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Ductus arteriosus and fetal echocardiography: Implications for practice

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ABSTRACT

The ductus arteriosus (DA) is a crucial part of the fetal circulation, both in the normal fetus and in critical congenital heart disease (CHD). It allows shunting between the pulmonary and systemic circulations. In physiological prenatal conditions, the DA lets the majority of right ventricular output bypass the fluid-filled, high-resistance lungs. The DA can cause hemodynamic compromise in the fetus and neonate when constricted or absent (in isolation or in patients with CHD) and may lead to pre- or postnatal sequelae within other systems when forming part of a vascular ring. In CHD, the DA can be interrogated by fetal echocardiography to infer information regarding severity of pulmonary outflow tract obstruction, adequacy of the sub-pulmonary ventricle to supply pulmonary blood flow, and to predict the likelihood of atrial septum restriction in transposition of the great arteries. A good understanding of the DA is crucial for fetal cardiologists.

1. Embryology

The ductus arteriosus (DA) is formed between the sixth and eighth weeks of gestation, after the right and left pulmonary arteries arise from the proximal end of the sixth branchial arch [1]. In normal hearts, the distal portion of the left sixth arch will not regress (in contrast to the right sixth arch) and a communication between the dorsal aorta and the pulmonary trunk remains, forming the DA. Less usually, the opposite occurs and there is a right DA instead.

2. Morphology/histology

In fetuses with normal anatomy, the DA is a direct continuation of the main pulmonary artery to the descending aorta [2]. The DA connects to the aorta just after the origin of the left subclavian artery. The location of DA insertion defines the inferior margin of the aortic isthmus. The fetal DA is of similar calibre to the descending aorta [3]. The DA is funnel-shaped, with the pulmonary artery end smaller than the aortic end [4]. During the course of pregnancy, it becomes longer, wider, and increasingly curved, and by the late third trimester most will have a markedly curved shape [4,5]. The media of the DA are composed primarily of smooth muscle, in contrast with the media of the pulmonary artery and aorta, which are comprised mainly of elastin [2]. In the third trimester, intimal cushions form due to smooth muscle cell proliferation and migration to the subendothelium [6].

Contraction of the muscle fibers in the media of the DA results in narrowing of the lumen and shortening of this structure, leading to functional closure, which usually occurs within 48 h of birth [3]. The process of DA constriction commences at the pulmonary end of the vessel [3].

3. Physiology

3.1. Fetus

Well-oxygenated blood from the placenta preferentially streams across the atrial septum to the left heart, and the right ventricle receives relatively poorly oxygenated blood. Animal and human studies have shown that approximately 80–90% of right ventricular output will pass through the DA with the remainder going into the pulmonary artery branches to ensure pulmonary irrigation and development [7]. The right ventricle supplies the vast majority of flow to the placenta via the DA [3]. The volume of blood passing through the DA increases exponentially as gestation advances [7].

Multiple factors are responsible for DA patency in utero. Prenatal ductal vasodilators include the relatively low arterial partial pressure of oxygen (PaO_2), circulating prostaglandins (particularly PGE_2) from the placenta, locally produced prostaglandin, and nitric oxide from the DA [3,6,8].

Normal ductal flow in utero is from right to left throughout the cardiac cycle and is biphasic, with a peak systolic velocity of 50–140 cm/s, end-diastolic velocities of 6–30 cm/s (these parameters increase with gestational age), and pulsatility index of 1.9–3 (throughout pregnancy) [9,10]. In the normal fetus, the DA is

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unrestrictive and therefore flow through the vessel is dictated by the relative differences in systemic versus pulmonary vascular resistance [3]. The fetal DA has a higher peak systolic blood flow velocity than in any other part of the cardiovascular system [9].

