Case report

Pulmonary hypertension associated with congenital heart disease; clinical decision scenario

Ali A. Alakhfash [a],[*], Abdullah Alqwaiee [a], Ghadeer Ali Alakhfash [b], Athkar Alhajjaj [c], Abdulrahman A. Almesned [a]

[a] Consultant Pediatric Cardiologist, Prince Sultan Cardiac Center-Qassim, Saudi Arabia
[b] Alrajehi University, Saudi Arabia
[c] PSCC-Qassim, Saudi Arabia

ARTICLE INFO

ABSTRACT

Pulmonary arterial hypertension associated with congenital heart disease (PAH-CHD) is one type under group 1 PH. Undiagnosed or delayed diagnosis of significant CHD might lead to significant PAH and at the end might lead to Eisenmenger syndrome. We could expect the degree of PAH in patients with CHD by proper clinical assessment as well as by the basic assessment tools including the chest x-ray (CXR), ECG, and transthoracic echocardiography (TTE).

We are presenting a three and half years old child with a delayed/missed diagnosis of large patent ductus arteries (PDA) who present with significant PAH. Clinical evaluation, CXR, ECG, TTE, as well as cardiac catheterization data are presented, with a review of the current guidelines regarding the management of pediatric patients with PAH-CHD.

1. Background

According to the new guidelines from the 6th World Symposium on Pulmonary Hypertension (WSPH) Task Force, pre-capillary pulmonary hypertension (PH) is defined as a mean pulmonary arterial pressure (mPAP) >20 mmHg, with a pulmonary vascular resistance (PVR) ≥3 Wood Units [1]. In comparison to adults, the majority of children have "transient" PAH in relation to either persistent PH of the newborn (PPHN) or treatable congenital cardiac heart defects. Around 34% of children with a diagnosis of PH had PH associated with developmental lung disease (bronchopulmonary dysplasia (BPD), congenital diaphragmatic hernia (CDH) and congenital pulmonary vascular abnormalities) and 27% of them have other forms of PAH (IPAH, PAH-CHD, PAH associated with connective tissue disease (CTD) and pulmonary veno-occlusive disease (PVOD)) [2–4].

Assessment of operability in PAH-CHD requires cardiac cath to measure the pulmonary valscular resistance (PVR), in addition to the clinical and echocardiographic findings [5,6].

Pulmonary hypertension associated with CHD is commonly secondary to left-to-right shunt defects or left heart obstructive lesions. Common defects include ventricular septal defect (VSD), atrial septal defect (ASD), and persistent ductus arteriosus (PDA) [7]. PH due to left heart disease is a separate entity and is considered as Group 2 in PH classification [6].

We are presenting a child with a large PDA associated with significant pulmonary hypertension. We will discuss how to manage such cases, with special emphasis on the importance of the clinical examination, the value of the CXR, ECG, and the interpretation of echocardiography in cases with left to right shunts.

1.1. Case presentation

Three years and 6 months old male child referred because of a history of easy fatigability and not coping with his peers during play with a history of shortness of breath. There is no history of fever, cough, or chest pain. He had a poor appetite and lost 3 kg in the last 1 month. No

