



The Paradoxical Protector: A Stretched Patent Foramen Ovale in Severe Pulmonary Arterial Hypertension and Right Heart Failure in an Adolescent — A Case Report

¹ Nurrahmah Latifa, ² Devi Nadilah, ³ Ganang Kusuma Ahimsa, ⁴ Liza Apsera, ⁵
Nurul Astari Sembiring, ⁶ Rezza Fitriansyah

^{1,2,5,6} General Practitioner, Awal Bros Bagan Batu General Hospital, Indonesia

³ Cardiologist, Awal Bros Bagan Batu General Hospital, Indonesia

⁴ Pediatrician, Awal Bros Bagan Batu General Hospital, Indonesia

Corresponding Email : nurrahmahlatifa@gmail.com

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ABSTRACT

Introduction: In severe pulmonary arterial hypertension (PAH), a small interatrial communication identified on echocardiography is frequently misinterpreted as the congenital lesion responsible for the disease. Physiologically, however, such a communication may function as a right atrial decompression pathway. The distinction is decisive, because closure of a decompressing shunt may precipitate fatal right heart failure.

Case report: A 17-year-old undernourished girl (weight 30 kg, height 140 cm; BMI 15.3 kg/m²) with pulmonary tuberculosis diagnosed in November 2024 and treated until May 2025 presented with a one-month history of progressive dyspnoea, abdominal distension and bilateral leg oedema, with acute worsening one day before admission. Examination revealed

central cyanosis (SpO₂ 89% on room air), tachypnoea, cardiomegaly, a grade 4/6 systolic murmur at the fourth left parasternal intercostal space, fixed splitting of S2, bibasal rales, ascites and pitting oedema. Laboratory tests showed microcytic hypochromic anaemia, hyponatraemia (128 mmol/L), severe hypokalaemia (2.6 mmol/L), hypochloraemia and hypoalbuminaemia. Electrocardiography demonstrated sinus tachycardia, right atrial enlargement and right ventricular hypertrophy with strain. Chest radiography and computed tomography showed cardiomegaly, pulmonary congestion, bilateral pleural effusions, pneumonia and ascites. Transthoracic echocardiography revealed right atrial and right ventricular dilatation, a small left ventricle with preserved ejection fraction (67%), severe tricuspid regurgitation (gradient 46 mmHg; estimated peak velocity $\approx$ 3.4 m/s), TAPSE 17 mm, a dilated main pulmonary artery and a small interatrial communication at the fossa ovalis. Treatment comprised intravenous furosemide, spironolactone, digoxin, sildenafil, beraprost, ceftriaxone and supportive measures; no septal intervention was undertaken.

Discussion: The size of the defect was disproportionate to the severity of pulmonary vascular disease. The clinical and echocardiographic profile is most consistent with group 1 pulmonary hypertension, either idiopathic PAH with a coincidental patent foramen ovale (PFO) or PAH with a small, coincidental defect, in which right atrial hypertension has stretched the foramen ovale open. The communication therefore represents a consequence rather than a cause of the disease and is not haemodynamically significant congenital heart disease. By permitting right-to-left decompression, it may help preserve left ventricular preload and systemic output at the expense of

hypoxaemia. Current guidelines consider closure of such defects contraindicated. Post-tuberculous lung disease and a post-capillary component must nevertheless be excluded by right heart catheterisation and targeted investigations.

Conclusion: A small interatrial communication in an adolescent with severe PAH and right heart failure should be interpreted as a potential “paradoxical protector” and managed as idiopathic PAH with risk-guided targeted therapy, correction of electrolyte and iron disturbances, and referral to a pulmonary hypertension centre. Closure should be avoided.

Keywords: Patent foramen ovale; Pulmonary arterial hypertension; Right heart failure; Adolescent; Interatrial shunt

INTRODUCTION

Background

Pulmonary hypertension (PH) is currently defined haemodynamically as a mean pulmonary arterial pressure (mPAP) >20 mmHg at rest measured by right heart catheterisation (RHC). Pre-capillary PH is characterised by a pulmonary arterial wedge pressure (PAWP) ≤ 15 mmHg and a pulmonary vascular resistance (PVR) >2 Wood units (WU). The clinical classification retains five groups: pulmonary arterial hypertension (PAH, group 1), PH associated with left heart disease (group 2), PH associated with lung disease and/or hypoxia (group 3), PH associated with pulmonary artery obstruction (group 4), and PH with unclear or multifactorial mechanisms (group 5). PAH is a progressive pulmonary vasculopathy in which the adaptive capacity of the right ventricle (RV), rather than the absolute level of pulmonary pressure, is the principal determinant of symptoms and survival.¹⁻³

In the paediatric and adolescent population, the aetiological spectrum differs from that of adults. Idiopathic PAH (IPAH) and PAH associated with congenital heart disease (PAH-CHD) predominate within group 1, whereas developmental lung disorders dominate group 3. The paediatric task force of the 7th World Symposium on Pulmonary Hypertension (WSPH) has emphasised that the classification of PAH-CHD must extend beyond the simple presence of a shunt, and that the role of atrial septal defects in paediatric PH should be reconsidered. Diagnosis in children and adolescents still relies on invasive haemodynamics performed in expert centres, while management is largely extrapolated from adult trials because of the paucity of paediatric randomised evidence.⁴⁻⁷

In low- and middle-income countries such as Indonesia, the burden of PH is compounded by delayed recognition of congenital heart disease, limited access to RHC and targeted therapies, and a high burden of infectious diseases. In the Indonesian COngenital HeART Disease in adult and Pulmonary Hypertension (COHARD-PH) registry, secundum atrial septal defect (ASD) accounted for 73.4% of adult congenital lesions, 77.1% of patients already had echocardiographic signs of PH,

and 66.9% had PAH confirmed by RHC. Tuberculosis adds a further, under-recognised dimension: a recent meta-analysis estimated the prevalence of PH at 42.4% among hospitalised or symptomatic post-tuberculosis patients and 9.4% among patients with active tuberculosis.^{8,9}

The foramen ovale is an essential component of the fetal circulation. After birth, the rise in left atrial pressure apposes the flap of the septum primum against the septum secundum. Fusion is incomplete in a substantial proportion of individuals: in a landmark autopsy study of 965 normal hearts, a patent foramen ovale (PFO) was present in 27.3%, with a maximal potential diameter of 1–19 mm (mean 4.9 mm). A PFO is therefore regarded as a normal anatomical variant rather than a structural defect. It remains functionally closed as long as left atrial pressure exceeds right atrial pressure, but it can be pushed open whenever right atrial pressure rises. This behaviour differs fundamentally from that of a secundum ASD, which is a true deficiency of septal tissue.^{10–13}

Paradoxically, in patients with severe PH an interatrial communication may be beneficial. Early observations linked patency of the foramen ovale with longer survival in primary pulmonary hypertension, and these observations provided the physiological rationale for therapeutic atrial septostomy. Similarly, adults with Eisenmenger syndrome have a more favourable haemodynamic profile and prognosis than adults with idiopathic disease of comparable severity. Contemporary cohorts, however, have not demonstrated an independent survival advantage associated with PFO in PH. They have instead shown that PFOs are detected more frequently in patients with dilated and dysfunctional right ventricles, which suggests that the foramen is stretched open by the disease rather than being congenitally patent.^{14–20}

This duality creates a recurring clinical dilemma. A small interatrial communication discovered in a young patient with severe PH is readily labelled as the causative congenital lesion, which may prompt referral for device closure. Current European guidelines, however, categorise PAH with small or coincidental defects as a distinct subgroup that behaves like IPAH, in which closure is contraindicated. Registry data also show that patients with small defects or previously corrected defects have the poorest survival among PAH-CHD subgroups.^{1,21–23}

Research Gap

Several gaps in knowledge justify the present report. First, available evidence on PFO in PH derives almost exclusively from retrospective or small prospective adult cohorts, which yielded conflicting conclusions on survival and did not address adolescents. Second, randomised data on the haemodynamic value of interatrial communications are lacking; the supporting evidence comes from uncontrolled septostomy series and meta-analyses of such series. Third, paediatric guidance on small interatrial defects in severe PH relies predominantly on expert consensus, and the applicability of adult PVR thresholds to adolescents remains debated. Fourth, the interplay between prior tuberculosis, chronic undernutrition and PAH in adolescents from tuberculosis-endemic, resource-limited settings, where RHC is frequently unavailable at presentation, has rarely been described. Finally, few published case reports explicitly model the bedside reasoning required to classify an interatrial shunt as a consequence rather than a cause, or to justify withholding closure.^{6,8,9,19,20,24}

Objectives

The **general objective** of this report is to describe, in a structured manner consistent with the CARE guidelines, the clinical presentation, diagnostic evaluation and management of an adolescent with severe PH, right heart failure and a small interatrial communication at the fossa ovalis. The **specific objectives** are: (i) to correlate the history, physical examination, laboratory, electrocardiographic, radiological and echocardiographic findings with their underlying pathophysiology; (ii) to explain the mechanism by which a stretched PFO may act as a “rescuer” in severe PH; (iii) to argue, on anatomical, haemodynamic and clinical grounds, that the PFO is a coincidental or consequential finding rather than causative congenital heart disease; (iv) to justify the provisional classification as group 1 PH while delineating the investigations needed to exclude groups 2–4; (v) to appraise the rationale and evidence base for each therapeutic agent administered; and (vi) to review the indications and contraindications for PFO closure and to explain why closure is contraindicated in this patient.^{1,25}

Benefits of the Report

From a **clinical** perspective, this report offers a practical framework that helps cardiologists, paediatricians, internists and emergency physicians avoid the potentially fatal error of closing a decompressing interatrial communication, and it highlights frequently overlooked, correctable contributors to decompensation such as severe hypokalaemia in patients receiving digoxin and loop diuretics, iron deficiency and infection. From an **academic** perspective, it integrates classical physiological observations with contemporary guidelines and registry data into a coherent teaching model for residents. From a **health-system** perspective, it underlines the need for timely referral pathways to PH centres, access to RHC and targeted therapies, and structured cardiopulmonary follow-up of tuberculosis survivors in endemic regions.^{5,8,9}

