10 Fetal Pulmonary Valvuloplasty: Natural History and Echocardiographic Evaluation of Critical Pulmonary Stenosis/Pulmonary Atresia with Intact Ventricular Septum

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Pulmonary atresia with intact ventricular septum (PAIVS) is a morphologically heterogeneous lesion characterized by variable dimensions of the right ventricle (RV) from a normal size to a variable degree of hypoplasia, often with associated anomalies of the coronary circulation. Critical pulmonary stenosis (CPS), also, is often present with an abnormal right ventricle.

Fetal diagnosis of PAIVS is relatively easy, although the differentiation between complete atresia and CPS may not be always feasible. The natural history of this complex anomaly diagnosed in utero and the predictors of neonatal outcome and of the type of postnatal correction (univentricular versus biventricular) are still objects of studies. The definition of anatomic features is fundamental for the prognosis and counseling in this anomaly.

10.1 Anatomic Features and Echocardiographic Evaluation

There is a wide anatomical spectrum involving all components of the RV.

Each echocardiographic examination should aim to:

- Achieve fetal biometry, calculation of C/T ratio, measures of the valves and ventricular chambers, and ratio of right to left heart dimensions including ventricular diameters and lengths and diameters of the atrioventricular valves and great arteries.

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- Assign *z*-scores for valvular and ventricular dimensions.[1]
- Study the flow across the cardiac valves and the interatrial septum, in the fetal umbilical artery and ductus venosus (DV) in the absence of fetal breathing or movements, using the color and pulsed wave Doppler.
- Evaluate the ductus arteriosus (DA) (morphology and the direction of the flow and systolic and diastolic velocities).

10.1.1 Tricuspid Valve (TV)

TV and mitral valve (MV) dimensions are measured at the hinge points at end-diastole, immediately before the closure of the atrioventricular valves; tricuspid-to-mitral valve (TV/MV) ratio and valve *z*-score are calculated.

The TV orifice is more frequently hypoplastic, sometimes associated with dysplasia of valve leaflets. The TV appears restricted in the opening because of an increased right ventricular pressure.

More rarely the TV may seem apparently normal, or with a dilated orifice, or may present Ebstein's malformation or dysplasia.

The tricuspid regurgitant (TR) jet is visible across the valve. Continuous wave or high-pulse repetition frequency Doppler records a high-velocity jet due to the raised right ventricular pressure. To assess its severity, the visual impression, the duration of the Doppler waveform in the cardiac cycle, and the extension of the regurgitant jet into the right atrium (RA) are considered. TR is graded as absent, mild, moderate, or severe (holosystolic trace extending into diastole, TR reaching the back of the RA) [1, 2]. See Fig. 10.1.

10.1.2 Right Atrium and Atrial Septum

RA enlargement is seen in the case of a moderate/severe TR and elevated right ventricular filling pressure.

Fetal assessment of the foramen ovale includes the evaluation of the septum mobility and the recording of the interatrial Doppler flow velocities: a poor mobility of the flap and a Doppler velocity >1.5 m/s indicate a restrictive communication.

Interrogation of the DV and inferior vena cava waveforms is used as indicator of raised systemic venous pressure and is estimated as normal in the presence of a positive end-diastolic velocity or abnormal if the end-diastolic flow is absent or reversed [3, 4].

Fetal right atrial pressure (RAP) score is calculated from the combination of the severity of TR, waveform characteristics of DV, and restriction of the interatrial septum, with each parameter having a score of 0–2 [5] (Table 10.1).

[1] *Z*-scores representing the number of standard deviations with respect to the data of the normal population for a given gestational age, derived from echocardiographic data – Boston criteria, *Circulation*. 2009;120(15):1482–1490.