3.2. Neonates

In normal babies, the transition from the fetal to neonatal circulation starts with clamping of the umbilical cord (resulting in separation from the low-resistance placental circulation and a reduction in circulating prostaglandins), expansion and increased perfusion of the lungs (leading to inactivation of circulating prostaglandins, a fall in pulmonary vascular resistance, and a rise in PaO_2) [11]. The degree of shunting via the DA is determined by its diameter, shape, length, elasticity, and the relative differences in systemic versus pulmonary vascular resistance. In the few hours after birth the DA might demonstrate bidirectional shunting, but as the pulmonary vascular resistance decreases, the shunt becomes solely left-to-right. This change leads to higher PaO_2 levels in the DA, which, in addition to the decrease in prostaglandin levels, results in DA constriction by means of contraction of the smooth muscle of the media [8,11].

Functional closure of the DA occurs within the first 72 h of life in the vast majority of term babies [12]. Beyond that it may be defined as a persistent patent ductus arteriosus (PDA). Anatomical closure follows within two to three weeks, by means of necrosis and fibrosis (triggered by cessation of flow within the lumen) leaving behind a structure named the ligamentum arteriosum [3].

4. Assessing the normal DA by fetal echocardiography

The DA forms part of the ductal arch, which can be demonstrated in the sagittal plane (Fig. 1). The ductal arch view demonstrates the main pulmonary artery arising from the right ventricle anteriorly, giving rise to the DA, which connects to the descending aorta. This ductal arch differs from the aortic arch in its morphology – the aortic arch has a tighter curve, arises more posteriorly within the heart (from the left ventricle) and gives rise to the head and neck vessels. The DA can also be seen in the cross-sectional plane as part of the three-vessel view (Fig. 2). This view was originally proposed by Yoo, and modified by Yagel to include the trachea and a transverse section of the aortic arch [13,14]. This view can be easily attained and the International Society of Ultrasound in Obstetrics and Gynecology now recommend that it is attempted as part of low-risk cardiac screening performed between 18 and 22 weeks gestational age.

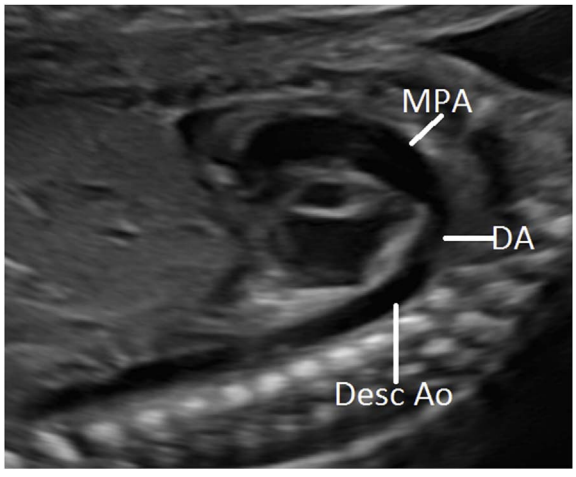

Fig. 1. Sagittal image demonstrating the ductal arch: the main pulmonary artery (MPA) leads through to the descending aorta (Desc Ao) via the arterial duct (DA).

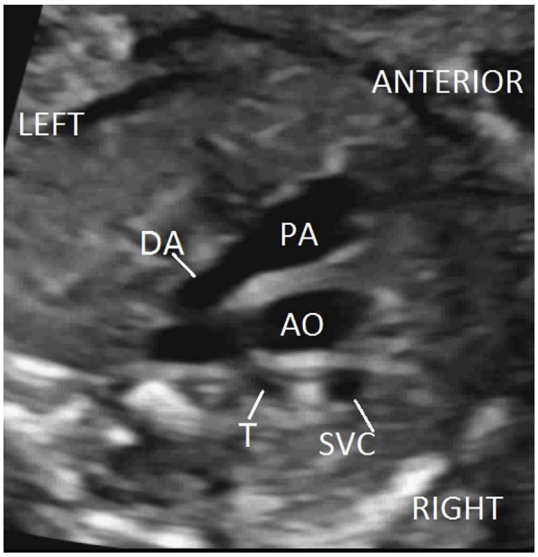

Fig. 2. Cross-sectional view showing the three-vessel and trachea view. The vessels (from left to right and anterior to posterior) are: pulmonary artery (PA), aorta (AO) and superior vena cava (SVC). The PA continues posteriorly via the duct (DA) and joins with the aorta to the left of the trachea (T).