Before PDA device closure   One day after PDA device closure
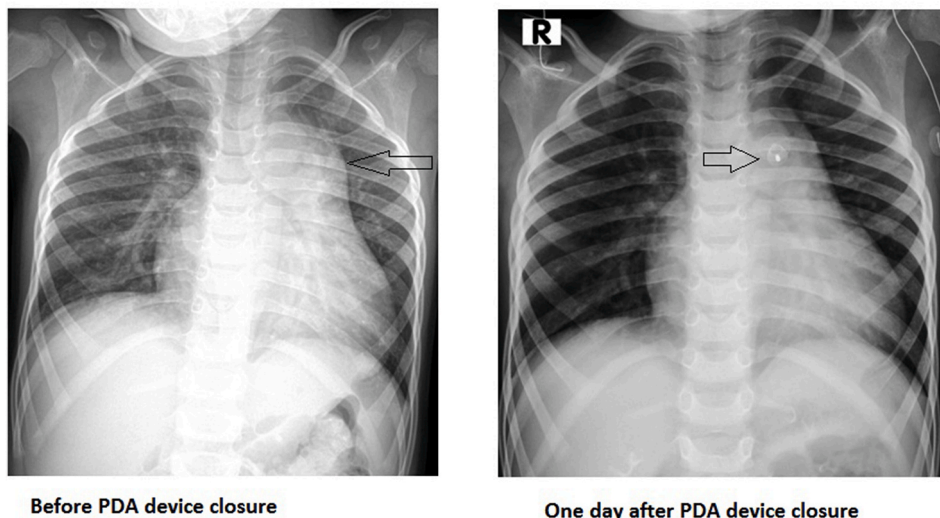
Fig. 1. Chest X-ray before and one day after PDA device closure. There is cardiomegaly with prominent pulmonary artery (PA)conus. Lung congestion is more significant before PDA device closure.(the arrows point to the PA conus and the PDA device).
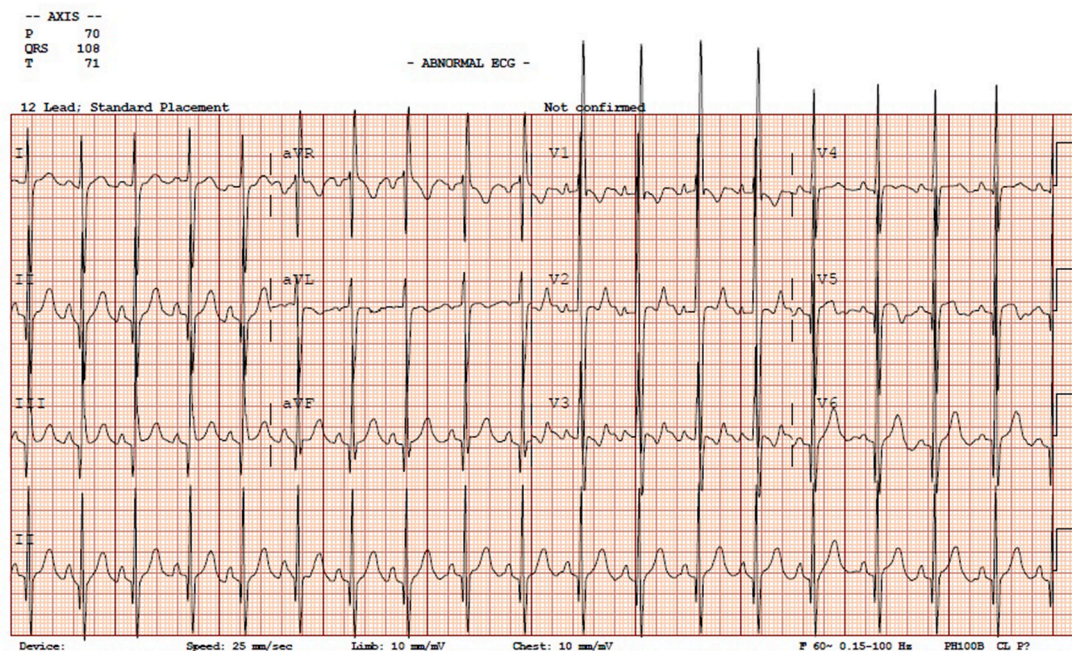

Fig. 2. 12 Lead ECG, showing evidence of right atrial enlargement, the axis is more toward the right side, with biventricular hypertrophy, mainly RVH.

other symptoms on review of other organ systems. He is the product of uneventful pregnancy with no NICU admission. His development is appropriate for his age. No family history of similar illness nor other illnesses.

Clinically: he is conscious, alert, no dysmorphic features and no signs of respiratory distress. His blood pressure is 110/54 mmHg, afebrile, and his saturation is 95% in the right upper limb (preductal) as well as in the lower limb (post-ductal). The weight and height were13.8 kg and 98 cm respectively (between the 25[th]and 50th percentile for his age and gender).

Cardiovascular examination revealed no central or peripheral cyanosis, palpable four limb pulses with no radio-femoral delay and no lower limb edema. On inspection: there is mild precordial bulging, but no retractions, nor visible pulsations. On palpation: no thrill, the apex beat was displaced laterally with a parasternal heave and palpable

pulmonary component of the 2nd heart sound (P2). On auscultation: the first heart sound is normal with accentuated P2. There is a systolic murmur grade 3/6 heard best at the pulmonary area and radiating to the left infraclavicular area.Other organ system examination was unremarkable.