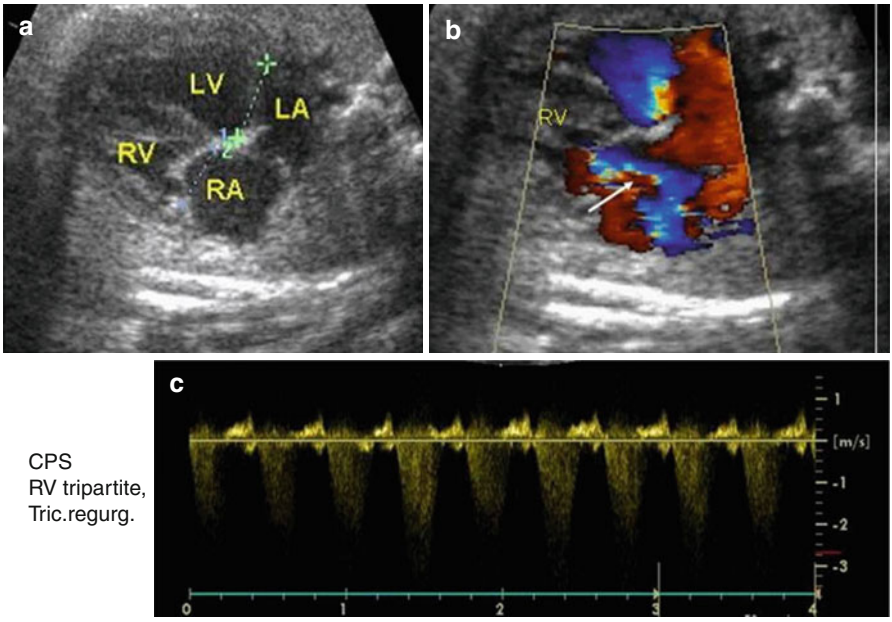


Fig. 10.1 Case with critical pulmonary stenosis with good RV (**a**), tricuspid regurgitation at color Doppler till the top of the right atrium (*RA*) in blue -arrow (**b**), and holosystolic regurgitant flow at pulsed Doppler. *LV* left ventricle, *LA* left atrium (**c**) Doppler gradient across the tricuspid valve

Table 10.1 RAP score

Points	0	1	2
Tricuspid regurgitation	None/mild	Moderate	Severe
Ductus venosus	Normal	Absent end-diastolic flow	Reversed end-diastolic flow
Foramen ovale	Normal right/left phasic flow velocities <1 m/s	Tense, bowing with moderate restriction; right/left velocities 1.0–1.5 m	Very restrictive Right/left velocities >1.5 m/s

10.1.3 Right Ventricle

The diameter of the RV is measured as the inlet length taken at closed TV from the midportion of the atrioventricular annulus to the apex of the RV at end diastole, in apical four-chamber view, to the endocardial surface [6].

The partiteness of the RV is morphologically evaluated by the number of parts of the RV not obliterated by trabecular muscular overgrowth:

- Tripartite: all three ventricular components – inlet, outlet, and trabecular – are present without intracavitary muscular overgrowth.
- Bipartite: overgrowth of the apical trabecular portion.
- Unipartite: muscular obliteration of both apical and infundibular portions.

The dimensions of the RV can worsen throughout the gestation to a pattern of a major hypoplasia with the RV progressively smaller in comparison with the left ventricle (LV). Parietal and trabecular RV hypertrophy is evident in this case and the right to left wall thickness is >1 [7]. Significant endocardial fibroelastosis is uncommon.

A septal displacement into the LV outflow tract may be present, and, when this bowing is extremely pronounced, an impairment of the left ventricular filling and function is possible.

More rarely a significant RV dilation with thin walls is observed, associated with a moderate or severe TR.

10.1.4 Pulmonary Valve (PV)

Differential diagnosis between pulmonary atresia and critical pulmonary stenosis (CPS) is difficult. In some cases severe pulmonary stenosis can progress to pulmonary atresia during the prenatal period [8–10].

Among different types of atresia, valvular atresia is more commonly *membranous* (in about 75%), due to a complete fusion of the valve leaflets with a patent infundibulum existing in the latter setting up to the level of the valvular tissue. At echocardiography this valve is visible also during the systole with a potential for a continuity between the RV and pulmonary trunk.

