



Case report

Partial anomalous pulmonary venous return: A case series with management approach

Karim El-Kersh^{a,*}, Elie Homsy^b, Curt J. Daniels^{c,d}, J. Shaun Smith^b

^a Department of Internal Medicine, Division of Pulmonary, Critical Care and Sleep Disorders Medicine, University of Louisville, Louisville, KY, USA

^b Department of Internal Medicine, Division of Pulmonary, Critical Care & Sleep Medicine, The Ohio State University Wexner Medical Center, USA

^c Department of Internal Medicine, Division of Cardiovascular Medicine, The Ohio State University Wexner Medical Center, USA

^d Department of Pediatrics, Division of Cardiovascular Medicine, Nationwide Children's Hospital, USA

ARTICLE INFO

Keywords:

PAPVR
PAH
CHD
ASD

ABSTRACT

Partial anomalous pulmonary venous return (PAPVR) is a rare congenital anomaly that results in a left-to-right shunt. Based on the shunt fraction, PAPVR has a wide spectrum of presentations. If a significant left-to-right shunt is left unrepaired, pulmonary vascular remodeling can occur resulting in the development of pulmonary arterial hypertension (PAH). Furthermore, if the condition is associated with an atrial septal defect (ASD), the patient can develop shunt reversal and Eisenmenger's syndrome in setting of severe PAH. Management plans include close observation, surgical repair, and treatment with pulmonary artery vasodilator therapies. Here, we present multiple cases of PAPVR to highlight the wide spectrum of presentations and the individualized treatment for each case.

1. Introduction

Anomalous pulmonary venous drainage was first described by Winslow in 1739 [1]. In partial anomalous pulmonary venous return (PAPVR), some of the pulmonary veins either drain into the systemic venous circulation or directly into the right atrium. This results in a left-to-right shunt that can have a wide spectrum of presentations. If a significant left to right shunt is left unrepaired, pulmonary vascular remodeling can occur resulting in the development of pulmonary arterial hypertension (PAH). Eventually, the patient can develop shunt reversal and Eisenmenger's syndrome if the PAPVR is associated with an atrial septal defect (ASD). Here, we present multiple cases of PAPVR highlighting a wide spectrum of presentations and their individualized treatment. (see [Table 1](#))

2. Cases

2.1. Case 1

A 42-year-old female presented for evaluation of pulmonary hypertension (PH). She had been experiencing a gradual increase in exertional dyspnea over the preceding two years with New York Heart Association functional class III (NYHA FC III) symptoms.

Transesophageal echocardiogram (TEE) showed moderate enlargement of the right ventricle (RV), mild RV hypokinesis, flattening of the septum, a right ventricular systolic pressure (RVSP) of 60 mmHg, a patent foramen ovale (PFO) and a 24mm sinus venosus ASD. Right heart catheterization (RHC) revealed step up in oxygen saturation at the level of right atrium with a calculated pulmonary-to-systemic flow ratio (Qp/Qs) of 2.3. The mean pulmonary artery pressure (mPAP) was 40 mmHg and the pulmonary vascular resistance (PVR) was 4.1 WU. Chest computed tomography (CT) with contrast revealed a persistent left superior vena cava (SVC) that was draining into a dilated coronary sinus and PAPVR of the right upper and right middle pulmonary veins at the junction of the right SVC and the right atrium (RA) ([Fig. 1](#)). The patient was started on tadalafil 40 mg PO daily and subsequently underwent surgical repair with ASD patch closure and baffling of the RV and RM PV to the left atrium and primary closure of the PFO. RV pressure at the end of her repair was 23/4 mmHg and she was weaned off tadalafil. On follow up three years later, the patient was asymptomatic with normal RV size and function and a normal RVSP.

2.2. Case 2

A 37-year-old female presented with progressive exertional dyspnea. TTE showed severe RV enlargement, septal flattening and normal

* Corresponding author. Department of Medicine, Division of Pulmonary, Critical Care and Sleep Disorders Medicine, Ambulatory Care Building, 550 S. Jackson Street, Louisville, KY, 40202, USA.

E-mail address: karim.elkersh@louisville.edu (K. El-Kersh).