Investigations: CBC, renal and liver functions, as well as serum electrolytes all, were normal, with a Hb of 13.2 gm/dl.CXR showed cardiomegaly, with plethoric lung congestion. There is significant prominence of the main pulmonary artery conus (Fig. 1A).

ECG revealed: Sinus rhythm with right atrial enlargement (peaked P wave). The QRS axis was toward the right side (110°). There is evidence of biventricular hypertrophy (R waves and S waves in both right and left precordial leads) with more ECG signs of RVH (Fig. 2).

Transthoracic Echocardiography revealed a large PDA with mainly left to right shunt. The peak instantaneous gradient (PG) across the PDA
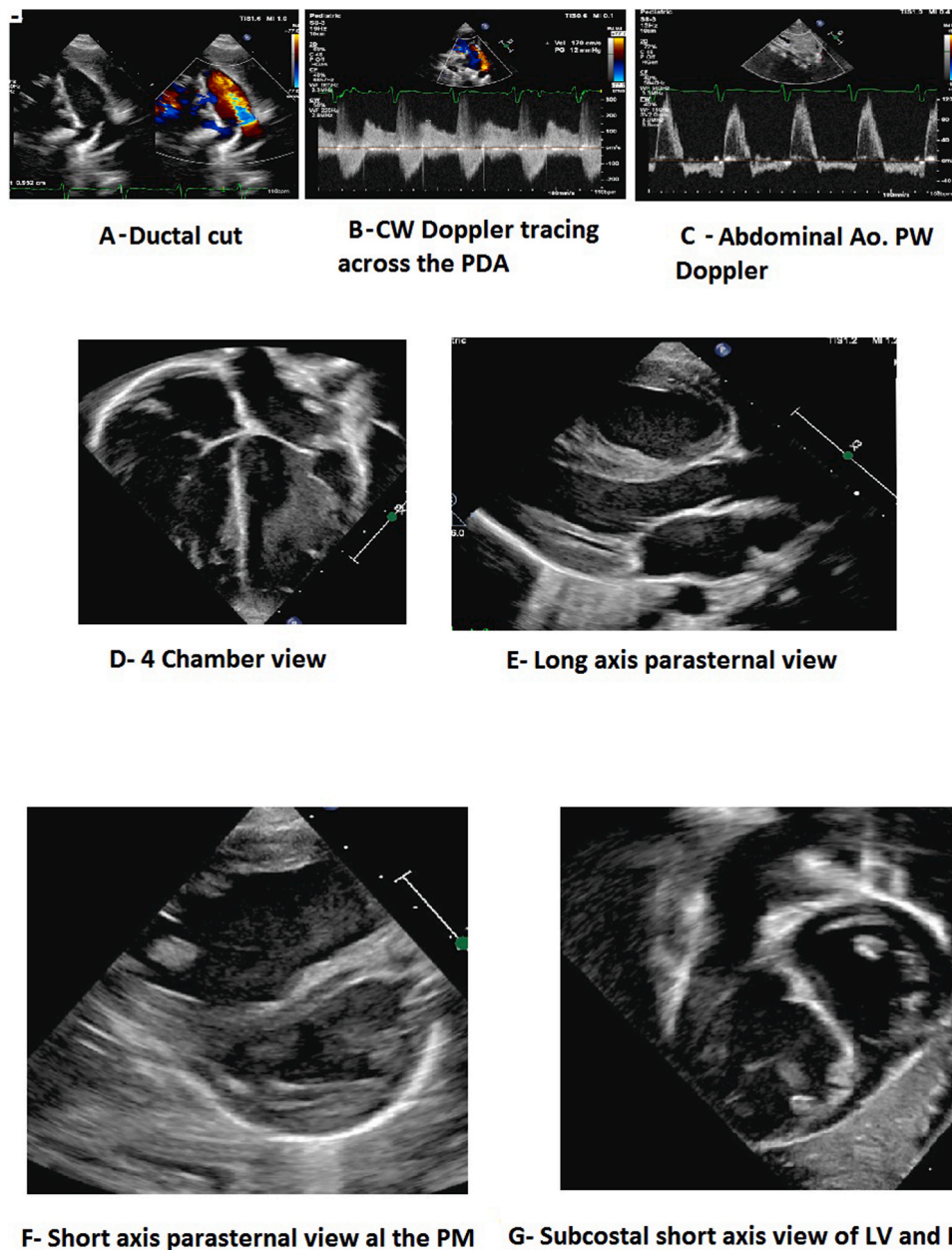
Fig. 3. Echocardiographic views before PDA device closure. A- Two Dimensional and color compare, high left parasternal view (ductal cut) (Ao = Aorta, PA = Pulmonary artery).B- Continuous-wave (CW) Doppler tracing of the flow across PDA (Low gradient between the aorta and the pulmonary artery). C- Abdominal aorta Pulse wave (PW) Doppler, showing pulsatile systolic flow with a holo-diastolic reversal.D- 4 Chamber view showing right ventricular (RV) dilatation. (LV = left ventricle). E− Long axis view, showing RV dilatation. F- Short axis parasternal view at the papillary muscle level. There is significant RV dilatation. The interventricular septum (IVS) is pushed toward the left ventricle (LV) (flattening of IVS and D-shaped LV). G- Short axis subcostalview. There is significant RV dilatation. The interventricular septum (IVS is pushed toward the left ventricle (LV). . (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