In a minority of cases, a *muscular* atresia with infundibular obliteration is present, without echocardiographic continuity between the RV and the pulmonary trunk.

In the cross-sectional view of the great vessels, a retrograde flow through the ductus confirms the diagnosis.

In the CPS the valvular orifice is reduced by the fusion of the commissures of the valve, thickened and doming. An accelerated forward pulmonary blood flow can be detectable, in addition to the reversed flow from the DA at color Doppler, in severe cases. See Fig. 10.2.

All vessel measurements are estimated at their maximum dimensions, at the end of systole, and *z*-score is calculated. Pulmonary/aorta ratio is obtained at the level of the annulus of both vessels. The PV and pulmonary trunk are usually smaller than normal for gestational age and of aortic annulus.

The pulmonary arteries are confluent ranging from slightly smaller dimensions in comparison with the normal values to a severe hypoplasia and are usually supplied in the fetal life in a retrograde way from the DA.

10.1.5 Ductus Arteriosus

An acute angled ductus tends to arise more proximally from the aortic arch than usual. The flow at color Doppler is interrogated – showing a total retrograde flow toward the valvular plane in the case of PAIVS (see Fig. 10.3) and a partial component of an anterograde flow in the case of CPS.

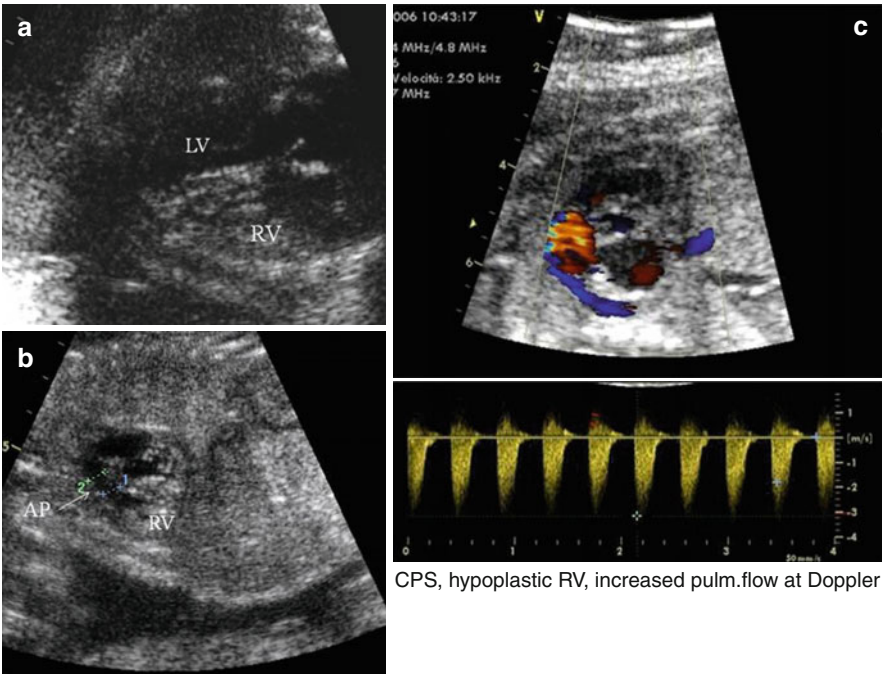


Fig. 10.2 Case with critical pulmonary stenosis with hypoplastic RV (**a**), small pulmonary valve annulus (**b**), and increased pulmonary flow at Doppler (**c**)

10.1.6 Ventriculocoronary Connections (VCCs)

Coronary artery anomalies in PAIVS include RV-to-coronary artery fistulae and/or coronary artery stenosis and occlusions.

VCCs occur as a persistence of the primitive connections in the condition of a high pressure, from the RV to the aorta in systole and from the aorta to the RV in diastole. They are reported both in cases of PAIVS and CPS [11].

VCCs are more frequent in cases with RV hypoplasia (z-score < -3) and major hypoplasia of the main pulmonary artery and the sigmoid shape of the DA [11, 12].

