	79 (17.2)

Abbreviations: COVID-19, coronavirus disease-19. IVC, inferior vena cava; ICD, intracardiac device; PFO, patent foramen ovale; LVAD, left ventricular assist device; AVM, arteriovenous malformation; HPS, hepatopulmonary syndrome; SVC, superior vena cava.
†Valvular heart disease includes tricuspid regurgitation, aortic regurgitation, tricuspid stenosis, pulmonary stenosis.
*Others include corrected transposition of great arteries, altered IVC orientation post liver transplant, dilated superior vena cava, aorta projection towards right atrium, ICD induced venous obstruction, pericardial effusion, coronary artery disease, Chiari malformation, obstructive sleep apnoea, thoracic aortic aneurysm, Budd Chiari syndrome, aortic tortuosity, ASD, autonomic dysfunction, bilateral large pleural effusions, fracture, eosinophilic endomyocardial disease, giant liver cyst, horizontal ascending aorta, hypovolemia, LVAD, obesity, paralysis post stroke, interatrial septal bulge, ascending aortic aneurysm, pulmonary AVM, right atrial thrombus, right atrial mass, abdominal compression, pericardial metastasis, right thoracoplasty, idiopathic cardiomyopathy, pulmonary tumour, thrombotic microangiopathy, high output heart failure, unfolding aorta, post resection of intrapericardial cyst, right middle lobe atelectasis, alpha agonist (metaraminol), dilated coronary sinus, post transcatheter aortic valve implantation, pulmonary metastasis, ascending aortic surgery, aortic dissection, post percutaneous coronary intervention, tetralogy of Fallot, post total hip replacement, post knee surgery, carcinoid, lymphoma of right atrium, bilateral lung transplantation, persistent left SVC.

Among the five patients receiving kidney replacement therapy (KRT) who had intracardiac shunts, two underwent percutaneous shunt closure, two underwent open surgical repair, and one received conservative management. One patient undergoing KRT required a thoracotomy and PFO repair when percutaneous closure failed. Another patient had open surgical repair addressing not only the PFO but also an atrial septal aneurysm and a redundant Eustachian valve. Conservative management, consisting of AVF ligation, was chosen for one patient due to a high perioperative risk and their unsuitability for surgery. Another was managed with oxygen and steroids for COVID-19 pneumonia with partial recovery of POS. Details of other treatment options are provided in the supplementary data (Table S4).

Table 4. Treatment and outcome of patients with platypnoea–orthodeoxia syndrome.

Treatment	n (%)
Percutaneous closure of PFO	395 (67)
Conservative management	52 (9)
Open surgical closure of PFO	38 (6)
Percutaneous closure of ASD	23 (4)
Open surgical closure of ASD	16 (3)
Other surgical repairs	3 (0.5)
Liver transplantation	3 (0.5)
Oxygen and physiotherapy	29 (5)
Steroids	5 (1)
Other	24 (4)
Outcomes	
Discharged	562 (95)
Died	27 (5)

Abbreviations: PFO, patent foramen ovale; ASD, atrial septal defect.

Of 589 patients with reported outcomes, 562 (95%) were discharged home, whereas 27 patients (4.5%) died (Table 4).

DISCUSSION

This scoping review includes the largest number of cases of POS recorded in the literature to date. The median age of patients in our review was 70 years. Others have reported similar findings with age ranging from 50 to 76 years [11,19-21]. One factor contributing to the increased occurrence of patent foramen ovale (PFO) among the elderly, especially when accompanied by intracardiac shunts, is the ageing process. With advancing years, several physiological changes occur, making it more conducive for venous blood from the inferior vena cava to travel towards the fossa ovale. These changes may involve a shift in the position of the mediastinum, a reduction in heart compliance, or a clockwise rotation or torsion of the heart [11,22].

From our review, intracardiac shunts accounted for 80% of cases of POS whereas extracardiac shunts accounted for 20% of cases. A previous review reported similar findings with intracardiac causes accounting for 87% of POS and extracardiac causes only 13% [1]. We found PFO to be the most common cause of intracardiac shunting and this was found in 74% of all cases and 92% in patients with intracardiac shunts compared to 67% and 88%, respectively, in previous reviews [1,11]. Atrial septal aneurysm was the most common secondary contributing factor from our

review and was present in one in five patients followed by aortic root dilatation and ascending aortic aneurysm, while right pneumonectomy accounted for 12%. Others have reported similar frequencies of contributing factors [1,11].