Working Hypothesis

We hypothesised that, in this adolescent, the small interatrial communication at the fossa ovalis is a stretched PFO that opened secondary to right atrial hypertension caused by severe pre-capillary pulmonary vascular disease. We further hypothesised that it acts as a partial decompression pathway, supporting left ventricular preload and systemic cardiac output at the cost of arterial desaturation, rather than being the cause of the pulmonary vascular disease, and consequently that its closure would be haemodynamically deleterious. Because a single case cannot test a hypothesis statistically, it is explored descriptively by confronting each clinical and investigational finding with the published physiological and clinical evidence.^{1,20,24}

Novelty

The novelty of this report lies in four aspects. It describes the “paradoxical protector” phenomenon in an adolescent rather than an adult. It occurs against a background of recently treated tuberculosis, severe chronic undernutrition and an Indonesian resource-limited setting. It explicitly reconciles the apparently contradictory evidence on PFO in PH (a mechanistic haemodynamic benefit versus a neutral effect on survival) and translates it into an actionable algorithm on whether an interatrial communication should be closed. Finally, it provides a transparent critical appraisal of the diagnostic and therapeutic gaps encountered in real-world practice, including the absence of haemodynamic confirmation. To our knowledge, comparable published cases have described PFO

reopening in adults with IPAH, but reports in adolescents from tuberculosis-endemic regions are scarce.^{6,9,25,26}

CASE REPORT

Patient Information and Presenting Complaint

A 17-year-old female adolescent was brought by her parents to the emergency department with shortness of breath that had progressed over one month and worsened markedly during the 24 hours before admission. Over the same month, she and her parents had noticed progressive abdominal enlargement and bilateral leg swelling. Fever, cough and weight loss were also reported. Please document: exertional versus resting dyspnoea, orthopnoea, paroxysmal nocturnal dyspnoea, syncope or presyncope, chest pain, haemoptysis, palpitations, menstrual history, exposure to anorexigens, stimulants or other drugs, and symptoms suggestive of connective tissue disease; these items are required for aetiological classification and risk stratification.^{4,25}

Pulmonary tuberculosis was diagnosed in November 2024, and the patient completed anti-tuberculosis therapy in May 2025. Specify the site of tuberculosis, diagnostic modality (sputum smear, Xpert MTB/RIF, culture or radiology), regimen, adherence, treatment outcome and HIV status. There was no family history of a similar illness, congenital heart disease or congenital anomalies. According to the mother, the patient had suffered frequent episodes of cough and fever since childhood, and her weight had never been appropriate for her age compared with her peers.^{9,25}

Regarding the perinatal history, the mother did not attend antenatal care regularly but reported no complaints during pregnancy. The patient was born by spontaneous vaginal delivery at 38–39 weeks of gestation, assisted by a midwife. She cried immediately after birth and was not cyanotic. Birth weight was 2,800 g, and birth length was recorded as 40 cm this value is implausibly short for a term neonate weighing 2,800 g; please verify. Her immunisation history was complete. The absence of neonatal cyanosis argues against a cyanotic congenital heart lesion or persistent pulmonary hypertension of the newborn.^{12,25}

Clinical Findings

On admission, her body weight was 30 kg, height 140 cm and body mass index 15.3 kg/m², with an overtly cachectic habitus (Figure 1A). For a 17-year-old girl, both height-for-age and BMI-

853

for-age fall below -2 standard deviations of the WHO 2007 growth reference, consistent with chronic undernutrition with stunting and thinness. Blood pressure was 110/71 mmHg, heart rate 105 beats/min, respiratory rate 26 breaths/min, and peripheral oxygen saturation 89% on room air. Add body temperature, jugular venous pressure, hepatojugular reflux and the presence or absence of digital clubbing.^{27,28}

Examination of the head and neck revealed normocephaly, black hair that was not dry or brittle, and pale conjunctivae; nasal flaring was absent and there was no nasal discharge. Central cyanosis of the lips and oral mucosa was evident. No peripheral lymphadenopathy was detected. On thoracic examination, inspection and palpation were unremarkable; percussion revealed minimal dullness over both lung bases, and auscultation revealed rales in both lung fields. The cardiac borders were enlarged. A grade 4/6 systolic murmur was audible at the fourth intercostal space along the left parasternal line, and the second heart sound was widely and fixedly split.^{1,28}

The abdomen was distended with normal bowel sounds. No organomegaly was palpable, although tense ascites may conceal hepatomegaly. Percussion was dull, with shifting dullness and a positive fluid wave indicating ascites. Both lower extremities showed pitting oedema (Figure 1B).²⁸



Figure 1. Clinical photographs. **(A)** General appearance showing marked cachexia and a thin habitus consistent with chronic undernutrition; the eye region is masked for de-identification. **(B)**

Bilateral lower-limb oedema with shiny, tense skin, consistent with systemic venous congestion from right heart failure compounded by hypoalbuminaemia.

Timeline

The chronology of relevant events is summarised in Figure 2. The interval between completion of anti-tuberculosis therapy and the onset of overt right heart failure was approximately two months.²⁵



*Month inferred from the date stamp of the transthoracic echocardiogram; exact admission date to be confirmed from the medical record.

Figure 2. Timeline of the clinical course, from childhood through tuberculosis diagnosis and treatment to presentation with right heart failure. The admission month is inferred from the echocardiographic date stamp **confirm exact admission date**. PDE5i, phosphodiesterase-5 inhibitor; TB, tuberculosis; TTE, transthoracic echocardiography.

Diagnostic Assessment

Laboratory investigations. The complete blood count showed mild microcytic hypochromic anaemia with a relatively preserved red cell count (Mentzer index MCV/RBC = 15.2), together with hyponatraemia, severe hypokalaemia, hypochloraemia, hypoalbuminaemia and a mild isolated elevation of aspartate aminotransferase. Renal function was preserved (Table 1). N-terminal pro-B-type natriuretic peptide (NT-proBNP), arterial blood gas analysis, iron indices, thyroid function, HIV serology, antinuclear antibodies and liver ultrasonography were not available **add if performed**.^{1,28}

Table 1. Laboratory findings on admission and their clinical interpretation

Parameter	Result	Reference range	Unit	Interpretation

Haemoglobin	11.7	12.0–16.0	g/dL	Mild anaemia; inappropriately low for a hypoxaemic patient
Haematocrit	39.7	35.3–51.2	%	Within range
Leucocytes	5,470	4,400–13,000	/μL	Within range
Lymphocytes	26.4	13–40	%	Within range
Monocytes	13.2	2–11	%	Monocytosis (infection or post-tuberculous inflammation)
Platelets	303,000	140,000– 440,000	/μL	Within range
Erythrocytes	5.11	4.0–5.2	×10 ⁶ /μL	High-normal count with microcytosis
MCV	77.6	80–100	fL	Microcytosis; Mentzer index 15.2 favours iron deficiency
MCH	23	26–34	pg	Hypochromia
MCHC	29.6	31–36	g/dL	Hypochromia (recorded as g% in source)
Erythrocyte sedimentation rate	17	verify; recorded as 2– 3	mm/h	Mildly elevated or upper normal
Sodium	128	136–145	mmol/L	Hyponatraemia: dilutional or diuretic- related; adverse prognostic marker
Potassium	2.6	3.5–5.1	mmol/L	Severe hypokalaemia:

				arrhythmic risk, potentiates digoxin toxicity
Chloride	79	98–107	mmol/L	Hypochloraemia (loop diuretic, contraction alkalosis)
Albumin	3.27	3.5–5.2	g/dL	Hypoalbuminaemia (undernutrition, congestion, inflammation); unit recorded as mg/dL
Urea	34.96	0.0–50.0	mg/dL	Within range
Creatinine	0.66	0.51–0.95	mg/dL	Preserved renal function
AST (SGOT)	35.8	0–32	U/L	Mild elevation, compatible with congestive hepatopathy
ALT (SGPT)	13.8	0–33	U/L	Within range

Bold values lie outside the reference range. AST, aspartate aminotransferase; ALT, alanine aminotransferase; MCH, mean corpuscular haemoglobin; MCHC, mean corpuscular haemoglobin concentration; MCV, mean corpuscular volume.

Chest radiography and computed tomography. The anteroposterior chest radiograph showed cardiomegaly with pulmonary congestion, bilateral pleural effusions and parenchymal opacities interpreted as pneumonia (Figure 3A). Cardiac size is overestimated on anteroposterior projection and should be interpreted with caution. Sagittal reformats of abdominal computed tomography confirmed a considerable volume of ascites (Figure 3B).^{1,28}

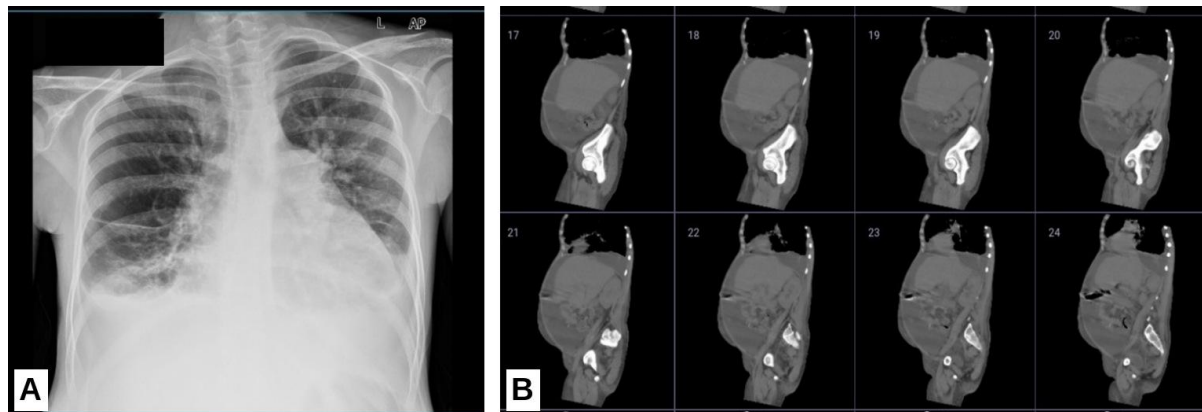


Figure 3. (A) Anteroposterior chest radiograph showing cardiomegaly, pulmonary congestion, bilateral pleural effusions (predominantly at the right base) and parenchymal opacities consistent with pneumonia; the patient identifier has been masked. **(B)** Sagittal computed tomography reformats of the abdomen demonstrating ascites.