was only 12 mmHg (Systolic BP 110 mmHg). There is a significant right ventricular (RV) dilatation with some early systolic bouncing of the interventricular septum (IVS) to the left side (Early systolic IVS flattening with D-Shaped LV). No ASD or VSD. Mild pulmonary insufficiency with a PG of 60 mmHg (estimated mean pulmonary artery pressure "PAP" 70 mmHg). Mild tricuspid valve insufficiency (TR) with a PG of 90 mmHg estimated PAP of 100 mmHg). Mildly dilated IVC (collapsible). Good systolic function. No pericardial effusion (Fig. 3).

He was admitted and prepared for diagnostic cardiac catheterization and possible PDA device closure.

Cardiac catheterization was performed. Hemodynamic assessment before closure of the PDA revealed the ratio of the pulmonary blood flow to the systemic blood flow (the Qp: Qs of 2.0 and the indexed pulmonary vascular resistance(PVRi) of 5.4 Wood.unit.m [2]. The pulmonary to the systemic vascular resistance (PVR: SVR) ratio was 0.4. Pre-PDA closure aortogram revealed a large PDA with good ampulla. The narrowest diameter was 4.5 mm. PDA device closure was done using a 6/8 Occlutech ductal Occluder device (Perfecting Performance) [8]. Before releasing the device, the PAP was measured through the side-port of the long delivery sheath. After PDA device closure hemodynamic assessment revealed a Qp: Qs of 1.0 and a PVRi of 3.5 Wood.unit.m [2]. The PVR: SVR ratio was 0.3. The patient was kept in room air prior to as well as after PDA device closure. The post-procedure angiogram revealed that the device is in a good position with no compromision to the arch
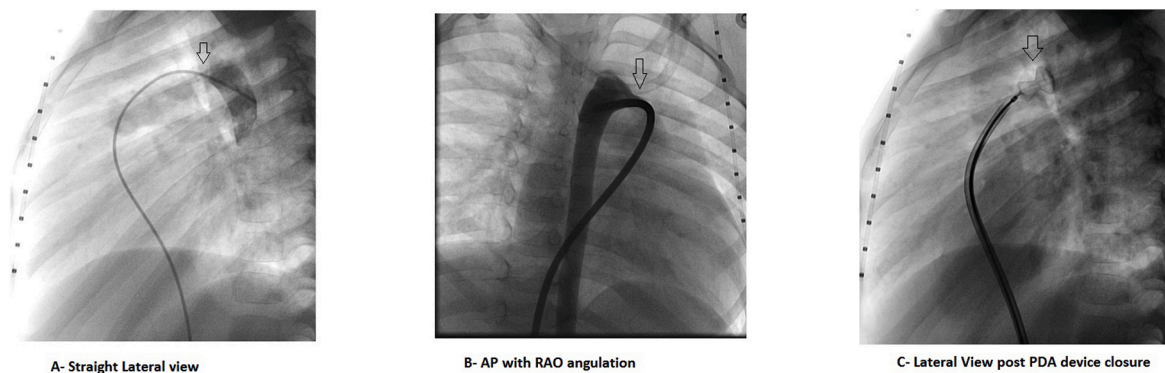
Fig. 4. Cardiac catheterization during PDA device closure (arrows point to the PDA and PDA device). A- Straight lateral view, showing the MPA2 catheter crossing from the pulmonary artery (PA) side to the aorta (AO). B- Postero-anterior view with 20° right anterior oblique (RAO) angulation, with an injection through the long delivery sheath. C- Lateral view post-PDA device closure. The Device still attached to the delivery cable.

or branch pulmonary arteries (PAs) (Fig. 4).