PFO with POS occurs when two conditions are present: an anatomical component, such as an interatrial shunt, and a functional component that redirects shunt flow when assuming an upright posture [22]. PFO is quite common, affecting around 25–30% of the general population, but many individuals with PFO do not experience POS symptoms due to the higher left atrial pressure, which keeps the atrial septum closed [23]. Shunting in the presence of inter-atrial communication can occur due to several mechanisms, including distortion of cardiac anatomy favouring blood passage into the interatrial communication with normal right atrial pressure (the "flow" phenomenon), transient right atrial pressure elevation (the "haemodynamic" explanation), or a combination of both [11,24]. Anatomical features like a hypermobile atrial septum, aortic root dilatation, and ascending aorta elongation can contribute to the "flow" phenomenon [19]. Aortic atherosclerosis, for example, can elongate the ascending aorta and cause aortic root dilation, allowing the PFO to open when upright [25]. Structural factors such as persistent Eustachian valve or Chiari's network, lipomatous hypertrophy of the atrial septum, and alterations in intrathoracic pressure or structure like kyphosis and hemidiaphragm paralysis can also influence shunting [19,26-28]. In patients with intracardiac shunts and elevated right atrial pressures, decreased right ventricular compliance is observed. Some authors have suggested that when standing upright, although there may be a drop in right ventricular pressure, compliance of the right ventricle may remain constant due to blood filling, while left ventricular compliance increases, thus favouring shunting [11]. Various medical conditions, such as pulmonary embolism [29,30], right ventricular myocardial infarction [31,32], pericardial effusion [33], constrictive pericarditis [34], age-related right ventricle stiffness, and chordae tendineae rupture causing tricuspid regurgitation and right pressure overload, can contribute to elevated right atrial pressures in these patients [35].

We found that the most common extracardiac cause of POS was HPS. In previous systematic reviews, the most common causes were pulmonary AVMs followed by pulmonary parenchymal diseases [1,11]. HPS is characterised by a triad of liver disease, arterial hypoxaemia and intrapulmonary vascular dilatations, with the latter in the presence of normal ventilation causing a V/Q mismatch [14]. The pulmonary vascular dilatations facilitate the rapid passage of mixed venous blood directly through intrapulmonary shunts into the pulmonary veins. Orthodeoxia in HPS results from rigid and fixed pulmonary vascular tone, which is not able to accommodate gravitational blood flow changes to ventilation in dependent alveolar units [36,37].

We found COVID-19 pneumonia as the second-most common extracardiac cause of POS. Physiological pulmonary shunts from basal-predominant lung parenchymal diseases such as COVID-19 pneumonia and chronic pulmonary diseases cause POS through severe V/Q mismatch [1,12,13]. In the presence of microthrombi and microangiopathy observed in severe COVID-19 pneumonia, the so-called zone one phenomenon is exaggerated [1,9,12,38,39].

In haemodialysis patients, SVC obstruction mostly occurs as a complication of central venous catheter placement [40]. As was found in our patient, SVC obstruction can result in the formation of an anatomical systemic-to-pulmonary venous collateral pathway and therefore extracardiac shunting of blood [41]. Our review found one case of kidney failure with SVC obstruction from multiple haemodialysis catheterisation and resultant systemic-to-pulmonary collateral vessel formation; however, there was no documented POS [40]. In our case study, the blood flow in the venovenous collateral blood vessels was augmented by the AVF flow, resulting in an increased shunt fraction. This gave the appearance of a functional equivalent to an ASD since microbubbles appeared in the left atrium within three cardiac cycles. From our scoping review, POS was extremely rare in patients on KRT, with only six cases reported. Only one patient on KRT had an extracardiac shunt as the primary cause of POS. One patient with a PFO had high-output heart failure from an AVF, which contributed to the shunt and POS.

In our review, percutaneous closure of intracardiac shunts was performed in most patients. Percutaneous transcatheter closure is the preferred method due to reduced morbidity, mortality and cost [2]. Open surgical repair of PFO or ASD was performed for patients with complex or two or more intracardiac shunts.

KRT patients who underwent percutaneous or surgical closure of the intracardiac shunt experienced complete resolution of POS symptoms, whereas the patient managed conservatively exhibited partial improvement in POS symptoms.

Management of extracardiac causes included oxygen, chest physiotherapy and steroids in cases of COVID-19 pneumonia and chronic pulmonary diseases. Some patients with HPS had liver transplantation; however, most were managed conservatively.

We found that nearly all patients were discharged home and mortality was low. Most mortalities were due to advanced age, comorbid conditions, or refusal by patients to undergo surgical repair. All patients on KRT were discharged from the hospital.

Limitations

There were some limitations in the scoping review. We were unable to access several full-text articles. Although studies diagnosed POS, the change in oxygen saturation or partial pressure of oxygen with position were not reported. Some of the larger case series may have included previously published case reports. This could have led to duplication of cases. Oxygen saturation for some patients were measured with a pulse oximeter whereas for others, arterial oxygen saturation was measured.