Electrocardiography. The 12-lead electrocardiogram showed sinus tachycardia, right atrial enlargement and right ventricular hypertrophy with a right ventricular strain pattern, as reported by the attending cardiologist. The tracing also shows a predominantly negative QRS complex in lead I with a positive complex in lead III, consistent with right-axis deviation, a dominant R wave in V1, and repolarisation abnormalities in the right precordial leads (Figure 4).^{1,14}

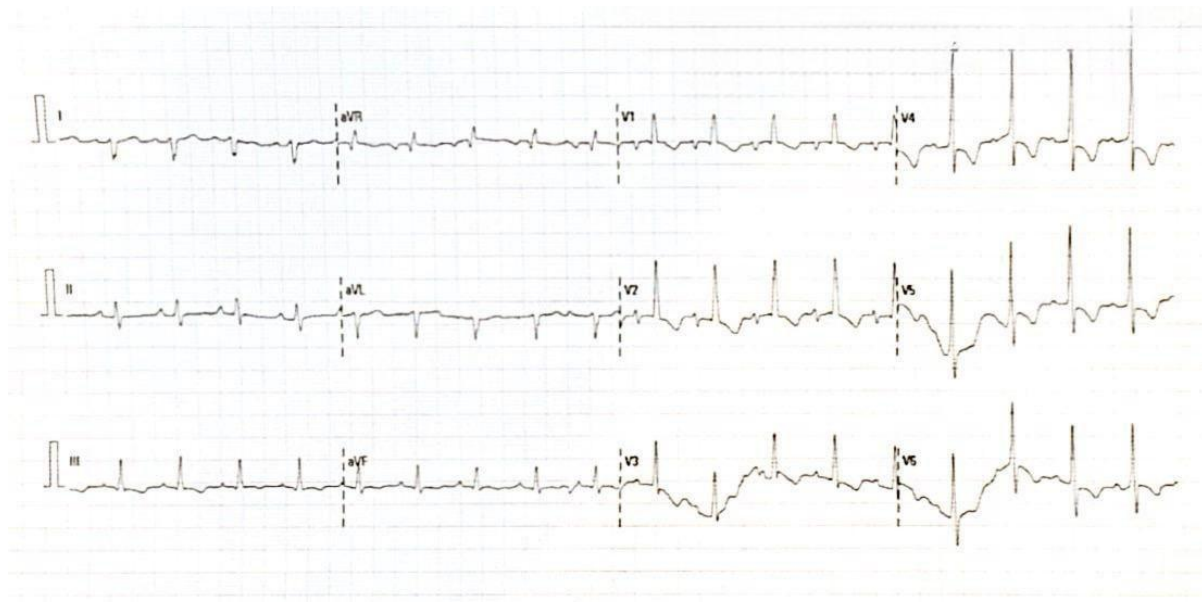


Figure 4. Twelve-lead electrocardiogram showing sinus tachycardia, right atrial enlargement, right-axis deviation and right ventricular hypertrophy with a strain pattern (dominant R wave in V1 with right precordial repolarisation abnormalities). The rhythm strip carrying a scanning watermark has been cropped.

Transthoracic echocardiography. Both the right atrium and right ventricle were dilated, and the left ventricle was small. Left ventricular systolic function was preserved (ejection fraction 67%), with normokinetic wall motion. Left ventricular diastolic function was reported as grade II dysfunction with elevated left atrial pressure. Tricuspid annular plane systolic excursion (TAPSE) was 17 mm, and RV contractility was described as good. There was severe tricuspid regurgitation with a peak systolic tricuspid valve gradient of 46 mmHg, and the main pulmonary artery was dilated. A small interatrial communication was demonstrated: the written report described a small secundum ASD of 0.5–0.7 cm with predominantly left-to-right flow, whereas the stored two-dimensional image labels the defect as a PFO measuring 3.9–4.2 mm (Figure 5) **reconcile defect type, size and shunt direction; agitated-saline contrast or transoesophageal echocardiography is recommended.** ^{1,29,30}

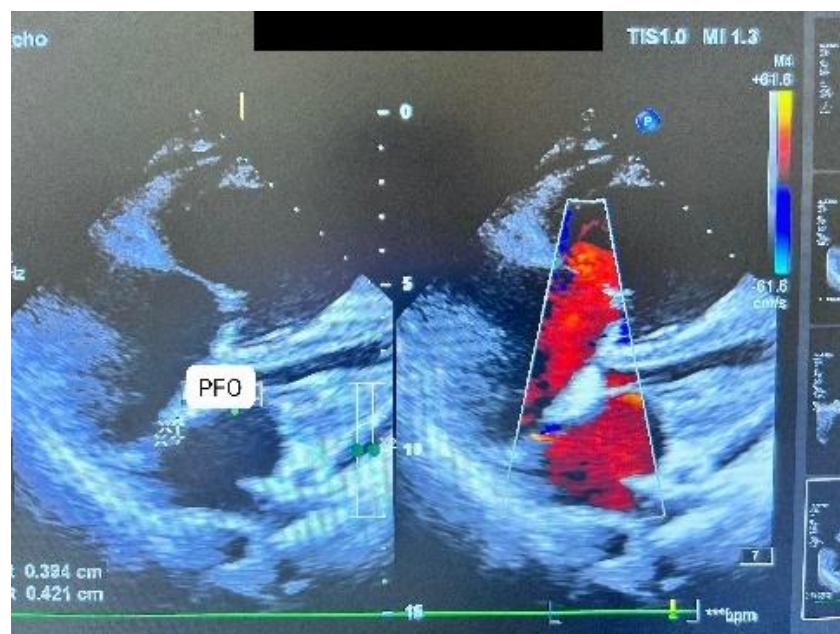


Figure 5. Transthoracic echocardiography, subcostal view. Left panel: two-dimensional image showing a small interatrial communication at the fossa ovalis (labelled “PFO”; calliper measurements 3.9 and 4.2 mm). Right panel: colour Doppler flow across the interatrial septum. The date stamp has been masked.

Table 2. Echocardiographic findings, derived indices and guideline-based interpretation

Parameter	Finding in this patient	Interpretation and reference thresholds
Right atrium	Dilated	Echocardiographic PH sign, category C (IVC/right atrium); RA area >18 cm ² supports PH RA area not measured
Right ventricle / left ventricle	RV dilated; LV small	Category A sign (RV/LV basal diameter ratio >1.0); LV underfilling due to reduced pulmonary venous return and septal shift (ventricular interdependence)

LV systolic function	EF 67%; normokinetic	Preserved; argues against LV systolic dysfunction as a cause of PH
LV diastolic function	Grade II dysfunction, raised LAP	May reflect LV underfilling and septal displacement rather than intrinsic LV disease; a post-capillary component cannot be excluded without PAWP measurement
TAPSE	17 mm	Below the conventional 18 mm threshold for reduced RV longitudinal function
Tricuspid regurgitation	Severe; peak gradient 46 mmHg	Peak TR velocity $\approx \sqrt{(46/4)} \approx 3.39$ m/s (range 2.9–3.4 m/s); with signs from ≥ 2 categories this gives a high echocardiographic probability of PH . Severe laminar TR may underestimate the true gradient
Estimated sPAP	46 mmHg + RAP	≈ 49 mmHg (RAP 3), ≈ 54 mmHg (RAP 8) or ≈ 61 mmHg (RAP 15) IVC diameter and collapsibility not reported
TAPSE/sPAP ratio	≈ 0.28 – 0.35 mm/mmHg (derived)	< 0.55 supports PH; < 0.31 suggests RV–PA uncoupling (Tello et al.); ESC/ERS risk thresholds: > 0.32 low, 0.19 – 0.32 intermediate, < 0.19 high
Main pulmonary artery	Dilated	Category B sign (PA diameter > 25 mm or larger than aortic root)
Interatrial septum	Small defect at fossa ovalis (3.9–4.2 mm on	Consistent with a stretched PFO or small secundum ASD; defect size is

	image; 5–7 mm in report)	disproportionate to the degree of pulmonary vascular disease
Not reported	—	Pericardial effusion, RA area, LV eccentricity index, RVOT acceleration time/notching, pulmonary regurgitation velocity, RV fractional area change, agitated-saline study

EF, ejection fraction; IVC, inferior vena cava; LAP, left atrial pressure; PA, pulmonary artery; PAWP, pulmonary arterial wedge pressure; RAP, right atrial pressure; RVOT, right ventricular outflow tract; sPAP, systolic pulmonary arterial pressure; TR, tricuspid regurgitation.^{1,29–31}

Diagnosis

The working diagnosis recorded by the attending team was: small secundum ASD with bidirectional shunt; severe tricuspid regurgitation with a high echocardiographic probability of PH; PH attributed to group 1, either idiopathic PAH or PAH associated with the interatrial defect; and right heart failure with ascites and pleural effusions. Community-acquired pneumonia, microcytic hypochromic anaemia, hyponatraemia, severe hypokalaemia, hypoalbuminaemia and chronic undernutrition were recorded as comorbid conditions. Following the WSPH and ESC/ERS frameworks, we reformulated the diagnosis as: **severe pre-capillary PH, provisionally group 1 (IPAH with a coincidental stretched PFO or PAH with a small coincidental interatrial defect), WHO functional class IV, with decompensated right heart failure**, pending haemodynamic confirmation. The differential diagnosis across the PH groups, and the investigations needed to resolve it, are presented in Table 3.^{1,2}

Table 3. Differential diagnosis according to the clinical classification of pulmonary hypertension

PH group / entity	Supporting features in this patient	Against / unresolved	Investigations required
Group 1: IPAH (or heritable	Young female; severe PH with RV failure;	RHC not performed; heritable, drug-,	RHC with vasoreactivity testing

PAH) with coincidental PFO	small defect disproportionate to PH; preserved LVEF	CTD-, HIV- and portal hypertension- associated PAH not excluded	once stable; HIV, ANA/ENA, liver ultrasound; genetic counselling
Group 1: PAH with small/coincidental defect	Interatrial communication present; clinical profile similar to IPAH	Defect too small to generate the observed PVR	TOE or agitated- saline study; Qp:Qs and shunt direction at RHC
Group 1: shunt- driven PAH-CHD / Eisenmenger	Cyanosis; interatrial flow	Small defect; no neonatal cyanosis; flow predominantly left-to-right on colour Doppler	As above; defect sizing and PVR
Group 2: left heart disease	Grade II LV diastolic dysfunction with raised LAP reported	Small, underfilled LV; normal LVEF; young age; no reported left atrial dilatation	PAWP/LVEDP at RHC; left atrial volume index
Group 3: post- tuberculosis lung disease / hypoxia	Tuberculosis 2024– 2025; pneumonia; hypoxaemia; recurrent childhood respiratory infections	Extent of parenchymal destruction unknown	HRCT; spirometry and DLCO; arterial blood gas; exclusion of TB relapse
Group 4: chronic thromboembolic PH	Chronic dyspnoea; reduced mobility	No documented venous thromboembolism	Ventilation/perfusion scintigraphy; CT pulmonary

			angiography if abnormal
Group 5 and mimics	Chronic haematological disorder possible (microcytosis); prior tuberculosis	Mentzer index favours iron deficiency; no pericardial findings reported	Iron studies ± haemoglobin analysis; assessment for tuberculous constrictive pericarditis