RV-to-coronary artery fistulae have been reported to occur in 31–68 % of patients with PAIVS [13–15].

RV-dependent coronary circulation (RVDCC) is defined by:

1. The presence of ventriculocoronary fistulae with severe obstruction of at least two major coronary arteries
2. Complete aortocoronary atresia
3. Situations in which a significant portion of the LV myocardium is supplied by the RV

PAIVS, reversed flow from the duct

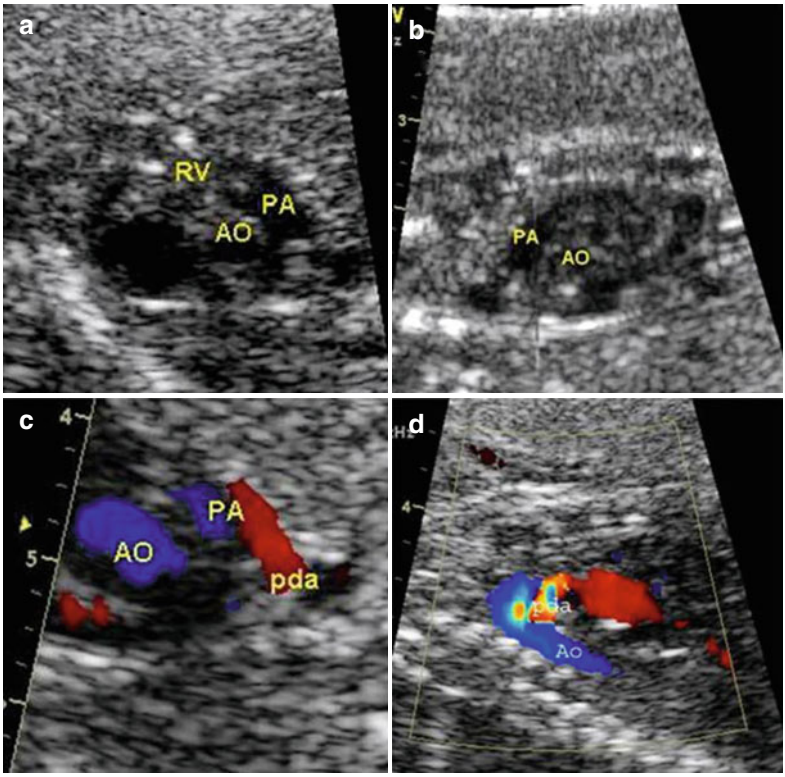


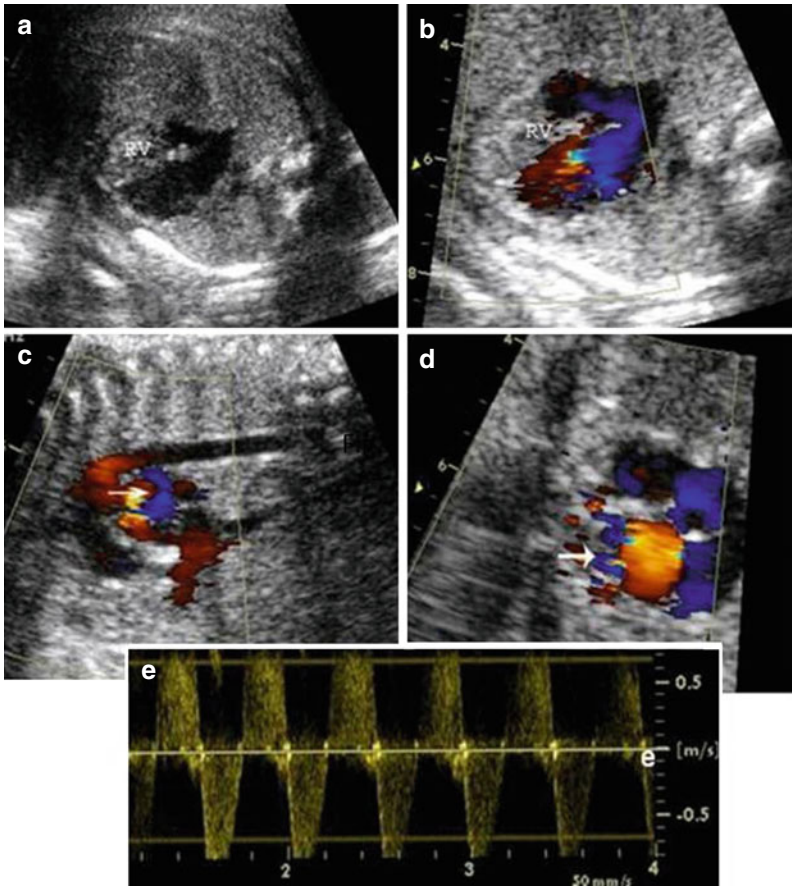
Fig. 10.3 Two-D echocardiographic images (**a** and **b**). Case with pulmonary atresia and intact septum (PAIVS) and reversed pulmonary flow from the duct at color Doppler – in *red* (**c**, **d**). *PA* pulmonary artery, *Ao* aorta, *pda* ductus arteriosus