CONCLUSIONS

Platypnoea–orthodeoxia syndrome is a rare condition. The most common cause of intracardiac shunt observed was a patent foramen ovale, whereas the most common extracardiac shunt was due to HPS. Intracardiac shunts were typically treated through percutaneous closure, whereas extracardiac shunts caused by pulmonary conditions were primarily managed medically, except in the case of HPS. Overall, the prognosis for individuals with POS was excellent, with a low mortality rate. There are only a limited number of documented cases of individuals receiving KRT. Identifying POS in KRT patients requires a high degree of clinical suspicion. Although intracardiac shunts were still the most prevalent cause of POS in KRT patients, SVC obstruction is another aetiology that should be considered specifically in patients who have a history of previous IJV haemodialysis catheters along with suggestive symptomatology, coupled with clinical features of SVC obstruction.

Supplementary materials

The supplementary materials are available on the *African Journal of Nephrology* website. They include Figure S1, Tables S1, S2, S3 and S4, and List S1.

Conflict of interest

The authors have no conflicts of interest to declare.

REFERENCES

1. Agrawal A, Palkar A, Talwar A. The multiple dimensions of platypnea-orthodeoxia syndrome: A review. Respir Med. 2017;129: 31-38.
2. Cheng TO. Editorial comment: editorial comment. Catheter Cardiovasc Interv. 1999;47: 64-66.
3. Burchell HB, Wood EH. Reflex orthostatic dyspnea associated with pulmonary hypotension. Am J Physiol. 1949;159: 563-564.
4. Altman M, Robin ED. Platypnea (Diffuse Zone I Phenomenon?). N Engl J Med. 1969;281: 1347-1348.
5. Robin ED, Laman D, Horn BR, Theodore J. Platypnea related to orthodeoxia caused by true vascular lung shunts. N Engl J Med. 1976;294: 941-943.
6. Roos CM, Romijn KH, Braat MC, van Leeuwen AM. Posture-dependent dyspnea and cyanosis after pneumonectomy. Eur J Respir Dis. 1981;62: 377-382.
7. Seward JB, Hayes DL, Smith HC, Williams DE, Rosenow EC, Reeder GS, et al. Platypnea-Orthodeoxia: Clinical profile, diagnostic workup, management, and report of seven cases. Mayo Clin Proc. 1984;59: 221-231.
8. Wadia S, Boateng S, Kenny D, Kavinsky C. Platypnea-orthodeoxia in patients on hemodialysis : A new approach to its pathophysiology and implications for treatment. Cardiology 2016;60612: 213-216.
9. Glenny RW. Teaching ventilation/perfusion relationships in the lung. Am J Physiol – Adv Physiol Educ. 2008;32: 192-195.
10. Covelli HD, Nessan VJ, Tuttle WK 3rd. Oxygen derived variables in acute respiratory failure. Crit Care Med. 1983;11: 646-649.
11. Rodrigues P, Palma P, Sousa-Pereira L. Platypnea-orthodeoxia syndrome in review: Defining a new disease? Cardiology. 2012;123: 15-23.
12. Tan GP, Ho S, Fan BE, Chotirmall SH, Tan CH, Lew SJW, et al. Reversible platypnea-orthodeoxia in COVID-19 acute respiratory distress syndrome survivors. Respir Physiol Neurobiol. 2020;282: 103515.
13. Mathew U, Mittal A, Vyas S, Ray A. Interstitial pneumonia with autoimmune features and platypnea-orthopnea syndrome. BMJ Case Rep. 2019;12: 12-15.
14. Sarkar M, Niranjan N, Banyal PK. Mechanisms of hypoxemia. Lung India. 2017;34: 47-60.
15. Talwar D, Kumar S, Acharya S, Hulkoti VS, Khanna S. Platypnea-orthodeoxia syndrome: A dangerous detour of intermediate syndrome with organophosphorus poisoning. J Family Med Prim Care. 2022;11: 4074-4078.
16. Soliman OII, Geleijnse ML, Meijboom FJ, Nemes A, Kamp O, Nihoyannopoulos P, et al. The use of contrast echocardiography for the detection of cardiac shunts. Eur J Echocardiogr. 2007;8: 2-12.
17. Hussain SF, Mekan SF. Platypnea-orthodeoxia : Report of two cases and review of the literature. South Med J. 2004;97: 657-662.
18. Soulaidopoulos S, Cholongitas E, Giannakoulas G, Vlachou M, Goulis I. Review article: Update on current and emergent data on hepatopulmonary syndrome. World J Gastroenterol. 2018;24: 1285-1298.
19. Othman F, Bailey B, Collins N, Lau E, Tanous D, Rao K, et al. Platypnea-orthodeoxia syndrome in the setting of patent foramen ovale without pulmonary hypertension or major lung disease. J Am Heart Assoc. 2022;11: e024609.
20. Experience TT. Percutaneous intervention to treat platypnea-orthodeoxia syndrome. JACC Cardiol Interv. 2016;9: 1928-1938.
21. Gama e Castro A, Luz A, Oliveira F, Brochado B, Santos R, Alexandre A, et al. Platypnoea orthodeoxia syndrome and patent foramen ovale closure: Single-centre experience and long-term follow-up. Hear Lung Circ. 2022;31: 1547-1552.