ANA/ENA, antinuclear/extractable nuclear antibodies; CTD, connective tissue disease; DLCO, diffusing capacity for carbon monoxide; HRCT, high-resolution computed tomography; IPAH, idiopathic PAH; LVEDP, left ventricular end-diastolic pressure; Qp:Qs, pulmonary-to-systemic flow ratio; TOE, transoesophageal echocardiography.^{1,2,6,9}

Therapeutic Intervention

The patient was admitted and treated medically. The regimen recorded in the medical file is shown in Table 4. Thoracocentesis and paracentesis were not performed, because the attending team judged the effusions and ascites to be manageable with diuretic therapy. No catheter-based or surgical septal intervention was undertaken. Document oxygen therapy (device, flow, target SpO₂), potassium replacement, fluid balance, daily weight and serum digoxin concentration, if available.^{1,28}

Table 4. Pharmacological regimen administered during hospitalisation (as recorded)

Agent	Regimen as recorded	Therapeutic target
Ringer's lactate (IV)	4 microdrops/min (keep-vein-open rate)	Vascular access with minimal volume load
Ceftriaxone (IV)	1 g every 12 h	Community-acquired pneumonia
Omeprazole (IV)	1 ampoule every 12 h	Gastric protection in acute illness with congestive gastropathy
Furosemide (IV)	40 mg every 6 h (160 mg/day ≈5.3	Relief of systemic venous congestion, effusions and ascites

	mg/kg/day)	
Spironolactone (oral)	50 mg once daily	Mineralocorticoid receptor antagonism; potassium sparing
Digoxin (oral)	1 tablet once daily specify strength	Modest inotropic support and heart-rate control in RV failure
Sildenafil (oral)	20 mg three times daily	PDE5 inhibition: pulmonary vasodilatation and antiproliferative effect
Beraprost sodium (oral)	Recorded as 0.2 µg twice daily verify: commercially available tablet is 20 µg	Oral prostacyclin analogue: IP-receptor-mediated vasodilatation
Cavicur® (oral)	1 tablet once daily	<i>Curcuma xanthorrhiza</i> (temulawak) extract; appetite stimulant/nutritional adjunct
Oral “albumin” supplement	1 tablet three times daily specify product	Nutritional protein supplementation for hypoalbuminaemia

IV, intravenous; PDE5, phosphodiesterase type 5. The rationale and evidence base for each agent are discussed in Section 3.8 and Table 7.^{1,32,33}

Follow-up and Outcomes

To be completed by the authors: length of hospital stay; changes in SpO₂, heart rate, respiratory rate, body weight, abdominal girth and oedema; serial electrolytes and renal function after correction; clinical response to pneumonia treatment; discharge WHO functional class; discharge medications and doses; referral to a pulmonary hypertension centre; RHC results if obtained; follow-up echocardiography including TAPSE/sPAP; six-minute walk distance; NT-proBNP; adverse drug events; readmissions; and status at the latest follow-up (with date). These data are required for a complete CARE-compliant report and for ESC/ERS follow-up risk assessment.^{1,25}

Patient and Family Perspective

Optional but recommended by CARE: a brief statement from the patient or her parents describing the illness experience, understanding of the diagnosis, and preferences regarding treatment and follow-up.²⁵

DISCUSSION

This case illustrates a clinically important paradox. In an adolescent with severe pre-capillary PH and decompensated right heart failure, echocardiography identified a small interatrial communication that could easily have been regarded as the culprit congenital lesion and a target for closure. Our analysis indicates the opposite: the communication is best understood as a stretched PFO, a consequence of right atrial hypertension that provides partial haemodynamic decompression. It is not causative congenital heart disease, and its closure would be contraindicated. The discussion first correlates the history, physical examination and investigations with established theory. It then explains the pathophysiology of the “rescuer” PFO, argues for its consequential nature and for group 1 classification, appraises the rationale for each therapeutic agent, and finally addresses the indications and contraindications for PFO closure.^{1,20,24}

Interpretation of the History

The triad of progressive dyspnoea, abdominal distension and bilateral leg oedema reflects the clinical syndrome of right heart failure. When RV systolic function can no longer match its afterload, cardiac output falls and right-sided filling pressures rise. The result is systemic venous congestion, manifested as hepatic and splanchnic congestion, ascites and peripheral oedema, together with exertional intolerance from a limited ability to augment cardiac output. Dyspnoea at rest with signs of right heart failure places the patient in WHO functional class IV, a high-risk feature at diagnosis.^{1,3,28}

Fever, cough and weight loss have several overlapping explanations. Community-acquired pneumonia was documented radiologically and is a well-recognised precipitant of decompensation in PAH. Chronic right heart failure itself produces cachexia through intestinal congestion, malabsorption, anorexia and a systemic pro-inflammatory state. In a patient who completed tuberculosis treatment only months before presentation, relapse and post-tuberculous lung disease

866

must also be considered, particularly because PH is frequent among symptomatic tuberculosis survivors.^{1,9,28}

The maternal report of recurrent respiratory infections and failure to thrive since childhood merits careful interpretation. Recurrent chest infections and poor weight gain are classical features of a large left-to-right shunt, which would favour a haemodynamically significant ASD. However, the small defect demonstrated on imaging cannot sustain a pulmonary blood flow sufficient to explain either those childhood features or the current severity of pulmonary vascular disease. Chronic undernutrition, recurrent infections and tuberculosis in a socioeconomically disadvantaged setting provide a more parsimonious explanation. In paediatric PAH, early symptoms are non-specific, and diagnostic delay of years is common, as reflected in Indonesian registry data showing that most adults with CHD already have PH at first evaluation.^{4,8,27}

The perinatal history, with a term delivery, immediate crying and no cyanosis, argues against cyanotic congenital heart disease and against clinically significant persistent pulmonary hypertension of the newborn. It also supports the concept that the foramen ovale was functionally closed after birth and reopened only later, when right atrial pressure rose. Female predominance is characteristic of IPAH in adolescents and adults, and the negative family history does not exclude heritable PAH because of incomplete penetrance.^{1,6,12}

Physical Examination: Findings and Their Theoretical Basis

Each physical sign in this patient has a coherent pathophysiological explanation (Table 5). Central cyanosis with SpO₂ of 89% is multifactorial. It results from right-to-left shunting across the interatrial communication whenever right atrial pressure exceeds left atrial pressure; from ventilation–perfusion mismatch caused by pneumonia and pleural effusions; and from a low mixed venous oxygen content secondary to reduced cardiac output. In a cohort of patients with IPAH, the presence of a PFO was associated with a higher prevalence of severe hypoxaemia, and deliberate atrial septostomy lowers arterial oxygen saturation by approximately 8 percentage points. Both observations underline the direct link between an open interatrial pathway and desaturation.^{1,19,24}

The grade 4/6 systolic murmur at the fourth left parasternal intercostal space is most consistent with functional tricuspid regurgitation secondary to annular dilatation. Such a murmur

typically increases with inspiration (Carvallo sign), which should be sought at the bedside. By contrast, the flow murmur of an ASD is a soft ejection murmur at the upper left sternal border and would not reach grade 4. Fixed splitting of S2 is classically attributed to an ASD, because the interatrial communication equalises respiratory variations in RV and left ventricular filling. In severe PH, however, the pulmonary component of S2 is accentuated. Splitting may also become wide and relatively fixed when RV ejection is prolonged by RV failure or right bundle branch block and RV stroke volume can no longer vary with respiration. Fixed splitting therefore does not in itself establish a haemodynamically significant shunt.^{1,28,29}

Enlarged cardiac borders reflect right atrial and RV dilatation. Bibasal dullness with rales indicates pleural effusions and pneumonia. Pleural effusions in PAH are generally modest and arise when elevated systemic venous pressure impairs lymphatic drainage of the pleural space. Ascites, shifting dullness and pitting oedema are cardinal signs of systemic venous congestion, aggravated by hypoalbuminaemia. Conjunctival pallor corresponds to the measured anaemia, which is relevant because a haemoglobin of 11.7 g/dL is inappropriately low in a hypoxaemic patient who would be expected to develop compensatory erythrocytosis. Finally, the cachectic habitus reflects both chronic undernutrition and cardiac cachexia.^{27,28,34}

Table 5. Correlation of physical findings with pathophysiology and clinical significance

Finding	Pathophysiological basis	Clinical significance
Central cyanosis; SpO ₂ 89%	Right-to-left interatrial shunt; V/Q mismatch (pneumonia, effusions); low mixed venous O ₂ from low cardiac output	Marker of disease severity; guides oxygen therapy; supports an open, decompressing interatrial pathway
Tachycardia (105/min), tachypnoea (26/min)	Compensation for fixed, low stroke volume; hypoxaemia; infection	Respiratory rate >20/min is associated with adverse outcome in hospitalised PAH with RV failure

Grade 4/6 systolic murmur, 4th left ICS	Functional TR due to RV dilatation and tricuspid annular enlargement	Severe TR worsens venous congestion and may underestimate the Doppler-derived sPAP
Wide, fixed splitting of S2	Interatrial communication equalising respiratory filling; prolonged RV ejection in RV failure	Not specific for a significant ASD in the setting of severe PH
Cardiomegaly on percussion	RA and RV dilatation (heterometric adaptation)	Indicates advanced, maladaptive RV remodelling
Bibasal dullness, rales	Pleural effusions from raised systemic venous pressure; pneumonia	Requires treatment of infection and decongestion
Ascites, shifting dullness, pitting oedema	Systemic venous congestion; hypoalbuminaemia	Signs of RV failure: high-risk criterion
Conjunctival pallor	Iron-deficiency anaemia or anaemia of chronic inflammation	Anaemia reduces O ₂ delivery; iron status should be corrected
Cachexia; height and BMI below –2 SD	Chronic undernutrition; cardiac cachexia (gut congestion, inflammation)	Impaired drug response, infection risk; needs nutritional rehabilitation