<https://doi.org/10.1016/j.rmcr.2019.100833>

Received 12 January 2019; Accepted 28 March 2019

2213-0071/© 2019 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Table 1
Patients' characteristics.

Case	Age/Sex	Qp/Qs	mPAP & PVR	Anomalous vein	Draining into	Interatrial septal defect	Treatment
1	42 F	2.3	40 mmHg 4.1 WU	Right upper and right middle PVs	Right SVC/RA junction	Sinus venosus ASD and PFO	Surgical repair (3 years follow up post-surgery)
2	37 F	2.8	19 mmHg 2 WU	The left lung had only one LLL segmental branch that drained into the left atrium.	Left innominate V.	None.	Surgical repair (3 years follow up post-surgery)
3	20 F	0.7	45mmHg 8.46 WU	1) Post. Segment of RUL 2) Ant and apical segment RUL 3) Medial segment RML 4) Lateral segment of RML	1) SVC at the level of carina 2) Lat. Aspect of SVC just above RA 3) RA at cavoatrial junction	ASD	Ongoing transplant evaluation, currently on intravenous Treprostinil at 235ng/kg/min Tadalafil 40 mg Ambrisentan 10 mg (9 years on treatment)
4	21 M	1.8	14 mmHg 0.8 WU	RUL	SVC	PFO	Clinical monitoring.
5	66 F	1.4	17 mmHg 1.34 WU	RUL	SVC	None	Clinical monitoring.

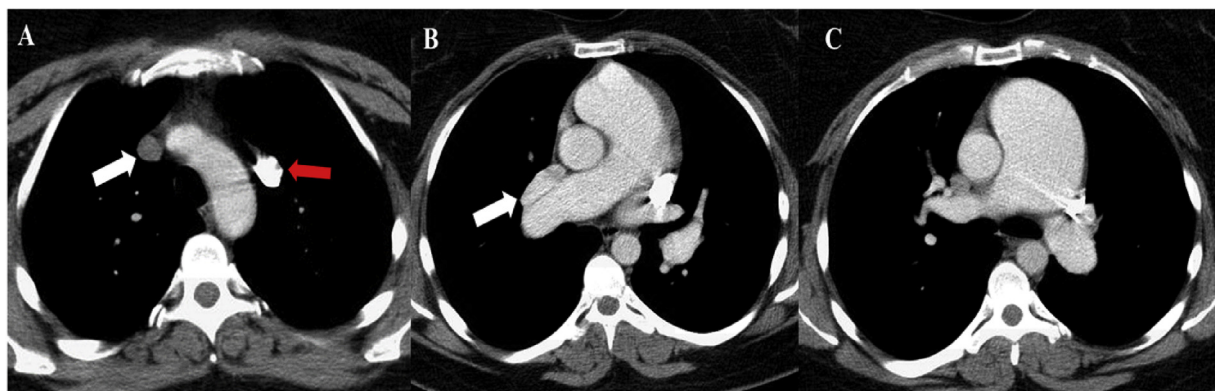


Fig. 1. CT chest with contrast shows A) Right sided SVC (white arrow) and left sided SVC (red arrow). B) PAPVR draining at the junction of right SVC and RA. C) Enlarged main pulmonary artery at 5.5 cm.

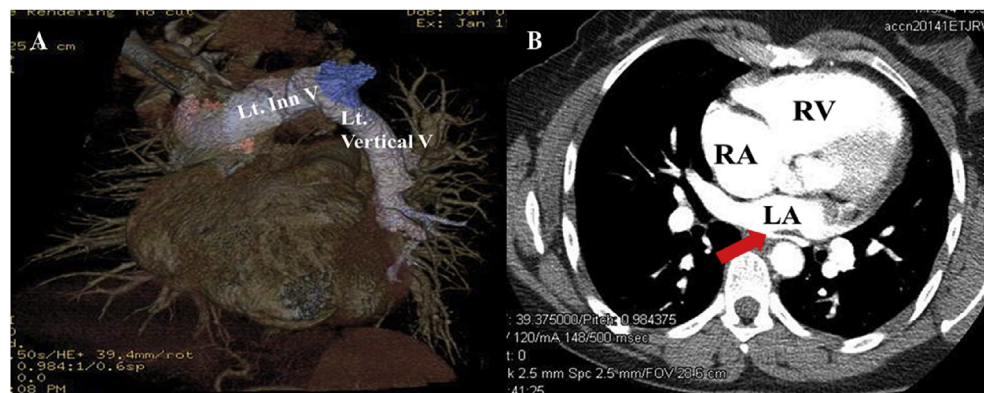


Fig. 2. Chest CT with contrast and 3D Reconstruction shows A) Near complete anomalous pulmonary venous return on the left. The left pulmonary veins drains into the left innominate vein at the upper mediastinum via left vertical vein. B) The left lung had only one left lower lobe segmental branch draining into the left atrium (red arrow).