22. Cheng TO. Mechanisms of platypnea-orthodeoxia : What causes water to flow uphill? Circulation. 2002;105: e47.
23. Akin E, Krüger U, Stroh E, Janicke I, Rezwanian R. The platypnea-orthodeoxia syndrome. Eur Rev Med Pharmacol Sci. 2014;18: 2599-2604.
24. Godart F, Rey C. Platypnea-orthodeoxia syndrome a probably underestimated syndrome? Chest. 2001;119: 1624-1625.
25. Hasegawa M, Nagai T, Murakami T, Ikari Y. Platypnoea-orthodeoxia syndrome due to deformation of the patent foramen ovale caused by a dilated ascending aorta: A case report. Eur Hear J Case Rep. 2020;4: 1-4.
26. Shakur R, Ryding A, Timperley J, Becher H, Leeson P. Late emergence of platypnea orthodeoxia: Chiari network and atrial septal hypertrophy demonstrated with transoesophageal echocardiography. Eur J Echocardiogr. 2008;9: 694-696.
27. Bashour T, Kabbani S, Saalouke M, Cheng TO. Persistent Eustachian valve causing severe cyanosis in atrial septal defect with normal right heart pressures. Angiology. 1983;34: 79-83.
28. Cheng TO. Right-to-left atrial shunting. Chest. 1991;99: 526-527.
29. Ray S, Qureshi SA, Stolagiewicz N, Sturridge L, Khan S. An unusual case of persisting hypoxia in a patient with a thrombolysed pulmonary embolism. Clin Med J R Coll Physicians London. 2020;20: 593-596.
30. de Figueiredo MG, Paula S, Almeida S, Gomes F, Ferreira F, Luz J, et al. Clinical Case 21—An unusual cause for hypoxemia and breathlessness. Cardiovasc Res. 2022;118: 2022.
31. Albaghdadi A, Teleb M, Porres-Aguilar M, Porres-Munoz M, Marmol-Velez A. The dilemma of refractory hypoxemia after inferior wall myocardial infarction. Baylor Univ Med Cent Proc. 2018;31: 67-69.
32. Saxena A, Saunders P, Frankel R, Friedman M, Adzic A, Moskovits N, et al. Percutaneous closure of the patent foramen ovale on right ventricular mechanical circulatory support. JACC Case Reports. 2020;2: 300-304.
33. Adolph EA, Lacy WO, Hermoni YI, Wexler LF, Javaheri S. Reversible orthodeoxia and platypnea due to right-to-left intracardiac shunting related to pericardial effusion. Ann Intern Med. 1992;116: 138-139.
34. Hashimoto M, Okawa Y, Baba H, Nishimura Y, Aoki M. Platypnea-orthodeoxia syndrome combined with constrictive pericarditis after coronary artery bypass surgery. J Thorac Cardiovasc Surg. 2006;132: 1225-1226.
35. Uchihashi M, Makino M, Kaimoto S, Imai Y, Hadase M, Kurata H, et al. Platypnea-orthodeoxia syndrome associated with spontaneously ruptured chordae tendineae of tricuspid valve. Case. 2019;4: 90-92.
36. Rodríguez-Roisin R, Krowka MJ. Hepatopulmonary syndrome – a liver-induced lung vascular disorder. N Engl J Med. 2008;358: 2378-2387.
37. Gómez FP, Martínez-Pallí G, Barberà JA, Roca J, Navasa M, Rodríguez-Roisin R. Gas exchange mechanism of orthodeoxia in hepatopulmonary syndrome. Hepatology. 2004;40: 660-666.
38. Anthonisen NR, Milic-Emili J. Distribution of pulmonary perfusion in erect man. J Appl Physiol. 1966;21: 760-766.
39. Fox SE, Li G, Akmatbekov A, Harbert JL, Lameira FS, Brown JQ, et al. Unexpected features of cardiac pathology in COVID-19 infection. Circulation. 2020;142: 1123-1125.
40. Valle EO, Mainardes LC, dos Santos Meira M, Dela Pascoa Toranzo MH, Elias RM. Systemic-to-pulmonary venous shunt in a hemodialysis patient with extensive thrombosis of superior and inferior vena cava. Kidney Int Rep. 2021;6: 2510-2513.
41. Grayet D, Ghaye B, Szapiro D, Dondelinger RF. Systemic-to-pulmonary venous shunt in superior vena cava obstruction revealed on dynamic helical CT. Am J Roentgenol. 2001;176: 211-213.