ICS, intercostal space; SD, standard deviation; V/Q, ventilation/perfusion.^{19,27,28,35}

Laboratory Findings in the Context of Right Heart Failure

The microcytic hypochromic indices with a relatively high red cell count (Mentzer index 15.2, above the threshold of 13) favour iron deficiency over thalassaemia trait, although iron studies are needed for confirmation. Iron deficiency is present in 43% of patients with IPAH, irrespective

of anaemia, and is associated with reduced exercise capacity. Elevated soluble transferrin receptor, found in 63% of patients with IPAH in another cohort, independently predicted survival. Hepcidin was inappropriately raised, which may limit oral iron absorption. Current guidelines recommend regular assessment of iron status and correction of iron deficiency in patients with PAH.^{1,34,36}

Hyponatraemia (128 mmol/L) is both a mechanistic and a prognostic marker. It results from non-osmotic vasopressin release in response to reduced effective arterial volume, neurohormonal activation, and treatment with loop diuretics. In a prospective PAH cohort, patients with serum sodium ≤ 136 mEq/L had higher right atrial pressure, lower stroke volume index, larger RV/LV area ratio and lower TAPSE, and their unadjusted risk of death was ten-fold higher. Among patients hospitalised for acute right heart failure in PAH, hyponatraemia independently predicted death or urgent transplantation.^{35,37}

Severe hypokalaemia (2.6 mmol/L) with hypochloraemia is most plausibly caused by intensive loop-diuretic therapy, secondary hyperaldosteronism from reduced renal perfusion, and poor oral intake. This abnormality is clinically dangerous: it predisposes to ventricular and atrial arrhythmias, which are poorly tolerated by a failing RV, and it potentiates digoxin toxicity. Prompt potassium replacement with close monitoring of electrolytes and, ideally, serum digoxin concentration is mandatory before and during digoxin therapy, and spironolactone offers additional potassium-sparing benefit.^{1,28}

Hypoalbuminaemia reflects the combined effects of undernutrition, inflammation and congestive enteropathy. It lowers plasma oncotic pressure, which favours oedema and effusions, and reduces the delivery of protein-bound loop diuretics to the renal tubule, contributing to diuretic resistance. The mildly elevated aspartate aminotransferase with normal alanine aminotransferase is compatible with congestive hepatopathy. Monocytosis and a modestly raised erythrocyte sedimentation rate are non-specific but warrant exclusion of tuberculosis relapse. Measurement of NT-proBNP, which is a core variable in ESC/ERS risk stratification, together with arterial blood gases, uric acid, thyroid function, HIV serology and autoimmune serology, would have strengthened the diagnostic and prognostic assessment.^{1,9,28}

Electrocardiographic, Radiological and Echocardiographic Correlates

Electrocardiography. Chronic RV pressure overload produces a characteristic constellation of right atrial enlargement (P-wave amplitude ≥ 2.5 mm in lead II), right-axis deviation, a dominant R wave in V1 (R/S >1), RV hypertrophy and a strain pattern with ST-segment depression and T-wave inversion in the right precordial and inferior leads. Sinus tachycardia reflects the dependence of cardiac output on heart rate when stroke volume is fixed. Although a normal ECG does not exclude PH, the presence of right-heart abnormalities increases the pre-test probability. In the early natural-history series of primary pulmonary hypertension, ECG evidence of right heart strain at presentation predicted survival of less than five years.^{1,14}

Chest radiography and computed tomography. Radiological signs of PH include cardiomegaly with RA and RV enlargement, a prominent pulmonary trunk and hilar arteries, and peripheral pruning. The reported pulmonary congestion is atypical for isolated pre-capillary PAH and may reflect pneumonia, the anteroposterior projection, or a coexisting post-capillary component, which again underlines the need for PAWP measurement. The pleural effusions and ascites are consistent with systemic venous congestion. Given the history of tuberculosis, high-resolution CT of the chest is indicated to quantify post-tuberculous parenchymal and airway sequelae.^{1,9,28}

Echocardiographic probability of PH. The ESC/ERS guidelines assign echocardiographic probability on the basis of peak tricuspid regurgitation velocity (TRV) combined with additional signs grouped into three categories: the ventricles, the pulmonary artery, and the inferior vena cava/right atrium. A TRV of 2.9–3.4 m/s accompanied by signs from at least two categories, or a TRV >3.4 m/s, confers a high probability. In this patient, the gradient of 46 mmHg corresponds to a TRV of approximately 3.39 m/s. Together with RV dilatation and a small LV (ventricular category), a dilated main pulmonary artery (pulmonary artery category) and right atrial dilatation (inferior vena cava/right atrium category), this establishes a high echocardiographic probability. The Doppler gradient may underestimate true systolic pulmonary pressure in severe, laminar tricuspid regurgitation, and decompression across the interatrial communication may further blunt

the gradient. The haemodynamic severity is therefore likely greater than the figure of 46 mmHg implies.^{1,29}

RV function and RV–pulmonary arterial coupling. TAPSE of 17 mm lies just below the conventional threshold of reduced longitudinal RV function. TAPSE interpreted in isolation, however, may appear “good” despite substantial afterload mismatch. The TAPSE/sPAP ratio is a validated non-invasive surrogate of RV–arterial coupling. In a pressure–volume loop study, a cut-off of 0.31 mm/mmHg discriminated RV–arterial uncoupling, and patients below this value had a worse prognosis. The 2022 ESC/ERS guidelines incorporated TAPSE/sPAP into risk stratification (>0.32 mm/mmHg low, 0.19 – 0.32 intermediate, <0.19 high risk). The derived ratio of approximately 0.28 – 0.35 mm/mmHg in this patient indicates impending or established uncoupling, which is concordant with the clinical signs of RV failure.^{1,29,30}

The small left ventricle and diastolic indices. RV pressure overload produces leftward septal displacement, pericardial constraint and reduced pulmonary venous return, all of which underfill the LV. The consequences are a small LV cavity, an impaired-relaxation pattern and altered Doppler indices of filling, in the absence of intrinsic myocardial disease. The reported grade II diastolic dysfunction with elevated left atrial pressure must therefore be interpreted cautiously. Algorithms for grading diastolic function were validated primarily in left-sided heart disease, and E/e' and mitral inflow patterns are confounded by ventricular interdependence. A normal-sized left atrium and preserved LVEF would argue against group 2 PH, but only direct PAWP measurement can exclude a post-capillary component.^{1,31,38}

Characterisation of the interatrial communication. The discordance between the written report (secundum ASD, 5–7 mm) and the stored image (labelled PFO, 3.9–4.2 mm) reflects a genuine diagnostic challenge in patients with RA dilatation. A PFO is a slit- or tunnel-like communication between the septum primum and septum secundum, without tissue deficiency. When the RA dilates, the septum secundum and the fossa ovalis are stretched, so that the flap no longer overlaps the limbus and a persistent gap with resting flow appears: the so-called “stretched” PFO. In a prospective series of 292 patients with PH, PFO was found in 22.9% of those with PAH and was more frequent with moderately or severely dilated and dysfunctional RVs, which led the

authors to conclude that such PFOs are stretched open rather than congenital. Transoesophageal echocardiography or agitated-saline contrast is recommended to define the anatomy, rims, size and shunt direction (Table 6).^{11,12,20,29}

Table 6. Differentiation of patent foramen ovale, stretched patent foramen ovale and secundum atrial septal defect

Feature	Patent foramen ovale	Stretched PFO (acquired incompetence)	Secundum ASD
Anatomical substrate	Failure of fusion of septum primum flap with septum secundum; no tissue deficiency	Anatomical PFO whose flap no longer overlaps because of RA and septal dilatation	True deficiency of septal tissue in the region of the fossa ovalis
Status as CHD	Normal variant ($\approx 25-27\%$ at autopsy)	Normal variant rendered patent by disease	Congenital heart defect
Morphology on TOE	Tunnel/flap valve; opens transiently when $RAP > LAP$ (e.g. Valsalva)	Displaced flap with persistent gap; resting flow	Round or oval hole with rims; no overlapping flap
Typical size	1–10 mm in 98% (mean 4.9 mm)	Usually a few millimetres; variable	Variable; defects too small to account for PVR elevation are classified as small/coincidental
Resting shunt	None, or transient right-to-left	Bidirectional or right-to-left when $RAP >$	Predominantly left-to-right with RV volume

		LAP	overload, unless PVR is markedly elevated
Role in PAH	Coincidental	Consequence; decompression pathway	Causal only if large with Qp:Qs >1.5 over years; otherwise coincidental
Closure in severe PAH	Contraindicated	Contraindicated	Contraindicated if small/coincidental or PVR ≥ 5 WU persisting despite therapy

ASD, atrial septal defect; CHD, congenital heart disease; LAP, left atrial pressure; PVR, pulmonary vascular resistance; RAP, right atrial pressure; TOE, transoesophageal echocardiography; WU, Wood units.^{1,10–12,20,21}

Pathophysiology: From Patent Foramen Ovale to “Rescuer”

In fetal life, the foramen ovale directs oxygenated umbilical venous blood from the inferior vena cava to the left atrium. At birth, pulmonary vascular resistance falls and left atrial pressure rises, pressing the flap of the septum primum against the septum secundum. Functional closure occurs within hours to days, and anatomical fusion usually follows during the first years of life. Where fusion remains incomplete, the channel persists as a potential communication that stays closed as long as the left-to-right atrial pressure gradient is maintained.^{10–12}

In PAH, progressive remodelling of the distal pulmonary arteries increases PVR and RV afterload. The RV initially adapts homeometrically by increasing contractility and wall thickness. Once this reserve is exhausted, it dilates (heterometric adaptation), RV–arterial coupling deteriorates, the tricuspid annulus enlarges and functional tricuspid regurgitation develops, and RV end-diastolic and right atrial pressures rise. The dilated right atrium stretches the interatrial septum. When right atrial pressure intermittently or persistently exceeds left atrial pressure, the flap valve is pushed open and a bidirectional or right-to-left shunt is established. Clinically, this stage coincides

874

with the appearance of central cyanosis and signs of systemic venous congestion, as observed in our patient (Figure 6).^{3,20,31,39}