RV systolic function. RHC showed normal pressures, however, the low SVC saturation was 95.4% consistent with left to right shunt. The calculated Qp/Qs ratio was 2.8. Chest CT with contrast demonstrated near complete anomalous pulmonary venous return of the left pulmonary veins. The left pulmonary veins drained into the left innominate vein at the upper mediastinum (Fig. 2). Both right-sided pulmonary veins had normal drainage into the left atrium. The patient underwent left lateral thoracotomy with ligation and division of the left vertical vein and anastomosis of the left pulmonary veins to the left atrial appendage. Her dyspnea resolved post operatively. Repeat TTE at 1 month after surgery showed a normal sized RA and RV and normal RV systolic function. The patient remained asymptomatic with normal echocardiography after three years of follow up.

2.3. Case 3

A 20-year-old female with a known sinus venosus ASD and PAH was referred for further evaluation. Four years prior to her presentation, she had been started on pulmonary artery vasodilator therapy that included tadalafil, ambrisentan and subcutaneous treprostinil and she was receiving warfarin for anticoagulation. At the time of her evaluation she was hypoxic with room air oxygen saturation of 85% and NYHA FC IV. TTE demonstrated a severely dilated and hypokinetic right ventricle. CT of the chest revealed three anomalous pulmonary veins (Fig. 3A and B). RHC revealed mPAP of 45 mmHg, PVR of 8.46 WU and Qp/Qs ratio of 0.7 consistent with Eisenmenger's physiology. The patient was referred for lung transplant evaluation. Oral pulmonary artery vasodilator