The patient was shifted to the CSICU for routine post cath care. He was discharged one day after the cath and started on Sildenafil 5 mg PO Q 8 hours for 3 months.

Chest X-ray one day after PDA device closure revealed a decrease in pulmonary congestion (Fig. 1 B). Echocardiography prior to discharge as well as one month after the cardiac cath revealed that there is still RV dilatation, but the LV is circular throughout systole. The TR PG dropped to 30 mmHg and the Pulmomonary regurge PG dropped to 25 mmHg. Biventricular systolic function is good with no pericardial effusion.

2. Discussion

The prevalence of PAH in adult patients with CHD is reported to be between 4.2 and 6% in developed countries [9]. [10]. The prevalence of PAH associated with CHD is much higher in developing countries, owing to delayed diagnosis, and or unavailability of proper and timely intervention [11,12]. The initial evaluation of pediatric patients with CHD and PH should include a comprehensive history and physical examination [13].

For every child with CHD, the clinical examination should focus also on common signs of PHT which might include: (1) left parasternal heave caused by the right ventricular enlargement, detected by placing the heel of the hand over the left parasternal region; (2) accentuation of the pulmonary component of the second heart sound (P2) (3) paradoxical splitting of the second heart sound, and (3) pulmonary regurgitation diastolic murmur. (4) The systolic murmur of the VSD might become softer and the machinery/diastolic murmur of PDA will disappear. Fig. 5

ECG, chest X-ray, and echocardiography are the first tools in the evaluation of patients with CHD. More frequent echocardiograms are recommended in the setting of changes in therapy or clinical condition [14].

The ECG in pediatric patients with PHT typically demonstrates right-sided cardiac strain associated with right ventricular hypertrophy (RVH) and right axis deviation (RAD). Fig. 5

Chest X-ray findings in children with PHT of any cause include (1) enlargement of the main and hilar pulmonary arteries, (2) tapering of the peripheral pulmonary arteries, and (3) right ventricular enlargement associated with loss of the retrosternal air space on the lateral view. The CXR can help in the assessment of the lung parenchyma and exclusion of lung/mediastinal/thoracic cage problems [14,15].

Some patients might have an increase in both the pulmonary blood flow as well as the pulmonary venous pressure, as a result of left-sided obstructive lesions associated with a shunt defect, increasing the risk for the development of PH.

Pulmonary artery pressure (PAP) can be estimated using Doppler echocardiography, in addition to the other 2-dimensional echocardiographic features [15]. Systemic blood pressure should be recorded at the time of echocardiogram.

In the absence of RVOT obstruction, and large VSD, the RV systolic pressure, and hence the PAP, can be estimated from the TR gradient. In cases of VSD and AVSD with a large VSD component, there might be equalization of the LV and RV pressures, and hence the TR gradient will reflect the systemic pressure rather than the PA pressure. In addition to that the VSD jet might be directed to the right atrium, and miss interpreted as TR. In such cases, the TR gradient should not be taken to estimate the PA pressure. In such cases (as well as in others) the PAP can be estimated from the Doppler gradient of the VSD shunt, PDA shunt, and PI gradient [16].

Using the 2-D echocardiogram, the position of the interventricular septum (IVS) can indicate the RV systolic pressure. When the RV systolic pressure is greater than half of the systemic pressure, there will be progressive leftward displacement and flattening of the interventricular septum. The eccentricity index (the ratio of the LV minor and major axes in the short-axis view at the level of the mitral tendinous chords) can be used to quantify this IVS flattening [17,18].

Echocardiography can help in assessing the severity of PAH and predicting the outcome. [19] Depending on the lesion, the timing of presentation and the overall clinical status, it is recommended to consider cardiac catheterization (to measure PVR index (PVRI) and to determine operability) for children with unrepaired significant structural heart defects. (*Class II; Level of Evidence B*) [13,20].