The “rescuer” effect follows directly from this physiology. Right-to-left shunting (i) decompresses the right atrium and RV, lowering right-sided filling pressure and RV wall stress; (ii) bypasses the obstructed pulmonary vascular bed, supplementing left atrial and LV preload that would otherwise be limited by the reduced transpulmonary flow; and (iii) thereby sustains systemic cardiac output. Although arterial oxygen content falls, systemic oxygen delivery, the product of cardiac output and arterial oxygen content, may be maintained or even increased, particularly during exercise, when pulmonary vascular resistance cannot fall adequately. A meta-analysis of 16 balloon atrial septostomy studies (204 patients) showed that creating such a pathway lowered right atrial pressure by 2.77 mmHg and increased cardiac index by 0.62 L/min/m² and left atrial pressure by 1.86 mmHg, at the cost of an 8.45% fall in arterial oxygen saturation. Blade and graded balloon septostomy abolished syncope, improved symptoms of right heart failure and increased systemic oxygen transport in severe primary pulmonary hypertension, including in children and young adults.^{15,16,24,40,41}

The same principle helps explain why patients with Eisenmenger syndrome, whose RV is unloaded by a non-restrictive shunt, have lower right atrial pressures and higher cardiac indices than patients with idiopathic disease at similar or even higher pulmonary pressures, and why their actuarial non-transplant survival at three years was 77% compared with 35% in primary pulmonary hypertension. Their RV also retains a fetal-like, hypertrophied morphology rather than dilating. An illustrative adult case report described a marked fall in pulmonary arterial pressure and sustained clinical improvement after cough-induced reopening of a PFO in severe IPAH.^{17,26,42}

The protective effect, however, should not be overstated. Early natural-history series associated PFO with longer survival, but later studies found a PFO prevalence in PH similar to that of the general population and detected no difference in resting haemodynamics, exercise tolerance or estimated survival. Two further cohorts showed that PFO was associated with more severe hypoxaemia and had no effect on long-term survival in IPAH or PH overall. The benefit is therefore primarily haemodynamic and symptomatic, and its magnitude depends on defect size. A restrictive

communication of approximately 4 mm, as in our patient, provides only partial decompression, which is consistent with her persisting right heart failure. The price includes worsening hypoxaemia, particularly when pneumonia coexists, and a risk of paradoxical embolism. The epithet “paradoxical protector” captures precisely this balance of benefit and harm.^{14,18–20,24,43}

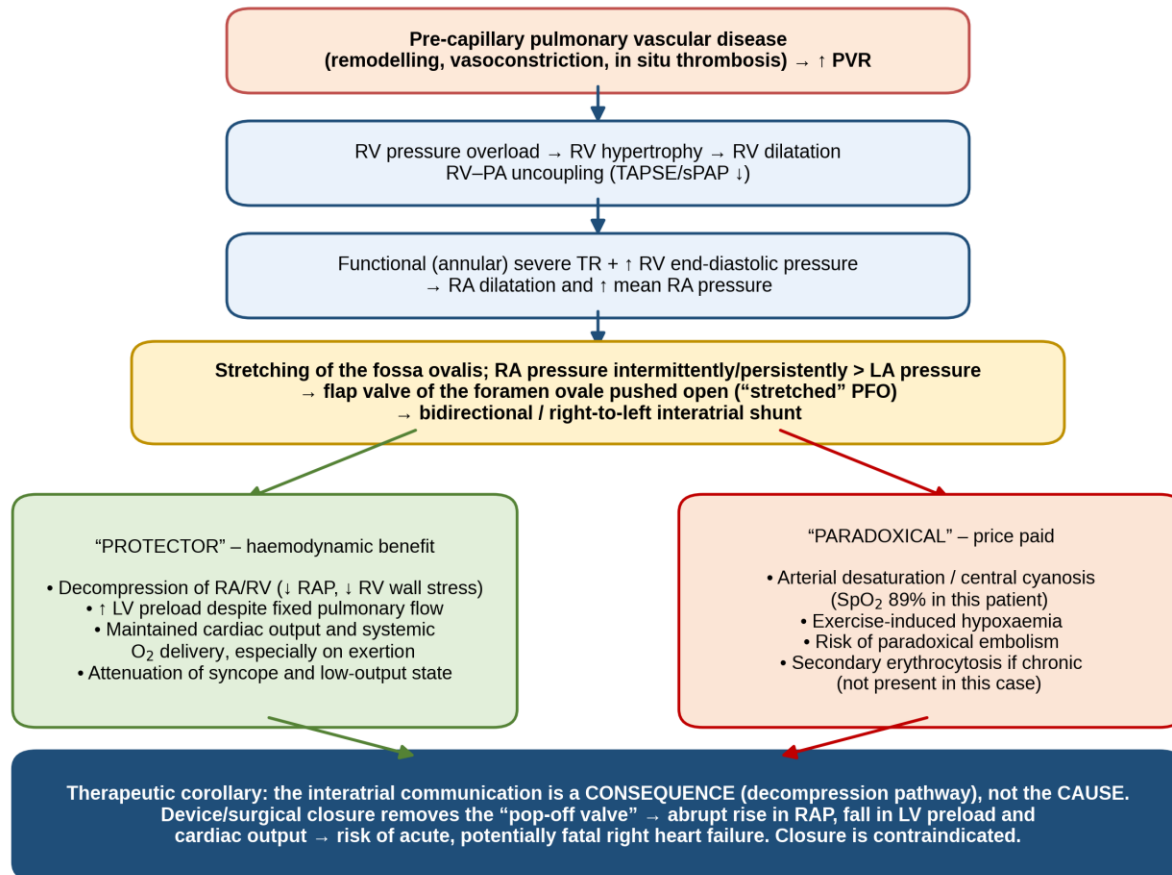


Figure 6. Proposed pathophysiological sequence by which severe pre-capillary pulmonary vascular disease stretches the foramen ovale open and converts it into a decompression pathway: haemodynamic benefit (“protector”) versus the price paid (“paradoxical”), and the therapeutic corollary that closure is contraindicated. LA, left atrium; LV, left ventricle; PA, pulmonary artery; PFO, patent foramen ovale; PVR, pulmonary vascular resistance; RA, right atrium; RAP, right atrial pressure; RV, right ventricle; sPAP, systolic pulmonary arterial pressure; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation.

The PFO as a Coincidental or Consequential Finding, Not the Cause

Five lines of reasoning support the conclusion that the interatrial communication did not cause the pulmonary vascular disease and does not constitute haemodynamically significant congenital heart disease. **First**, size: a communication of approximately 4–7 mm cannot generate the chronic pulmonary overcirculation needed to induce pulmonary vascular remodelling. Post-tricuspid shunts expose the pulmonary circulation to both volume and pressure, whereas pre-tricuspid shunts cause PH only when large and long-standing. The ESC/ERS classification explicitly recognises PAH with small or coincidental defects, in which marked PVR elevation coexists with defects that do not themselves account for it. **Second**, flow: the colour Doppler flow was small and predominantly left-to-right, without the RV volume-overload physiology of a significant ASD, while the clinical picture showed right-to-left desaturation driven by right atrial hypertension.^{1,21,44}

Third, anatomy and epidemiology: the stored image demonstrates a communication at the fossa ovalis compatible with a PFO. A PFO is found in about one quarter of the general population and in a similar proportion of patients with PH, and its detection increases with RV dilatation and dysfunction. **Fourth**, natural history: patients with an isolated small secundum ASD rarely develop severe PAH with RV failure in adolescence, whereas the present course, with rapid decompensation, cachexia and overt RV failure, resembles that of IPAH. **Fifth**, the neonatal history excludes early cyanotic physiology. Taken together, these arguments indicate that the defect is a normal variant that has been rendered patent by the disease: a consequence, not a cause.^{10,18,20,23}

This distinction has direct prognostic and therapeutic consequences. Patients with PAH and small or coincidental defects should be managed as patients with IPAH. In a contemporary Italian cohort, this subgroup and the subgroup with previously corrected defects had the worst survival among PAH-CHD phenotypes (15-year survival 66% for small defects versus 87% for Eisenmenger syndrome). A Thai cohort likewise identified PAH with a small defect as an independent mortality risk. In paediatric registry data, the role of ASDs in PH has been called into question, supporting classification of such defects as coincidental.^{7,22,23,45}

Classification as Group 1 Pulmonary Hypertension and Risk Stratification

Within the WSPH/ESC classification, PAH associated with congenital heart disease (group 1.4.4) comprises Eisenmenger syndrome, PAH with prevalent systemic-to-pulmonary shunts, PAH with small or coincidental defects, and PAH after defect correction. The paediatric task force of the 7th WSPH has expanded this framework further. Our patient therefore fits group 1 in one of two closely related ways: IPAH (group 1.1) with a coincidental, stretched PFO, or PAH with a small/coincidental defect (group 1.4.4). Management is identical in both scenarios. The 7th WSPH also reintroduced long-term responders to calcium-channel blockers as a subgroup of IPAH, which reinforces the value of vasoreactivity testing during RHC once the patient is clinically stable.^{1,2,6,44}

The group 1 classification must nevertheless be regarded as provisional. The haemodynamic definition requires RHC, which was not performed, and three alternative or contributory mechanisms require specific exclusion. (i) **Group 3 PH** related to post-tuberculous lung disease and hypoxia. Tuberculosis-associated PH is increasingly recognised as an under-appreciated entity, most plausibly mediated by parenchymal and vascular lung damage and hypoxia, and may coexist with pulmonary vascular disease; HRCT, spirometry with diffusing capacity, and arterial blood gases are essential. (ii) **Group 2 PH**, given the reported diastolic indices, which requires PAWP measurement. (iii) **Group 4 PH**, to be excluded by ventilation/perfusion scintigraphy. Associated forms of PAH, including HIV-, connective tissue disease-, portal hypertension- and drug-associated disease, must also be screened for. The EPPVDN consensus provides specific recommendations for these evaluations in low- and middle-income regions.^{1,5,9}

Using the ESC/ERS three-strata model at diagnosis, WHO functional class IV and clinical signs of right heart failure place this patient in the high-risk category, even though her TAPSE/sPAP ratio lies in the intermediate range and NT-proBNP and six-minute walk distance were unavailable. Hyponatraemia, tachypnoea and severe tricuspid regurgitation add prognostic weight, as they independently predict death or urgent transplantation in patients hospitalised for right heart failure in PAH. This high-risk profile justifies urgent referral to a PH centre and an intensive therapeutic strategy.^{1,6,35,37}