4.1. In-utero pathologies of the DA with normal intracardiac anatomy

Fetal echocardiography can be used for diagnosis and surveillance of pathologies of the DA.

4.2. Constrictive DA (incidence, causes, fetal findings, neonatal physiology, neonatal echo findings, neonatal management, and outcome)

Intrauterine constriction of the DA is a relatively rare diagnosis and most often occurs in the third trimester of pregnancy [15,16]. Milder forms are most likely under-ascertained, with prenatal diagnosis usually made only in moderate/severe cases with secondary pathology detected on obstetric scanning, or in patients at high risk due to ingestion of substances known to cause ductal constriction. A recent retrospective study reported the diagnosis of complete fetal DA closure in 1.3% of 602 cases referred for echocardiography due to suspected abnormality of the heart or great vessels [17].

Ductal constriction is often idiopathic; however, in the majority of reported cases it has been associated with maternal exposure to prostaglandin synthase inhibitors, e.g. non-steroidal anti-inflammatory drugs or corticosteroids or intake of polyphenol-rich foods such as green tea, dark chocolate, and grape juice [15,18–20]. The likelihood of ductal constriction increases with advancing gestational age, with a sharp increase in risk occurring from 32 weeks of gestation [16].

Prenatal constriction of the DA exposes the right ventricle (RV) to the relatively high fetal pulmonary vascular resistance, which may lead to right heart failure, and results in increased pulmonary blood flow, which may lead to remodelling of the pulmonary vascular bed or to dilation of the pulmonary arteries [21]. Histological examination in cases of prenatal DA constriction have demonstrated pulmonary artery dilation with medial hypertrophy and intimal proliferation [22,23].

On fetal echo assessment of the DA itself, findings include a small diameter, aliasing of flow on colour Doppler, and high systolic and diastolic Doppler velocities ($>$ 95th percentiles for gestational age) with a decreased pulsatility index ($<$ 1.9) [10,24]. Secondary fetal echo findings include: cardiomegaly, dilation of the right atrium, RV and pulmonary artery, RV hypertrophy and dysfunction, and high-velocity tricuspid and pulmonary valve regurgitation [17,19,25,26]. Ductal constriction may lead to RV failure, signaled by short duration monophasic RV inflow Dopplers, abnormal systemic venous Doppler, and an