RVDCC may cause RV "steal" in the presence of fistulae alone and ischemia, coronary isolation, or myocardial infarction in the presence of coronary stenosis [13, 16].

The coronary stenosis is usually not detectable prenatally by echocardiography, while a more precise evaluation of the VCCs is possible by a postnatal angiography.

Echocardiographic Evaluation The evaluation of the fetal coronary circulation is now possible with high-resolution 2-D imaging and with new color Doppler techniques.

The coronary arteries in normal heart are difficult to detect by fetal echocardiography. In PAIVS or CPS, the systematic evaluation to assess VCCs involves scanning the aortic root and the right ventricular myocardium using color Doppler mapping with a low-velocity setting.



PAIVS,
+
sinusoids

Fig. 10.4 Case of PAIVS and hypoplastic RV (**a**, **b**), reversed flow from the duct (**c**), and turbulent flow at color Doppler due to sinusoids (**d**), with systodiastolic flow at pulsed Doppler (**e**)

When turbulent color signal is identified only on the epicardial surface of the myocardium and within trabeculations of the RV, *minor fistulae or sinusoids* may be suspected (see Fig. 10.4). In this case there is a connection between trabeculations of the RV and coronary capillaries with a slight filling of nondilated coronary arteries. In the presence of intracavitary right ventricular connections, the coronary turbulent diastolic flow pattern is best seen at the transverse section of the fetal heart, immediately over the five-chamber view, but sometimes this flow is difficult to record.

The existence of a VCC between the right ventricle and right coronary artery (*mayor fistulae*) is suspected when a dilated vessel along the right ventricular wall is observed, and color flow imaging reveals that this blood flow arises from the

aortic root and faces the right ventricular chamber. The pulsed Doppler interrogation shows a forward diastolic and reversed systolic flow.

Multiple VCCs with the possibility of RVDCC are suspected when other abnormal blood flows are found between the right ventricular wall and the left coronary artery [13, 17–19].

10.1.7 Other Abnormalities

LV: very rarely, it is possible to observe spongiform noncompactile interventricular septum, dysplastic MV, or concentric LV hypertrophy [20].

Also left superior caval vein, right aortic arch, and aberrant subclavian artery are rarely described.

Associated extracardiac or chromosomal anomalies are reported: chromosome 22 deletion and, rarely, chromosome 4p deletion and Dandy-Walker syndrome [20, 21].

10.2 Natural History

When the right heart is small in the second and third trimester, its dimensions can worsen during the remaining gestation to a pattern of a major degree hypoplasia. Equally, severe pulmonary valvular stenosis can progress to a complete atresia [22].

The possibility of the development of a hypoplastic RV led to the idea of performing an early valvuloplasty already in utero with the aim of making possible a postnatal biventricular repair: the selection criteria of cases and the results obtained until now will be treated in a specific chapter.