Rationale of the Therapy Administered

Decongestion. Diuretics are recommended for patients with PAH who have signs of RV failure and fluid retention. The loop diuretic furosemide relieves systemic venous congestion, pleural effusions and ascites, reduces RV dilatation and tricuspid regurgitation, and thereby may improve LV filling through reduced ventricular interdependence. Spironolactone antagonises secondary hyperaldosteronism, potentiates natriuresis and limits potassium loss. The recorded dose of intravenous furosemide (160 mg/day, ≈ 5.3 mg/kg/day) is substantial for a 30-kg adolescent. Because RV output in PAH is highly preload-sensitive, over-diuresis can precipitate hypotension, prerenal azotaemia and worsening electrolyte disturbances. Daily weight, fluid balance, renal function and electrolytes should guide dose titration, and hypokalaemia must be corrected promptly. The minimal maintenance infusion of Ringer's lactate is appropriate to avoid iatrogenic volume loading.^{1,28,31}

Digoxin. In patients with PAH and RV dysfunction, a single intravenous dose of digoxin produced a modest increase in cardiac output (from 3.49 to 3.81 L/min) and a significant reduction in circulating noradrenaline. Evidence for chronic use, however, is limited. In a propensity-matched retrospective cohort, chronic digoxin use in PAH was associated with higher mortality and heart failure hospitalisation, although residual confounding by disease severity is likely. Current guidelines therefore reserve digoxin mainly for rate control of atrial tachyarrhythmias. If it is continued, weight-appropriate dosing, correction of hypokalaemia and monitoring of serum concentration are essential.^{1,46,47}

Sildenafil. By inhibiting phosphodiesterase type 5, sildenafil augments nitric oxide–cyclic guanosine monophosphate signalling, producing pulmonary vasodilatation and antiproliferative effects. In the SUPER-1 trial, sildenafil 20 mg three times daily increased the placebo-corrected six-minute walk distance by 45 m and improved haemodynamics and functional class. In treatment-naïve children aged 1–17 years (STARTS-1), medium and high doses improved peak oxygen consumption, functional class and haemodynamics, whereas low doses were ineffective. The STARTS-2 extension raised concern about increased mortality with high doses, which has shaped

weight-based paediatric dosing recommendations. The regimen of 20 mg three times daily in this 30-kg adolescent is consistent with those recommendations.^{5,48–50}

Beraprost. Beraprost sodium is an orally active prostacyclin analogue that acts through the prostacyclin (IP) receptor and cyclic adenosine monophosphate signalling. In the ALPHABET trial, beraprost at a median dose of 80 µg four times daily improved six-minute walk distance by 25 m at 12 weeks, with greater benefit in primary pulmonary hypertension. In a 12-month trial, the benefit was evident at 3–6 months but attenuated thereafter. Treatment is typically initiated at 20 µg three to four times daily and titrated to tolerance. The recorded dose of 0.2 µg twice daily is therefore almost certainly a transcription error for 20 µg and must be verified. Beraprost is approved in several Asian countries but not in Europe or North America, and it is not part of the ESC/ERS treatment algorithm.^{1,32,33,51}

Positioning against current recommendations. For patients at high risk at diagnosis, the 2022 ESC/ERS guidelines advise considering initial combination therapy with a phosphodiesterase-5 inhibitor, an endothelin receptor antagonist and an intravenous or subcutaneous prostacyclin analogue. Patients at low or intermediate risk should receive initial dual oral combination therapy with a phosphodiesterase-5 inhibitor and an endothelin receptor antagonist. The 7th WSPH paediatric task force has proposed an updated paediatric risk tool and treatment algorithm. Where parenteral prostanoids are unavailable, as is common in resource-limited settings, the combination of sildenafil with an endothelin receptor antagonist (for example, bosentan, for which paediatric formulations and experience exist) is better supported by evidence than sildenafil plus beraprost. Treatment escalation should be planned in collaboration with a PH centre, and inotropic support may be required if low-output right heart failure supervenes.^{1,5,6}

Anti-infective and supportive therapy. Infection is a recognised precipitant of right heart failure decompensation in PAH, so empirical ceftriaxone for community-acquired pneumonia is appropriate. Sputum examination for *Mycobacterium tuberculosis* should nevertheless be repeated to exclude relapse. Omeprazole may be justified as short-term gastric protection in an acutely ill patient with congestive gastropathy but should be reviewed at discharge. Cavicur®, a *Curcuma xanthorrhiza* extract, and oral “albumin” supplements are nutritional adjuncts without evidence of

benefit in PAH, and potential herb–drug interactions have not been systematically evaluated. Structured nutritional rehabilitation with dietetic input is a more rational approach to cachexia and hypoalbuminaemia.^{1,9,28}

Measures not documented but recommended. Supplemental oxygen is recommended when arterial oxygen tension is persistently below 8 kPa (60 mmHg), acknowledging that its effect on saturation is limited when desaturation results mainly from right-to-left shunting. Iron deficiency should be corrected; intravenous iron is often preferable because hepcidin-mediated impairment of oral absorption is common in PAH. Other recommended measures include immunisation against influenza, *Streptococcus pneumoniae* and SARS-CoV-2; counselling on the high maternal risk of pregnancy in PAH, with provision of effective contraception, which is particularly pertinent in an adolescent girl; and psychosocial support. Routine anticoagulation is no longer generally advocated in PAH and should be individualised. In patients who deteriorate despite maximal therapy, balloon atrial septostomy or a Potts shunt may serve as palliation or as a bridge, and early evaluation for lung transplantation should be considered.^{1,6,24,36}

Table 7. Rationale, supporting evidence and recommendations for each therapeutic component

Agent / measure	Mechanism and rationale	Key evidence / guideline position	Comments for this patient
Furosemide	Loop diuretic; relieves systemic congestion; reduces RV dilatation and TR	Recommended in PAH with RV failure and fluid retention (ESC/ERS 2022)	High dose (≈ 5.3 mg/kg/day); risk of over-diuresis in a preload-dependent RV; monitor K^+ , Na^+ , creatinine and weight
Spironolactone	MRA; counters hyperaldosteronism; K^+ -sparing	Standard adjunct in right-sided heart failure	Helpful given K^+ 2.6 mmol/L; still requires active K^+

			replacement
Digoxin	Na ⁺ /K ⁺ -ATPase inhibition; modest inotropy; sympatholytic	Acute ↑ cardiac output in PAH (Rich 1998); chronic use associated with worse outcomes in observational data (Chang 2023)	Hypokalaemia potentiates toxicity; verify dose and serum level; mainly for atrial tachyarrhythmias
Sildenafil	PDE5 inhibition → ↑cGMP; vasodilatation, antiproliferation	SUPER-1: +45 m 6MWD; STARTS-1/2: efficacy at medium doses, mortality signal at high doses	20 mg t.i.d. appropriate for 30 kg; consider adding an ERA
Beraprost	Oral prostacyclin analogue (IP receptor → ↑cAMP)	ALPHABET: +25 m at 12 weeks; benefit attenuated by 9–12 months; not in ESC/ERS algorithm	Recorded 0.2 µg likely denotes 20 µg; verify; ERA preferable if available
Ceftriaxone	Treatment of community-acquired pneumonia	Infection is a recognised trigger of RV failure decompensation	Repeat TB microbiology to exclude relapse
Omeprazole	Gastric acid suppression	No PAH-specific evidence	Short-term only; review at discharge
Ringer's lactate (KVO)	Venous access with minimal volume	Avoid volume loading in RV failure	Appropriate
Cavicur® /	Nutritional adjuncts	No evidence in PAH	Replace with

oral albumin			structured nutritional rehabilitation
Oxygen (not documented)	Corrects hypoxic vasoconstriction; improves O ₂ delivery	Recommended if PaO ₂ persistently <8 kPa	Limited response expected with right-to-left shunt; titrate to target
Iron repletion (not documented)	Corrects iron deficiency	Iron deficiency is common and prognostic in IPAH	Obtain ferritin and TSAT; IV iron preferred
Potassium replacement (not documented)	Corrects hypokalaemia	Essential with loop diuretics and digoxin	Urgent

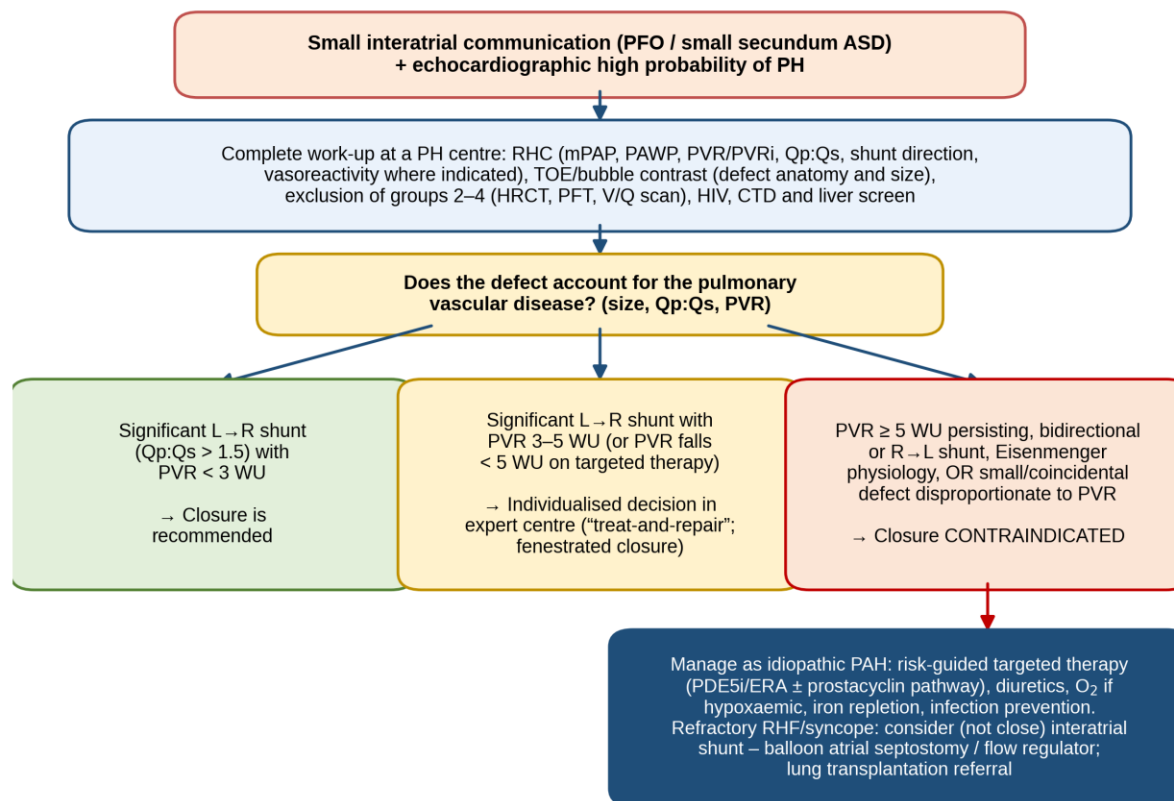
6MWD, six-minute walk distance; cAMP/cGMP, cyclic adenosine/guanosine monophosphate; ERA, endothelin receptor antagonist; KVO, keep vein open; MRA, mineralocorticoid receptor antagonist; TSAT, transferrin saturation.^{1,32,34,46–51}