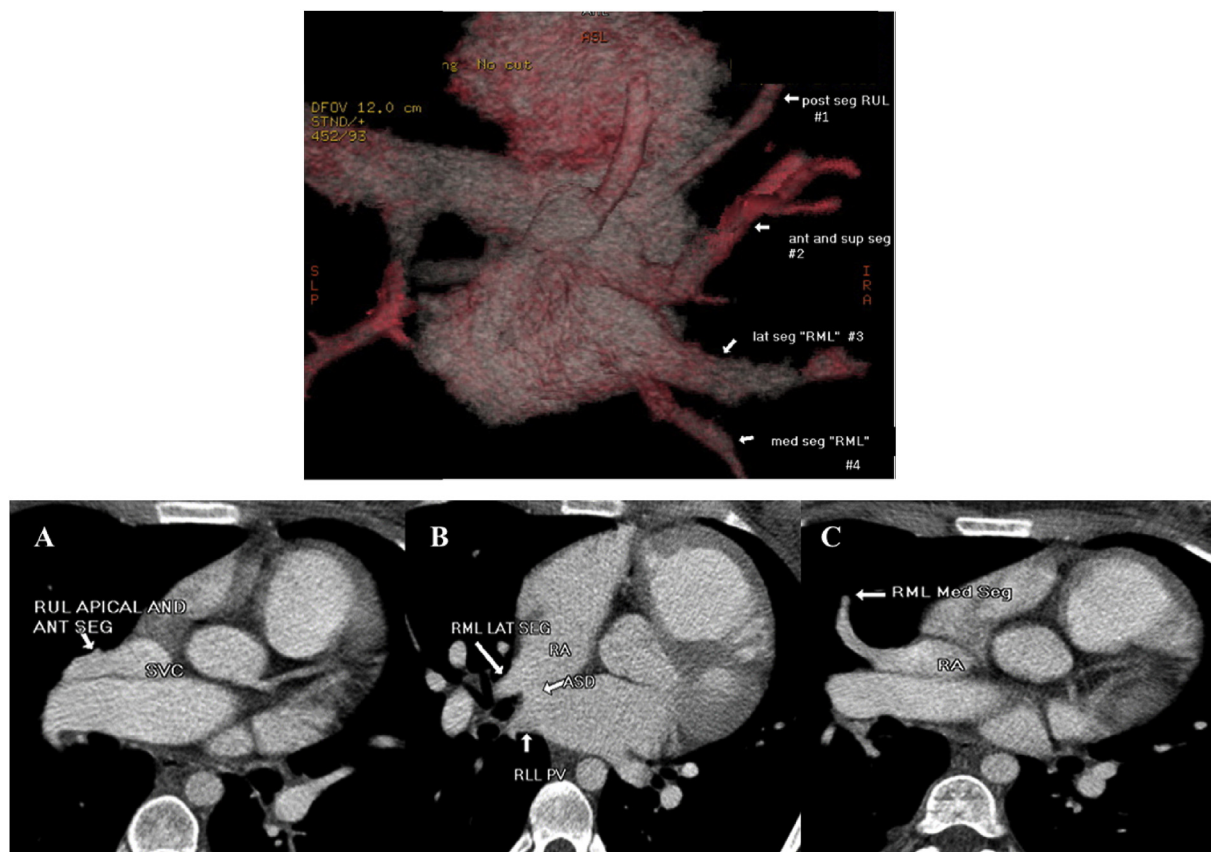


Fig. 3. A- Chest CT with contrast and 3D reconstruction shows the anomalous pulmonary veins. B-Chest CT with IV contrast shows anomalous pulmonary veins and ASD.

therapy was continued and treprostinil was transitioned to the intravenous route with subsequent up-titration. At five years of follow up, the patient had NYHA FC II/III symptoms on a treprostinil dose of 235 ng/kg/min and she is undergoing transplant evaluation.

2.4. Case 4

A 21-year-old male presented for evaluation of pulmonary hypertension after TTE showed moderate RV dilation with normal RV function, a flattened septum and a PFO. RHC showed normal pressures with a step up in oxygen saturation from 61.2% at the high SVC to 81.2% at the RA. The catheter was advanced into the pulmonary vein that was draining into the mid SVC and the oxygen saturation was noted to be 98.4%. The calculated Qp/Qs was 1.8. CT chest with three-dimensional reconstruction showed PAPVR from the right upper lobe to the mid SVC (Fig. 4A). The patient was referred for surgical repair evaluation but he elected not to undergo surgery at this point and favored close monitoring.

2.5. Case 5

A 66-year-old female presented for evaluation of dyspnea on exertion in the setting of moderate RV enlargement with mildly reduced function and an RVSP of 32 mmHg. RHC showed normal right sided pressures with a step up in oxygen saturation from 68% at the SVC to 82% at the RA. The catheter was advanced into the pulmonary vein that was draining into the mid SVC and the oxygen saturation was noted to be 96% there (Video 1). CT chest showed PAPVR from the right upper lobe to the mid SVC (Fig. 4B). The calculated Qp/Qs was 1.4. The patient was evaluated for surgical repair but due to advanced age and multiple comorbidities, she elected to forgo any invasive intervention in

favor of close monitoring.

Supplementary video related to this article can be found at <https://doi.org/10.1016/j.rmcr.2019.100833>.

3. Discussion

During embryogenesis, the left atrium and the pulmonary veins develop separately. The lung buds arise from the foregut and drain through a vascular bed into the cardinal and umbilicovitelline veins which are systemic veins. Outpouchings from the primitive atrium form the common pulmonary vein that then communicates with the pulmonary vascular bed [2]. Eventually, the connections between the pulmonary vascular bed and the systemic venous system regress. Failure of this process results in persistent partial or total anomalous pulmonary drainage into the systemic venous circulation [2].

While total anomalous venous return is a congenital heart disease that is detected in the newborn, PAPVR often goes undiagnosed as it can be asymptomatic in most cases. Autopsy series report that the incidence of PAPVR is 0.4% while a more recent retrospective study examining chest CTs identified PAPVR in only 0.1% of the examined images [3,4].