Severe anomalies of the tricuspid valve as Ebstein or non-Ebstein anomaly with important valvular regurgitation may predispose to the hydrops fetalis and intrauterine death [23].

Fetal growth may be restricted in some cases of PAIVS and CPS.

Failed differentiation between CPS and PAIVS in fetal life will not in any case affect the prenatal and postnatal management of the case, because of a similar strategy.

10.2.1 Postnatal Treatment

Postnatally, a ductus-dependent circulation with desaturation and cyanosis is present, often with a need of a respiratory assistance. The first procedure after birth is the prostaglandin treatment. Then, after a reevaluation of the cardiac features, the decision is taken with regard to the possibility of the RV decompression in suitable cases (without VCCs), by means of pulmonary valvuloplasty, usually with the need of radiofrequency opening of the valve, establishing so the RV-PA continuity with a potential for the subsequent RV and TV growth. Otherwise, systemic pulmonary

shunt is performed, in alternative to the ductal stenting. This approach may be needed also after the valvuloplasty, if the arterial saturation does not improve, due to inadequacy of the RV to provide a valid pulmonary flow [24].

A disproportional growth of the tricuspid valve with respect to the somatic growth can occur, especially in patients with small tricuspid valves and lower right ventricular pressures after decompression [25].

The size of the TV and RV will determine the type of the final repair – the possibility of a Fontan operation. Long-term outcome after Fontan is comparable to other complex cardiac anomalies treated this way.

Management of Cases with VCCs A main surgical option is the creation of a systemic-to-pulmonary shunt. However, there is a rather relevant postnatal mortality due to ischemia/coronary events, in these cases. Subsequently, a single-ventricle palliation provides a good long-term clinical outcome even in this category of patients [26]. In some cases, however, there may be a progression of the size and numbers of coronary fistulae at the long term, with clinical symptomatology of ischemia at exercise, and this should be kept in mind.

More rarely, an option of the tricuspid valve closure is chosen [27].

10.2.2 Predictors for the Postnatal Outcomes and Treatment

Different studies have used tricuspid and pulmonary valve fetal *z*-scores to predict a postnatal biventricular or univentricular repair.

For Gardiner et al. [5], the TV *z*-score was a good predictor in all cases studied, but the best predictive scores for a postnatal biventricular repair were the PV *z*-score > −1 and the median TV *z*-score > −3.4 before 23 weeks, the median TV score > −3.95 before 26 weeks, the combination of median PV *z*-score and the median TV/MV ratio (at 26–31 weeks), and the combination of median TV *z*-score and median TV/MV ratio (>31 weeks). The RAP score and the evidence of coronary fistulae were good independent predictors: RAP score > 3 predicted biventricular repair, and the detection of fistulae usually predicted a univentricular route.

In the study of Salvin et al. [11] on 13 fetuses with a midgestation fetal TV *z*-score < −3, only 1 achieved biventricular repair, compared with 5 of 5 with a TV *z*-score > −3. Of 13 fetuses with a midgestation fetal TV *z*-score < −3, 8 were diagnosed postnatally with a right ventricular-dependent coronary circulation, compared with none who had a TV *z*-score > −3.

The average rate of TV growth between mid- and late fetal echocardiograms was significantly lower in patients who did not achieve biventricular repair.

The presence of TR was found to be a good predictor of a better outcome with a biventricular repair, having these fetuses larger RV dimensions, without VCCs [28]. This is in agreement with the study of Peterson et al. [29], who suggest that TR can facilitate the growth of the RV and TV despite the pulmonary atresia. Also, in this study, both a fetal TV *z*-score of −4 or less beyond 23 weeks of gestation and a fetal

TV annulus of 5 mm or less beyond 30 weeks of gestation were predictive of poor postnatal outcomes. In addition, right/left ventricular length or width less than 0.5 and/or the absence of TR were predictive of poor outcome.