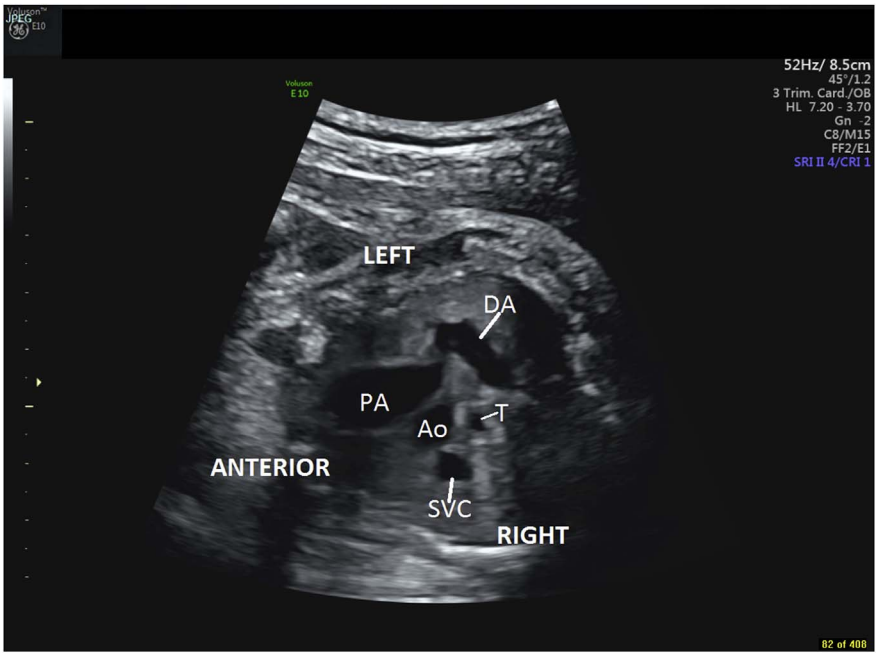

Fig. 3. Three-vessel view, demonstrating a ductal aneurysm. The arterial duct (DA) is elongated, dilated, and tortuous. The pulmonary artery (PA), aorta (Ao), trachea (T), and superior vena cava (SVC) are normal in appearance and orientation.

increased RV Tei index [25,26]. In the most severe cases there may be hydrops and fetal demise [22,23].

If a causative agent can be found, this should be discontinued (resulting in normalization of ductal flow in the majority) [9]. Early delivery may be considered when there is evidence of progressive right heart dysfunction and to preclude further damage to the pulmonary vasculature [17,26]. A recent literature review concluded that complete closure of the DA with or without hydrops should prompt immediate delivery [15].

The degree of compromise caused by ductal constriction depends on the severity of the ductal constriction and the gestational age at which it develops [15].

Postnatal echocardiograms show a spectrum of mild-to-severe RV hypertrophy, with the worst cases even causing the RV to be bipartite and "collapsed," with associated diastolic dysfunction [17]. There are rare reports of prolapse of tricuspid valve leaflets and rupture of chords [17,27]. There are also reports of pulmonary valve abnormalities, e.g. stenosis or agenesis, in association with DA constriction [17].

Following delivery these babies are at risk of persistent pulmonary hypertension of the newborn (PPHN), with right-to-left shunting at ductal and atrial levels resulting in cyanosis, and RV dysfunction due to high afterload. These babies are challenging to manage and can have severe hypoxia and low cardiac output, which, if not responsive to treatment, may cause refractory acidosis and death [18]. PPHN occurs in 18–28% of babies with DA constriction [15,19].

Clinical management of PPHN is targeted at reduction of pulmonary vascular resistance (including supplementary oxygen, mechanical ventilation, and use of nitric oxide) and the support of RV function and cardiac output (which may even require extracorporeal membrane oxygenation in the most severe cases). Gewillig et al. reported a postnatal mortality of 25% and no intrauterine deaths [17]. A recent literature review regarding prenatal DA closure yielded a perinatal mortality rate of 10.3%, and hydrops was reported as a significant risk factor for PPHN and death [15]. It appears that those who survive the perinatal period experience regression of the pulmonary hypertension and have good medium-term outcomes [15,19].

4.3. Aneurysmal DA (incidence, causes, fetal findings, neonatal physiology, neonatal echo findings, neonatal management, and outcome)

Congenital ductal aneurysm is a saccular or fusiform dilation and elongation of the DA and develops exclusively in the third trimester of pregnancy [28]. Congenital ductal aneurysms occur in 1.5–2.2% in the third trimester [29,30]. It is likely that ductal aneurysms are underascertained in clinical practice since the majority of fetal echocardiograms are performed in the second trimester. Ductal aneurysms are often only diagnosed postnatally when there are symptoms and can go undiagnosed with spontaneous resolution when the DA closes. Prospective studies have reported an incidence of 5.7–8.8% in full-term neonates, and in one of those reports all neonates were asymptomatic or had symptoms not related to the aneurysm [12,31]. A study including serial echocardiograms from prenatal to postnatal life demonstrated a more than threefold increase in the percentage with DA aneurysms after delivery [30]. All new postnatal diagnoses had DA dilation prior to delivery and the proportion with prenatally diagnosed DA aneurysm or dilation increased as gestation advanced with dilation progressing from the aortic end towards the pulmonary artery end [30].

The etiology of ductal aneurysms is unknown. Associations have been reported with large and small for gestational age fetuses, poorly controlled maternal gestational diabetes, low Apgar scores, and mothers with blood group A; however, a causative relationship has not been established [12,30]. A multi-center study reported a 25% association with chromosomal abnormalities and syndromes, but this is likely an overestimate due to ascertainment bias [29]. There is an association with connective tissue disorders, including Marfan and Loeys–Dietz syndromes [29].