PAPVR can occur on either side or bilaterally. In 80–90% of cases, the PAPVR is right sided draining into the SVC and is usually associated with a sinus venosus ASD. It can also drain into the RA or into the inferior vena cava. The scimitar syndrome occurs when a right sided pulmonary vein drains into the IVC in association with hypoplasia of the right lung and right pulmonary artery and dextroposition of the heart [5–7]. In left sided PAPVR the anomalous vein usually drains into the left innominate vein via an anomalous vertical vein. In bilateral PAPVR, the interatrial septum may be intact if the drainage occurs into the left innominate vein and the SVC [5].

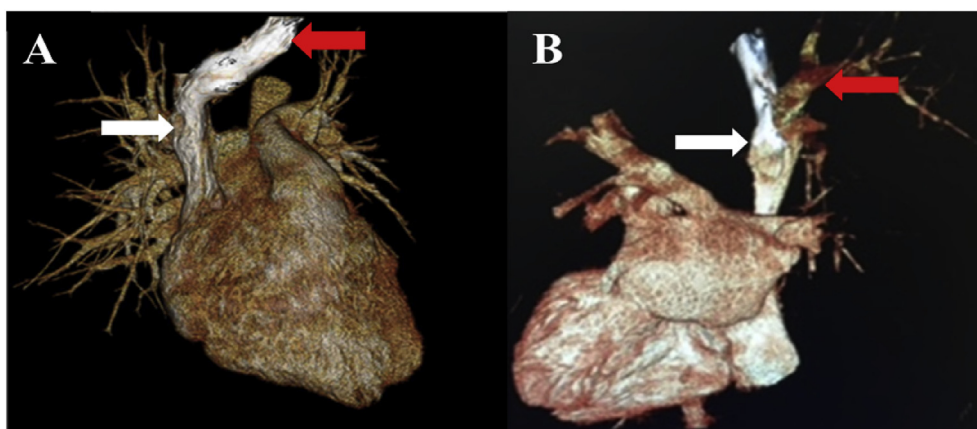


Fig. 4. A and B: Chest CT with contrast and 3D reconstruction shows PAPVR from RUL (red arrow) to mid SVC (white arrow).

$$\text{Oxygen consumption} = \text{blood flow} \times \text{A-V O}_2 \text{ difference across the organ} \quad (\text{A})$$

$$\text{Indexed pulmonary blood flow (Qp)} = \text{O}_2 \text{ consumption} / \text{PV sat} - \text{PA sat} \quad (1)$$

$$\text{Indexed systemic blood flow (Qs)} = \text{O}_2 \text{ consumption} / \text{Ao sat} - \text{MV sat} \quad (2)$$

$$\text{Qp/Qs} = \text{Ao sat} - \text{*MV sat} / \text{PV sat} - \text{PA sat}$$

$$\text{*MV sat} = (3 \text{ SVC}) + \text{IVC} / 4 \quad (\text{B})$$

Fig. 5. Calculation of Qp/Qs. Formula (1) and (2) can be derived from the oxygen consumption formula (A). Formula (B) is Flamm equation for mixed venous saturation. (PV: pulmonary vein, PA: pulmonary artery, Ao: Aorta, MV: mixed venous, sat: saturation) [8].

As demonstrated in our case series, patients with PAPVR can present at any age. The diagnosis is seldom made on transthoracic echocardiography due to poor visualization of the superior posterior atrial septum. Usually the only clue to the diagnosis is a step up in oxygen saturation during RHC. Important during right heart catheterization is to obtain a high SVC saturation above the innominate vein (pre-shunt saturation). Shunt fraction calculation is recommended when a step up in oxygen saturation is encountered during RHC (Fig. 5) as it can affect treatment decisions [8]. Occasionally, cannulating the anomalous vein itself during RHC is possible; however, any abnormal step up in oxygen saturation should be followed with cardiac magnetic resonance imaging (MRI) or a venous phase chest CT with contrast to accurately assess the anatomy of the shunt. Besides defining shunt anatomy, cardiac MRI can accurately quantify the shunt fraction and provide information regarding right ventricular size and function [9].