The current recommendations on the evaluation and management of PH in Children and young adults with CHD (PAH-CHD, PHVD-CHD) state that children with a PVRi < 6 WU.m^2 and a PVR/SVR ratio < 0.3, in the absence of additional risk factors, are eligible for shunt closure [5,13,20].(Figure/algorithm 5). After cardiac intervention (cardiac catheterization or surgery) such patients need close follow up because they are still at risk for persistent PHT. This PHT might progress to resemble that of idiopathic PAH [21–24]. Fig. 5

In our case, echocardiography gives an indication of the presence of significant PAH. This was reflected by the low gradient across the PDA by CW Doppler, the RV dilatation, IVS flattening and D-Shaped LV in systole, and the degree of TR and PI gradient. This was confirmed by cardiac catheterization. The PVRi was 5.4 Wood.unit.m [2] with a PVR: SVR ratio of 0.4. After PDA closure, the PVRi dropped to 3.5 Wood.unit. m [2]' and the PVR: SVR ratio dropped to 0.3. Hemodynamics was performed based on the current guidelines [5,25].

After PDA closure, there was a significant improvement in the echocardiographic parameters. Such patients need close follow up and might need to be given some specific therapy for PAH. Our patient was kept on Sildenafil 5 mg PO every 8 hours for three months. He remained asymptomatic with a functional class I.
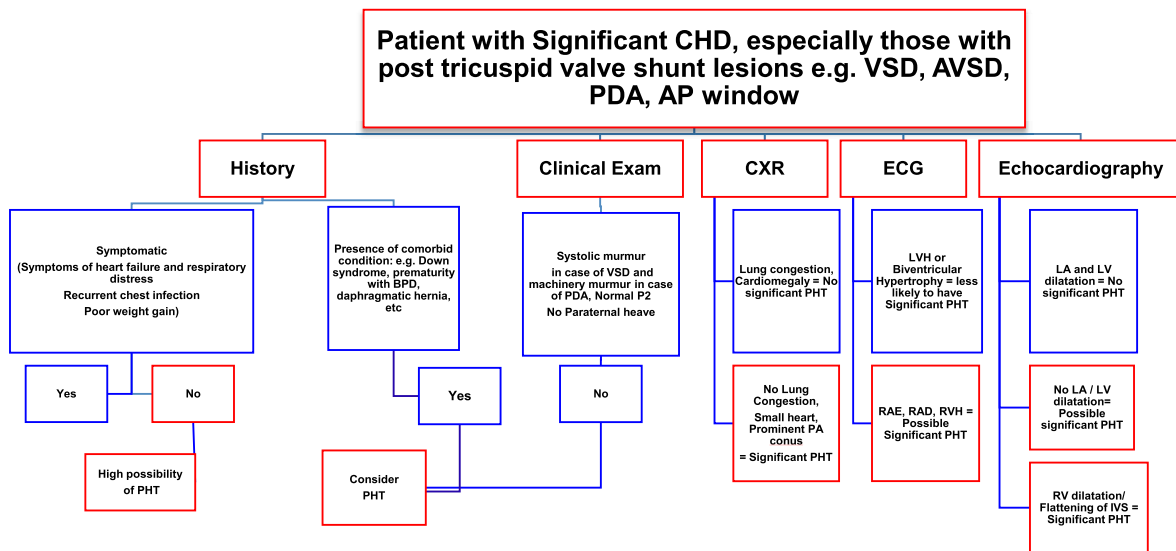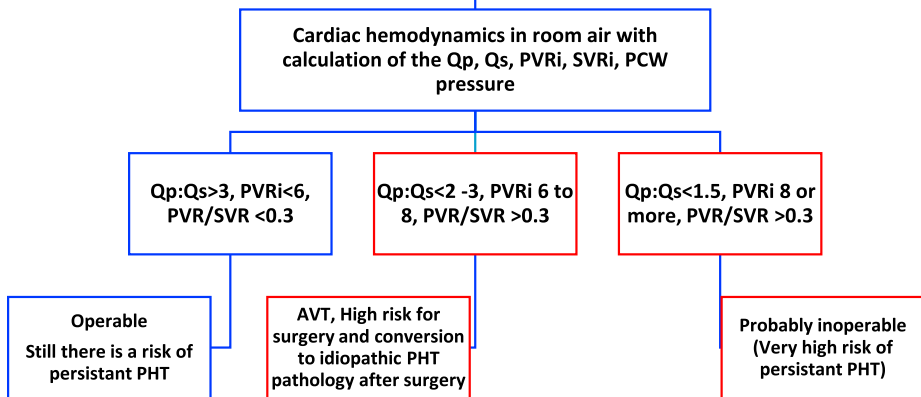
Fig. 5. Clinical assessment and management algorithm of patients with significant post-tricuspid valve shunt (When to consider the presence of significant pulmonary valscular disease/Pulmonary hypertension).