One theory regarding pathogenesis is that ductal aneurysms occur when there is delayed closure at the aortic end of the DA, leaving the vessel exposed to high pressures at a time when it is involuting – although this would not explain prenatal occurrences [32]. Lund et al. theorized that DA aneurysms result from congenital wall weakness secondary to necrosis and mucoid degeneration of the media. Dyamenhalli demonstrated that sometimes there is absence of the intimal cushions or defective elastin in the DA [29,33]. Lund et al. also suggested that increased flow through the DA in utero in the presence of wall weakness could also be a factor [33]. Given its relatively high

neonatal incidence, Jan et al. proposed that small ductal aneurysms may even represent a normal variant of spontaneous ductal closure [12].

The most frequent fetal echo referral indication is a suspicion of arch abnormality [29]. The characteristic finding is of a dilated, tortuous DA, with a diameter > 95th percentile, which protrudes leftward of the aortic arch and can be appreciated from the three-vessel view [4,29] (Fig. 3). Colour Doppler interrogation may demonstrate turbulence within the DA. Postnatally, a round mass may be noted in the left superior mediastinum on the chest X-ray [34].

Jan et al. reported a very low prevalence of symptoms, and a benign natural history in the majority of affected neonates with spontaneous resolution, occurring by either ductal constriction or progressive thrombus formation and subsequent fibrosis within the DA aneurysm [12,31]. Complications may occur, with the most frequent being compression of adjacent structures (including airways, phrenic and recurrent laryngeal nerves), thromboembolism, rupture, or infection [29,32]. It is likely that patients with connective tissue disorders are at higher risk of rupture of the DA aneurysm [29].

Surgery should be considered if the DA remains patent after the neonatal period or earlier if there is a connective tissue disorder, thrombus extending into other vessels, evidence of thromboembolism, or if symptoms occur [12,28,29]. Surgical resection of the DA aneurysm on cardiopulmonary bypass is recommended rather than ligation, which may risk inadequate discontinuation of flow and not eliminate the risk of sudden rupture [29].

5. Role of the DA in congenital heart disease pre- and postnatally

In fetuses with critical right or left outflow obstruction, the patency of DA is required for hemodynamic stability.

5.1. In pulmonary outflow tract obstruction

It has long been recognized that in the setting of severe pulmonary outflow tract obstruction (POFTO) or pulmonary atresia, there is retrograde flow in the fetal DA [35]. In some infants with moderate POFTO, it can be challenging to predict whether a neonatal operation or intervention will be required. It has recently been shown, even in complex cases with functionally univentricular anatomy and POFTO, that retrograde fetal DA flow is the single best marker to predict the need for neonatal surgery or intervention to augment pulmonary blood flow, with high sensitivity and specificity [36]. Thus, identification of retrograde DA flow on fetal echo may contribute to planning location of delivery and predict the need for prostaglandin therapy. Conversely, anterograde flow in the DA is in keeping with non-critical POFTO and parents can be counselled appropriately in this regard.

In addition, in the setting of POFTO, the morphology and position of the DA may be abnormal. In cases of moderate or severe POFTO, the DA is often smaller than usual, which may relate to reduced ductal flow or, in the setting of reverse ductal flow, could be secondary to constriction due to blood with high PaO_2 passing through it from the aorta [37]. The position and orientation of the DA is also more likely to be abnormal in severe POFTO/pulmonary atresia, where the DA often arises from the undersurface of the aortic arch, at an acute angle to the descending aorta [37,38]. The size and orientation of the DA in POFTO can make it a challenging structure to locate and assess on fetal echocardiography. The DA may be absent in tetralogy of Fallot or it may arise from an innominate or subclavian artery. It is important for the fetal echocardiographer to be aware that the duct may arise abnormally, in order to identify the abnormal origin of the DA (which may otherwise be erroneously labelled as absent).