In the asymptomatic patients with low shunt fraction and no evidence of RV dysfunction, conservative management is recommended with close monitoring. Development of symptoms, RV enlargement, or presence of significant left to right shunt ($\text{Qp/Qs} > 1.5$) are the main indications for surgical repair which can lead to rapid and enduring cure [10,11]. Surgical outcomes for PAPVR are generally excellent with a low complication rate. The one exception is the scimitar syndrome where the complication rate is higher due to the complexity of the anatomy and the repair [5]. The most common postoperative complications are sinus node dysfunction and systemic or pulmonary venous stenosis [12].

With continued left to right shunt, pulmonary vascular remodeling can progress with subsequent increase of PVR and development of pulmonary hypertension. The 2015 and the 2018 pulmonary hypertension guidelines proposed PVR cut-off of 4.6 WU ($\text{PVRi} > 8 \text{ WU.m}^2$) for correction of congenital heart disease with prevalent systemic-to-pulmonary shunts [13,14]. Pulmonary vasodilators can be considered as a bridge to surgery but this “treat-and-repair approach” is still being investigated [15].

In patients with an indication for surgical repair of PAPVR, the 2018 adult congenital heart disease (ACHD) guidelines recommends the systolic PA pressure to be $< 50\%$ of the systemic pressure and the PVR to be $< 1/3$ of systemic vascular resistance. Patients who don't meet these criteria should be carefully evaluated by PH and ACHD experts [10].

Acute vasoreactivity test (AVT) can be used to assess PH reversibility during the evaluation of patients for potential operability. Although specific hemodynamic criteria for defining a positive AVT in adult PAH patients associated with shunt are lacking, special attention should be given to the PVR and not only to the pulmonary artery pressure [14]. For example, patients with significant shunt may respond to the vasodilator agent with a decrease in PVR and an increase in pulmonary flow resulting in no significant change in mean pulmonary artery pressure [16].

With continued vascular remodeling and further increase in PVR, shunt reversal may occur ($\text{Qp/Qs} < 1$) with development of Eisenmenger's physiology/syndrome in cases of PAPVR associated with

ASD. In this case surgical repair is contraindicated because of high surgical risk, the possibility of compromising cardiac output and inducing right heart failure and the low likelihood of reversal of severe pulmonary artery remodeling [15,17]. In this situation, pulmonary artery vasodilator therapies should be considered. This is supported by small studies that have shown symptomatic and hemodynamic benefits in patients with Eisenmenger's syndrome who were treated with pulmonary artery vasodilator therapies [18]. Lung transplantation with concomitant repair of cardiovascular defects or heart–lung transplantation can be considered in patients who continues to deteriorate despite optimized pulmonary artery vasodilator therapy [10]. In our experience with Eisenmenger's syndrome due to PAPVR and ASD, aggressive up-titration of pulmonary vasodilator therapy can improve functional status and delay the need for transplantation.

In conclusion, PAPVR is rare and it is often a silent congenital anomaly. In some patients, pulmonary over-circulation will eventually result in dyspnea with exertion and development of PAH. Evaluating patients for step up in oxygen saturation during the RHC is imperative to avoid misdiagnosing this potentially curable condition. Early surgical repair is the treatment of choice in symptomatic patients. In advanced cases with severe pulmonary hypertension, we recommend early and aggressive pulmonary vasodilator therapy.

Authors' disclosure

- Karim El-Kersh: Speaker; United Therapeutics.
- Curt J. Daniels: None.
- Elie Homsy: None
- J Shaun Smith: Speaker; Actelion Pharmaceuticals, Bayer, United Therapeutics, and Gilead Sciences.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