Roman et al. [30] suggested a four-criteria scoring system to predict the postnatal outcome of PAIVS/CPS. They found the best sensitivity and specificity for a non-biventricular outcome as follows: TV/MV ratio <0.7, RV/LV length ratio <0.6, TV inflow duration <31.5 % of cardiac cycle length, and the presence of RV sinusoids. If three of these four criteria were fulfilled, this predicted a non-biventricular outcome with sensitivity of 100 % and specificity of 75 %.

In conclusion, the echocardiographic diagnosis of PAIVS/CPS is feasible. However, as reported above, both outcomes and management are still under evaluation.

References

1. Bolger AF, Eigler NL, Maurer G. Quantifying valvular regurgitation. Limitations and inherent assumptions of Doppler techniques. Circulation. 1988;78:1316–8.
2. Rivera JM, Vandervoort PM, Vazquez de Prada JA, et al. Which physical factors determine tricuspid regurgitation jet area in the clinical setting? Am J Cardiol. 1993;72:1305–9.
3. Kiserud T, Eik-Nes. SH, Blaas HG, Hellevik LR. Ultrasonographic velocimetry of the fetal ductus venosus. Ultrasound Obstet Gynecol. 1991;338:1412–4.
4. DeVore GR, Horenstein J. Ductus venosus index: a method for evaluating right ventricular preload in the second-trimester fetus. Ultrasound Obstet Gynecol. 1993;3:338–42.
5. Gardiner HM, Belmar C, Tulzer G, Barlow A, Pasquini L, Carvalho JS, Daubeney PE, Rigby ML, Gordon F, Kulinskaya E, Franklin RC. Morphologic and functional predictors of eventual circulation in the fetus with pulmonary atresia or critical pulmonary stenosis with intact septum. J Am Coll Cardiol. 2008;51(13):1299–308.
6. Tan J, Silverman NH, Hoffman JIE, Villegas M, Schmidt KG. Cardiac dimensions determined by cross-sectional echocardiography in the normal human fetus from 18 weeks to term. Am J Cardiol. 1992;70:1459–67.
7. Hornberger LK, Benacerraf BR, Bromley BS, Spevak PJ, Sanders SP. Prenatal detection of severe right ventricular outflow tract obstruction: pulmonary stenosis and pulmonary atresia. J Ultrasound Med. 1994;13:743–50.
8. Gardiner HM. Progression of fetal heart disease and rationale for fetal intracardiac interventions. Semin Fetal Neonatal Med. 2005;10:578–85.
9. Shinebourne EA, Rigby ML, Carvalho JS. Pulmonary atresia with intact ventricular septum: from fetus to adult. Heart. 2008;94:1350–7.
10. Sharland GK, Tynan M, Qureshi SA. Prenatal detection and progression of right coronary artery to right ventricle fistula. Heart. 1996;76:79–81.
11. Salvin JW, McElhinney DB, Colan SD, Gauvreau K, del Nido PJ, Jenkins KJ, Lock JE, Tworetzky W. Fetal tricuspid valve size and growth as predictors of outcome in pulmonary atresia with intact ventricular septum. Pediatrics. 2006;118:e415–20.
12. Maeno YV, Boutin C, Hornberger LK, McCrindle BW, Cavallé-Garrido T, Gladman G, Smallhorn JF. Prenatal diagnosis of right ventricular outflow tract obstruction with intact ventricular septum, and detection of ventriculocoronary connections. Heart. 1999;81:661–8.
13. Giglia TM, Mandell VS, Connor AR, Mayer JE, Lock JE. Diagnosis and management of right ventricle-dependent coronary circulation in pulmonary atresia with intact ventricular septum. Circulation. 1992;86:1516–28.
14. Calder AL, Co EE, Sage MD. Coronary arterial abnormalities in pulmonary atresia with intact ventricular septum. Am J Cardiol. 1987;59:436–42.