3. Conclusion

PAH is a common association of CHD. In developing countries, the delayed diagnosis as well as the unavailability of timely and proper diagnosis and intervention might complicate the picture. The clinical assessment as well as the basic investigations including CXR, ECG, and transthoracic echocardiography will give a good estimation of the degree of PH and PA pressure.

CRediT authorship contribution statement

Ali A. Alakhfash: Writing - original draft, Writing - review & editing, spends timewriting and reviewing the manuscript. **Abdullah Alqwaiee:** Writing - original draft, Writing - review & editing, reviewed the case and shared in writing and review of the manuscript. **Ghadeer Ali Alakhfash:** Writing - original draft, Writing - review & editing, Prepared the case, reviewed the literature, and shared in manuscript writing. **Athkar Alhajjaj:** Writing - original draft, Writing - review & editing, Prepared the case, reviewed the literature, and shared in manuscript writing. **Abdulrahman A. Almesned:** Writing - original draft, Writing - review & editing, reviewed the case and shared in writing and review of the manuscript.

Declaration of competing interest

All authors have no conflicts of interest to disclose. They indicated that they have no financial relationships relevant to this article to disclose.

References

[1] D.F. Condon, N.P. Nickel, R. Anderson, S. Mirza, V.A. de Jesus Perez, The 6th World Symposium on Pulmonary Hypertension: what's old is new, F1000Research 8 (2019) 888, https://doi.org/10.12688/f1000research.18811.1.

[2] R.L.E. van Loon, M.T.R. Roofthooft, H.L. Hillege, et al., Pediatric pulmonary hypertension in The Netherlands, Circulation 124 (16) (2011) 1755–1764, https://doi.org/10.1161/CIRCULATIONAHA.110.969584.

[3] MJ. del C. Marín, A.S. Rotés, A.R. Ogando, et al., Assessing pulmonary hypertensive vascular disease in childhood. Data from the Spanish registry, Am. J. Respir. Crit. Care Med. 190 (12) (2014) 1421–1429, https://doi.org/10.1164/rccm.201406-1052OC.

[4] L. Li, S. Jick, S. Breitenstein, G. Hernandez, A. Michel, D. Vizcaya, Pulmonary arterial hypertension in the USA: an epidemiological study in a large insured pediatric population, Pulm. Circ. 7 (1) (2017) 126–136, https://doi.org/10.1086/690007.

[5] E.B. Rosenzweig, S.H. Abman, I. Adatia, et al., Paediatric pulmonary arterial hypertension: updates on definition, classification, diagnostics and management, Eur. Respir. J. 53 (1) (2019) 1801916, https://doi.org/10.1183/13993003.01916-2018.

[6] G. Simonneau, D. Montani, D.S. Celermajer, et al., Haemodynamic definitions and updated clinical classification of pulmonary hypertension, Eur. Respir. J. 53 (1) (2019) 1801913, https://doi.org/10.1183/13993003.01913-2018.

[7] E. Pascall, R.M. Tulloh, Pulmonary hypertension in congenital heart disease, Future Cardiol. 14 (4) (2018) 343–353, https://doi.org/10.2217/fca-2017-0065.

[8] F. Godart, A. Houeijeh, O. Domanski, M.-P. Guillaume, M. Brard, H. Lucron, Is the new Occlutech duct occluder an appropriate device for transcatheter closure of patent ductus arteriosus? Int. J. Cardiol. 261 (2018) 54–57, https://doi.org/10.1016/j.ijcard.2018.03.059.

[9] M.G.J. Duffels, P.M. Engelfriet, R.M.F. Berger, et al., Pulmonary arterial hypertension in congenital heart disease: an epidemiologic perspective from a Dutch registry, Int. J. Cardiol. 120 (2) (2007) 198–204, https://doi.org/10.1016/j.ijcard.2006.09.017.

[10] G.-P. Diller, M a Gatzoulis, Pulmonary vascular disease in adults with congenital heart disease, Circulation 115 (8) (2007) 1039–1050, https://doi.org/10.1161/CIRCULATIONAHA.105.592386.