Should the Patent Foramen Ovale Be Closed? Indications and Contraindications

Percutaneous PFO closure has well-defined indications in patients **without** significant PH. In selected patients aged approximately 18–60 years with a PFO-associated ischaemic stroke and a high probability of a causal role of the PFO, randomised evidence supports closure plus antiplatelet therapy over medical therapy alone. The European position papers and the SCAI guidelines also address closure for arterial deoxygenation syndromes such as platypnoea–orthodeoxia without PH, for selected divers with decompression illness and, as an investigational indication, for migraine with aura. The common denominator of all these indications is that pulmonary vascular resistance and right-sided pressures are normal, so that the PFO serves no physiological purpose and acts only as a conduit for paradoxical embolism or desaturation.^{52–54}

The situation is fundamentally different in severe PH. In the ESC/ERS and ESC adult congenital heart disease guidelines, closure of an ASD with a significant left-to-right shunt is recommended when PVR is <3 WU, should be individualised in expert centres when PVR is 3–5 WU, and is not recommended when PVR remains ≥ 5 WU despite targeted therapy. Closure is likewise not recommended in patients with PAH and small or coincidental defects, or in Eisenmenger physiology (Figure 7, Table 8). In paediatric patients, indexed PVR thresholds and expert-centre evaluation apply.^{1,6,21}

In our patient, PFO closure is **contraindicated** for several converging reasons: the PH is severe and pre-capillary in nature; the RV is failing and uncoupled; the interatrial flow is bidirectional or right-to-left; the defect is small and coincidental; and there is active infection. Closure would abruptly abolish the decompression pathway. Right atrial and RV end-diastolic pressures would rise, RV wall stress and myocardial oxygen demand would increase, tricuspid regurgitation would worsen, and LV preload and cardiac output would fall. The likely result is acute, potentially fatal right heart failure with low-output shock. The unfavourable survival of patients with PAH after defect correction (20-year survival 36%) offers indirect clinical support for this concern. The rationale for creating, rather than closing, interatrial communications in refractory PAH through balloon atrial septostomy provides the mirror-image argument. Should the patient become refractory to maximal medical therapy, the relevant consideration would be enlargement of the communication by graded septostomy in an experienced centre, not closure.^{1,16,22,24,41}



PVR thresholds as per 2022 ESC/ERS PH guidelines (adults); in children, indexed PVR (PVRi) thresholds and paediatric expert-centre evaluation apply. PAH, pulmonary arterial hypertension; PDE5i, phosphodiesterase-5 inhibitor; ERA, endothelin receptor antagonist.

Figure 7. Proposed decision algorithm for a small interatrial communication identified in a patient with a high echocardiographic probability of pulmonary hypertension, based on the 2022 ESC/ERS pulmonary hypertension and 2020 ESC adult congenital heart disease guidelines. CTD, connective tissue disease; HRCT, high-resolution computed tomography; L→R, left-to-right; PAWP, pulmonary arterial wedge pressure; PFT, pulmonary function tests; PVR(i), (indexed) pulmonary vascular resistance; R→L, right-to-left; RHC, right heart catheterisation; TOE, transoesophageal echocardiography; V/Q, ventilation/perfusion; WU, Wood units.

Table 8. Indications and contraindications for closure of a patent foramen ovale or small interatrial defect

Indications (normal pulmonary haemodynamics)	Contraindications / not recommended

PFO-associated ischaemic stroke in selected patients aged 18–60 years with a high probability of causal PFO (large shunt and/or atrial septal aneurysm)	Severe PH with PVR ≥ 5 WU persisting despite targeted therapy
Arterial deoxygenation syndromes (e.g. platypnoea–orthodeoxia) in the absence of PH	PAH with small or coincidental defects (defect does not account for PVR)
Selected cases of decompression illness in divers	Eisenmenger physiology or predominant right-to-left shunting that decompresses the right heart
Migraine with aura: investigational only	Decompensated RV failure in which the interatrial pathway supports LV preload
Secundum ASD with Qp:Qs >1.5 and PVR <3 WU (individualised evaluation if PVR 3–5 WU)	Active systemic infection or sepsis; intracardiac thrombus; unsuitable anatomy; contraindication to antiplatelet therapy

ASD, atrial septal defect; LV, left ventricle; PAH, pulmonary arterial hypertension; PFO, patent foramen ovale; PH, pulmonary hypertension; PVR, pulmonary vascular resistance; Qp:Qs, pulmonary-to-systemic flow ratio; RV, right ventricle; WU, Wood units.^{1,21,52–54}

Implications for Resource-Limited Settings

This case reflects several structural challenges documented in Indonesia: late presentation, limited availability of RHC outside tertiary centres, restricted access to endothelin receptor antagonists and parenteral prostanoids, and a high burden of tuberculosis and undernutrition. The EPPVDN consensus was the first to formulate specific recommendations for paediatric PH care in middle- and low-income regions. Echocardiography, ECG, oximetry and basic laboratory tests can support a robust provisional classification and risk assessment, but they cannot replace haemodynamic confirmation. Networked referral to national PH centres, such as those contributing

to the COHARD-PH registry, and structured cardiopulmonary follow-up of tuberculosis survivors could shorten diagnostic delay and prevent inappropriate interventions.^{5,8,9}

Strengths and Limitations

The strengths of this report include a comprehensive, CARE-structured clinical description, a systematic correlation of findings with pathophysiology, and an evidence-based appraisal of therapy and septal intervention drawn from guidelines, randomised trials, registries and physiological studies. Its limitations must be acknowledged. It describes a single patient, so causal inference and generalisation are not possible. RHC was not performed, so the haemodynamic definition, PVR, PAWP, Qp:Qs and vasoreactivity remain unknown, and the group 1 classification is provisional. The interatrial communication was not characterised by transoesophageal echocardiography or agitated-saline contrast, and the source record contains discrepancies in defect type, size and shunt direction. Key prognostic variables (NT-proBNP, six-minute walk distance, arterial blood gases, iron studies) and investigations to exclude groups 3 and 4 were unavailable. Finally, follow-up and outcome data were not available at the time of writing.^{1,25}

CONCLUSION AND RECOMMENDATIONS

Conclusion

This report describes a 17-year-old undernourished girl with recently treated tuberculosis who presented with severe PH, decompensated right heart failure, central cyanosis and a small interatrial communication at the fossa ovalis. Integrated analysis of the history, physical examination, laboratory, electrocardiographic, radiological and echocardiographic findings supports provisional group 1 PH, either IPAHA with a coincidental PFO or PAH with a small coincidental defect. In this setting, the PFO has been stretched open by right atrial hypertension.^{1,2,20}

The interatrial communication is a consequence rather than a cause of the disease and does not represent haemodynamically significant congenital heart disease. It acts as a “paradoxical protector”: it decompresses the right heart and helps sustain LV preload and systemic output, at the price of hypoxaemia and a risk of paradoxical embolism. Although its haemodynamic benefit is physiologically robust, current evidence does not demonstrate an independent survival advantage.

Closure is contraindicated, because removal of this decompression pathway may precipitate acute, potentially fatal right heart failure.^{19,21,22,24}

The management administered, comprising loop and mineralocorticoid-antagonist diuretics, digoxin, sildenafil, beraprost and antibiotics, addresses congestion, pulmonary vasodilatation and infection. It should nevertheless be optimised by urgent correction of severe hypokalaemia, verification of the beraprost and digoxin doses, oxygen supplementation when indicated, iron repletion, nutritional rehabilitation, and escalation to guideline-based combination therapy under the supervision of a PH centre.^{1,32,34,46}

Recommendations

- 1. For this patient:** refer urgently to a paediatric/adult PH centre for RHC (mPAP, PAWP, PVR/PVRI, Qp:Qs, shunt direction, and vasoreactivity testing once stable); transoesophageal echocardiography or agitated-saline contrast to define the interatrial communication; HRCT, spirometry with DLCO, arterial blood gases and ventilation/perfusion scintigraphy to exclude groups 3 and 4; and screening for HIV, connective tissue disease and portal hypertension.^{1,5,6}
- 2. Risk stratification and therapy:** measure NT-proBNP and six-minute walk distance where feasible, repeat TAPSE/sPAP assessment, and apply ESC/ERS and 7th WSPH paediatric risk tools. Consider adding an endothelin receptor antagonist to sildenafil, reserve parenteral prostacyclin for high-risk status where available, and avoid interventions that close the interatrial communication.^{1,6,30}
- 3. Safety measures:** correct hypokalaemia and hyponatraemia with close monitoring, titrate diuretics to daily weight and renal function, confirm digoxin strength and monitor serum levels, and correct the documented beraprost dose.^{28,37,47}
- 4. Comprehensive care:** provide iron studies and repletion, structured nutritional rehabilitation, immunisation, contraceptive and pregnancy-risk counselling, psychosocial support, and a planned transition from paediatric to adult PH care.^{1,5,36}
- 5. For clinicians:** a small interatrial communication in a patient with severe PH should never be closed on the basis of echocardiography alone; defect size must be weighed against PVR, and small or coincidental defects should be managed as IPA.²¹⁻²³

6. **For health systems and research:** strengthen referral networks and access to RHC and targeted PAH therapies in Indonesia; implement cardiopulmonary screening of symptomatic tuberculosis survivors; and conduct prospective paediatric and adolescent registries that characterise PFO and small defects with invasive haemodynamics, TAPSE/sPAP and long-term outcomes.^{7–9}

DECLARATIONS

Informed consent: Written informed consent for publication was obtained from the patient's legal guardians, and assent was obtained from the patient. **Insert date.**

Ethics: **Insert institutional ethics committee approval or waiver statement per target journal policy.**

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