15. Powell AJ, Mayer JE, Lang P, Lock JE. Outcome in infants with pulmonary atresia, intact ventricular septum, and right ventricle-dependent coronary circulation. Am J Cardiol. 2000;86:1272–4.
16. Guleserian KJ, Armsby LB, Thiagarajan RR, del Nido PJ, Mayer Jr JE. History of pulmonary atresia with intact ventricular septum and right-ventricle-dependent coronary circulation managed by the single-ventricle approach. Ann Thorac Surg. 2006;81:2250–8.
17. Cha HH, Choo YS, Seong WJ. Prenatal diagnosis of multiple ventriculocoronary connections in pulmonary atresia with an intact ventricular septum: a case report. J Obstet Gynaecol Res. 2015;41:1278–81.
18. Chaoui R, Tennstedt C, Goldner B, Bollmann R. Prenatal diagnosis of ventriculo-coronary communications in second-trimester fetus using transvaginal and transabdominal color Doppler sonography. Ultrasound Obstet Gynecol. 1997;9:194–7.
19. Sandor GG, Cook AC, Sharland GK, Ho SY, Potts JE, Anderson RH. Coronary arterial abnormalities in pulmonary atresia with intact ventricular septum diagnosed during fetal life. Cardiol Young. 2002;12:436–44.
20. Daubeney PEF, Delany DJ, Anderson RH, et al. Pulmonary atresia with intact ventricular septum: range of morphology in a population-based study. J Am Coll Cardiol. 2002;39:1670–9.
21. Vesel S, Rollings S, Jones A, Callaghan N, Simpson J, Sharland GK. Prenatally diagnosed pulmonary atresia with ventricular septal defect: echocardiography, genetics, associated anomalies and outcome. Heart. 2006;92:1501–5.
22. Todros T, Presbitero P, Gagliotti P, Demarie D. Pulmonary stenosis with intact ventricular septum: documentation of development of the lesion echocardiographically during fetal life. Int J Cardiol. 1988;19:355–60.
23. Song TB, Lee JY, Kim YH, Oh BS, Kim EK. Prenatal diagnosis of severe tricuspid insufficiency in Ebstein's anomaly with pulmonary atresia and intact ventricular septum: a case report. J Obstet Gynaecol Res. 2000;26:223–6.
24. Mallula K, Vaughn G, El-Said H, Lamberti JJ, Moore JW. Comparison of ductal stenting versus surgical shunts for palliation of patients with pulmonary atresia and intact ventricular septum. Catheter Cardiovasc Interv. 2015;85:1196–202.
25. Huang SC, Ishino K, Kasahara S, Yoshizumi K, Kotani Y, Sano S. The potential of disproportionate growth of tricuspid valve after decompression of the right ventricle in patients with pulmonary atresia and intact ventricular septa. J Thorac Cardiovasc Surg. 2009;138:1160–6.
26. Yoshimura N, Yamaguchi M. Surgical strategy for pulmonary atresia with intact ventricular septum: initial management and definitive surgery. Gen Thorac Cardiovasc Surg. 2009;57:338–46.
27. Waldman JD, Karp RB, Lamberti JJ, Sand ME, Ruschhaupt DG, Agarwala B. Tricuspid valve closure in pulmonary atresia with important RV-to-coronary artery connections. Ann Thorac Surg. 1995;59:933–41.
28. Iacobelli R, Pasquini L, Toscano A, Raimondi F, Michielon G, Tozzi AE, Sanders SP. Role of tricuspid regurgitation in fetal echocardiographic diagnosis of pulmonary atresia with intact ventricular septum. Ultrasound Obstet Gynecol. 2008;32:31–5.
29. Peterson RE, Levi DS, Williams RJ, Lai WW, Sklansky MS, Drant S. Echocardiographic predictors of outcome in fetuses with pulmonary atresia with intact ventricular septum. J Am Soc Echocardiogr. 2006;19:1393–400.
30. Roman KS, Fouron JC, Nii M, Smallhorn JF, Chaturvedi R, Jaeggi ET. Determinants of outcome in fetal pulmonary valve stenosis or atresia with intact ventricular septum. Am J Cardiol. 2007;99:699–703.