It is not uncommon to have proximal branch pulmonary artery stenosis (particularly on the left) in tetralogy of Fallot. This may evolve as the DA constrictions postnatally might be due to extension of ductal tissue into the proximal pulmonary artery. Rarely, the pulmonary artery branches are non-confluent and one pulmonary artery branch is supplied by the DA [39]. This anatomy occurs more often in the setting of congenital heart disease (CHD), e.g. common arterial trunk or tetralogy of Fallot, than in isolation. The disconnected pulmonary artery is found on the contralateral side to the aortic arch and there may either be uni- or bilateral arterial ducts in this situation [39]. On fetal echocardiography it is important to assess the confluence of the pulmonary arteries, as, if the pulmonary flow to one lung depends on the DA, then this should be considered a “duct-dependent” condition for which a prostaglandin infusion is required postnatally.

In pulmonary atresia with a ventricular septal defect, the pulmonary blood supply is either from a DA or major aortopulmonary collateral arteries (MAPCAs) [40]. If the MAPCAs supply a lung, then it is extremely rare for there to be an ipsilateral DA. MAPCAs and DA can coexist when there are non-confluent pulmonary arteries, with MAPCA supply to one lung and a DA to the other.

5.2. In isolated coarctation of the aorta

Prenatal diagnosis of coarctation of the aorta is associated with a reduction in mortality and morbidity, therefore it is an important condition to detect; however, it is often missed [41]. Typically coarctation occurs opposite the insertion of the DA and patency of the DA in utero often masks the classical postnatal features of coarctation [42]. In coarctation, a sling of ductal tissue extends into the aorta and the classical posterior “shelf” may only be unmasked when the DA begins to constrict postnatally [42]. For this reason, when there is a prenatal suspicion of coarctation, fetal cardiologists may consider advising a period of close observation in the neonatal period without initial administration of prostin to allow echo confirmation of the diagnosis as the DA constricts. Delivery should take place in a center equipped to perform adequate clinical and echocardiographic assessments of the newborn. Prostin therapy may be recommended to facilitate safe transfer if delivery in a unit such as this is not possible, or if additional critical cardiac defects have been identified. Fetal cardiologists should counsel the prospective parents that confirmation of the diagnosis may not occur until several days after delivery has taken place.

Secondary markers (related to redistribution of blood flow), such as a dilated right heart or hypoplasia of the transverse arch, are often indicators that lead to prenatal suspicion of coarctation. In coarctation, the DA is generally larger than usual – secondary to flow redistribution in order to bypass the obstructed left heart [43]. The ratio between diameters of the isthmus and the DA is lower in coarctation, and has been proposed as a fetal echo marker for condition [44]. Another proposed fetal echo marker is the more acute angle formed by the DA with the descending aorta in this condition [44].

5.3. In vascular rings

One of the most frequently occurring forms of vascular ring involving the DA is a right aortic arch with a left-sided DA from an aberrant left subclavian artery [45]. Other, rarer, forms of vascular ring may also include the DA as a component of the ring. The DA is not part of the vascular ring in a double aortic arch, but always left-sided in this situation as documented in all fetal series. Vascular rings may coexist with other forms of CHD.

Vascular rings are generally easier to diagnose by fetal than postnatal echocardiography. The fetal fluid-filled lungs provide a better acoustic window than postnatal air-filled lungs, allowing the fetal echocardiographer to obtain cross-sectional views of the mediastinum that cannot be obtained postnatally. Prenatally, the airway can be seen with relative ease on the three-vessel and trachea view, which allows easy identification of the sidedness of the aortic arch. Colour Doppler readily confirms the presence of an aberrant subclavian artery running behind the trachea. Another factor influencing the ease of prenatal diagnosis of a vascular ring is the patency of the DA, which is often not

the case on postnatal assessments.