[11] K. Dimopoulos, S.J. Wort, M.A. Gatzoulis, Pulmonary hypertension related to congenital heart disease: a call for action, Eur. Heart J. 35 (11) (2014) 691–700, https://doi.org/10.1093/eurheartj/eht437.

[12] B.M. Schaefer, M.B. Lewin, K.K. Stout, P.H. Byers, C.M. Otto, Usefulness of bicuspid aortic valve phenotype to predict elastic properties of the ascending aorta, Am. J. Cardiol. 99 (5) (2007) 686–690, https://doi.org/10.1016/j.amjcard.2006.09.118.

[13] S.H. Abman, G. Hansmann, S.L. Archer, et al., Pediatric pulmonary hypertension, Circulation 132 (21) (2015) 2037–2099, https://doi.org/10.1161/CIR.0000000000000329.

[14] A.V. LaRaia, A.B. Waxman, Pulmonary arterial hypertension: evaluation and management, South. Med. J. 100 (4) (2007) 393–399, https://doi.org/10.1097/SMJ.0b013e31802f2ff1.

[15] M. D'Alto, K. Dimopoulos, W. Budts, et al., Multimodality imaging in congenital heart disease-related pulmonary arterial hypertension, Heart 102 (12) (2016) 910–918, https://doi.org/10.1136/heartjnl-2015-308903.

[16] A. Pande, A. Sarkar, I. Ahmed, et al., Non-invasive estimation of pulmonary vascular resistance in patients of pulmonary hypertension in congenital heart disease with unobstructed pulmonary flow, Ann. Pediatr. Cardiol. 7 (2) (2014) 92, https://doi.org/10.4103/0974-2069.132475.

[17] J.H. Huston, B.A. Maron, J. French, et al., Association of mild echocardiographic pulmonary hypertension with mortality and right ventricular function, JAMA Cardiol 4 (11) (2019) 1112, https://doi.org/10.1001/jamacardio.2019.3345.

[18] K. Okumura, C. Slorach, D. Mroczek, et al., Right ventricular diastolic performance in children with pulmonary arterial hypertension associated with congenital heart disease, Circ Cardiovasc Imaging 7 (3) (2014) 491–501, https://doi.org/10.1161/CIRCIMAGING.113.001071.

[19] M.-J. Ploegstra, M.T.R. Roofthooft, J.M. Douwes, et al., Echocardiography in pediatric pulmonary arterial hypertension, Circ Cardiovasc Imaging 8 (1) (2015), https://doi.org/10.1161/CIRCIMAGING.113.000878.

[20] F.R. Olguntürk, An update on the diagnosis and treatment of pediatric pulmonary hypertension, Expet Opin. Pharmacother. 13 (2020) 1–15, https://doi.org/10.1080/14656566.2020.1757071. Published online May.

[21] H. Kaemmerer, M. Gorenflo, M. Hoeper, D. Huscher, P. Ewert, D. Pittrow, Pulmonalarterielle Hypertonie bei angeborenen Herzfehlern: problemstellung und Versorgungslage, DMW - Dtsch Medizinische Wochenschrift 138 (23) (2013) 1247–1252, https://doi.org/10.1055/s-0033-1343189.

[22] R. Neidenbach, K. Niwa, O. Oto, et al., Improving medical care and prevention in adults with congenital heart disease—reflections on a global problem—part II: infective endocarditis, pulmonary hypertension, pulmonary arterial hypertension and aortopathy, Cardiovasc. Diagn. Ther. 8 (6) (2018) 716–724, https://doi.org/10.21037/cdt.2018.10.16.

[23] R. Alonso-Gonzalez, C.J. Lopez-Guarch, M.T. Subirana-Domenech, et al., Pulmonary hypertension and congenital heart disease: an insight from the REHAP National Registry, Int. J. Cardiol. 184 (2015) 717–723, https://doi.org/10.1016/j.ijcard.2015.02.031.

[24] R.J. Barst, D.D. Ivy, A.J. Foreman, M.D. McGoon, E.B. Rosenzweig, Four- and seven-year outcomes of patients with congenital heart disease–associated pulmonary arterial hypertension (from the REVEAL registry), Am. J. Cardiol. 113 (1) (2014) 147–155, https://doi.org/10.1016/j.amjcard.2013.09.032.

[25] J.L. Wilkinson, Congenital heart disease: haemodynamic calculations in the catheter laboratory, Heart 85 (1) (2001) 113–120, https://doi.org/10.1136/heart.85.1.113.