- [1] Winslow J. Mem. Acad. Roy. Sci. 1739:113.
- [2] L.A. Latson, L.R. Prieto, Congenital and acquired pulmonary vein stenosis, *Circulation* 115 (1) (2007) 103–108.
- [3] J.E. Healey Jr., An anatomic survey of anomalous pulmonary veins: their clinical significance, *J. Thorac. Surg.* 23 (1952) 433–444.
- [4] M.L. Ho, S. Bhalla, A. Bierhals, F. Gutierrez, MDCT of partial anomalous pulmonary venous return (PAPVR) in adults, *J. Thorac. Imaging* 24 (2009) 89–95.
- [5] B. Alsoufi, S. Cai, G.S. Van Arsdell, et al., Outcomes after surgical treatment of children with partial anomalous pulmonary venous connection, *Ann. Thorac. Surg.* 84 (2007) 2020.
- [6] M.G. Bourassa, The scimitar syndrome: report of two cases of anomalous venous return from a hypoplastic right lung to the inferior vena cava, *Can. Med. Assoc. J.* 88 (1963 Jan 19) 115–120.
- [7] F. Senocak, S. Ozme, A. Bilgic, S. Ozkutlu, S. Ozer, M. Saraçlar, Partial anomalous pulmonary venous return. Evaluation of 51 cases, *Jpn. Heart J.* 35 (1994) 43–50.
- [8] K. El-Kersh, M. Howsare, A. Zaidi, M.P. Flaherty, J.S. Smith, Pulmonary hypertension and atrial septal defect: management dilemma, *Am. J. Therapeut.* 24 (5) (2017) e602–e605 Sep/Oct.
- [9] K. Debl, B. Djavidani, S. Buchner, N. Heinicke, F. Poschenrieder, S. Feuerbach, G. Riegger, A. Luchner, Quantification of left-to-right shunting in adult congenital heart disease: phase-contrast cine MRI compared with invasive oximetry, *Br. J. Radiol.* 82 (977) (2009 May) 386–391.
- [10] K.K. Stout, C.J. Daniels, J.A. Aboulhosn, et al., 2018 AHA/ACC guideline for the management of adults with congenital heart disease: a report of the American college of cardiology/American heart association task force on clinical practice guidelines, *J. Am. Coll. Cardiol.* (2018) Aug 10. pii: S0735-1097(18)36846-3.
- [11] E.H. Sears, J.M. Aliotta, J.R. Klinger, Partial anomalous pulmonary venous return presenting with adult-onset pulmonary hypertension, *Pulm. Circ.* 2 (2) (2012 Apr-Jun) 250–255.
- [12] C. Pace Napoleone, E. Mariucci, E. Angeli, G. Oppido, G.D. Gargiulo, Sinus node dysfunction after partial anomalous pulmonary venous connection repair, *J. Thorac. Cardiovasc. Surg.* 147 (5) (2014 May) 1594–1598.
- [13] N. Galiè, M. Humbert, J.-L. Vachiery, et al., 2015 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension: the joint task force for the diagnosis and treatment of pulmonary hypertension of the European society of cardiology (ESC) and the European respiratory society (ERS): endorsed by: association for European paediatric and congenital cardiology (AEPC), international society for heart and lung transplantation (ISHLT), *Eur. Respir. J.* 46 (2015) 903–975.
- [14] E.B. Rosenzweig, S.H. Abman, I. Adatia, M. Beghetti, D. Bonnet, S. Haworth, D.D. Ivy, R.M.F. Berger, Paediatric pulmonary arterial hypertension: updates on definition, classification, diagnostics and management, *Eur. Respir. J.* (2018 Dec 13) 1801916, <https://doi.org/10.1183/13993003.01916-2018> ([Epub ahead of print]).
- [15] K. Dimopoulos, A. Peset, M.A. Gatzoulis, Evaluating operability in adults with congenital heart disease and the role of pretreatment with targeted pulmonary arterial hypertension therapy, *Int. J. Cardiol.* 129 (2) (2008 Sep 26) 163–171.
- [16] C. Apitz, G. Hansmann, D. Schranz, Hemodynamic assessment and acute pulmonary vasoreactivity testing in the evaluation of children with pulmonary vascular disease. Expert consensus statement on the diagnosis and treatment of paediatric pulmonary hypertension. The European Paediatric Pulmonary Vascular Disease Network, endorsed by ISHLT and DGPK, *Heart* 102 (Suppl 2) (2016 May) i223–i29.
- [17] M.A. Gatzoulis, R. Alonso-Gonzalez, M. Beghetti, Pulmonary arterial hypertension in paediatric and adult patients with congenital heart disease, *Eur. Respir. Rev.* 18 (113) (2009 Sep) 154–161.
- [18] R. Condliffe, P. Clift, K. Dimopoulos, R.M.R. Tulloh, Management dilemmas in pulmonary arterial hypertension associated with congenital heart disease, *Pulm. Circ.* 8 (3) (2018 Jul-Sep) 2045894018792501, Epub 2018 Jul 23.