With increasing use of the three-vessel view on obstetric screening, an increasing proportion of vascular rings are diagnosed prenatally [45]. It is challenging to predict the likelihood of a fetus with a vascular ring going on to have symptoms of airway or esophageal compression, since many asymptomatic cases would likely previously have gone undiagnosed. Very rarely, vascular rings can cause prenatal compression of the esophagus and/or trachea, leading to polyhydramnios or even congenital high-airway obstruction syndrome – if this occurs, delivery planning is required to ensure that any emergent airway issues can be dealt with if necessary [46]. In all cases with a vascular ring, appropriate postnatal surveillance should be planned to assess for airway or tracheal compression and surgical division of the ring, if needed.

5.4. In transposition of the great arteries

Patients with transposition of the great arteries (TGA) have parallel systemic and pulmonary circulations. We limit our discussion to the DA in simple TGA (intact ventricular septum or non-significant ventricular septal defects) as complex TGA (large VSD, with or without outflow tract obstruction and single ventricles) may have a very different clinical presentation and the role of the DA may differ.

5.4.1. Simple TGA

In prenatal TGA, blood passing through the DA has a higher oxygen content than normal. The quantity of flow passing through the DA is also lower in TGA than usual [47,48]. This combination of factors likely explains the relatively small DA diameter in TGA [49]. Some cases of TGA have been noted to have ductal constriction prenatally, which may in part explain the relatively high incidence of PPHN in the neonate with TGA [49].

Blood passing into the pulmonary arteries in TGA also has a higher oxygen content than normal. In the setting of oxygen-mediated reduction in pulmonary vascular resistance (as evidenced by a high proportion with bidirectional DA flow), there is an increase in pulmonary venous return, which may raise left atrial pressure, reducing right-to-left atrial shunting or perhaps causing restriction of the atrial septum [49]. This reduction in right-to-left atrial shunting reduces the oxygen content of blood entering the fetal lungs and may encourage development of aortopulmonary collateral arteries, leading to a combination of hypoxic blood within the pulmonary arteries and exposure of the small pulmonary arteries to increased pressure, a combination which has been hypothesized to promote pulmonary vascular disease [48].

Prenatal diagnosis of TGA confers a reduction in neonatal morbidity and mortality [50]. Following delivery, cases with a highly restrictive atrial septum are severely cyanotic, acidotic and, in the absence of intervention, have a high rate of mortality. Prenatal prediction of which babies will have a highly restrictive atrial septum facilitates planning for delivery timing and location in a center capable of providing a potentially lifesaving emergency balloon atrial septostomy.

Fetal echocardiographers can assess the intrinsic characteristics of the atrial septum, such as thickness, hypermobility, and size of the foramen ovale relative to atrial septal length in babies with TGA [51,52]. Unfortunately, fetal echo prediction of atrial septum restriction in the setting of TGA lacks sensitivity [51,53]. Assessment of the DA provides additional information, with evidence showing that DA restriction and bidirectional flow are associated with the need for emergent septostomy [47,51]. The combination of restriction of both foramen ovale and the DA on fetal echo assessment is highly associated with early neonatal hemodynamic compromise [49,53].

5.5. In Ebstein anomaly/tricuspid valve dysplasia

Ebstein anomaly and tricuspid valve dysplasia (TVD) are often analyzed together, due to their similar physiology prenatally. There is a wide spectrum of pathophysiology in these conditions and at the worst end of the spectrum there is severe tricuspid regurgitation, massive cardiomegaly, cardiac failure, fetal hydrops, and high rates of intrauterine death. Fetuses with severe Ebstein anomaly or TVD are at high risk of perinatal mortality and morbidity [54]. Anatomical pulmonary atresia may coexist or functional pulmonary atresia can occur if the right heart is unable to generate adequate systolic pressure to open the pulmonary valve. In this setting, there is retrograde flow in the DA, which is a well-recognized risk factor for mortality [54]. Echocardiographic findings evolve during pregnancy, including an increase in the proportion of fetuses with retrograde DA flow, so ongoing surveillance is required as gestation progresses [55]. If there is retrograde DA flow, it is likely that a prostaglandin infusion will be required after delivery, at least initially until the pulmonary vascular resistance falls, or, for babies with anatomical pulmonary atresia, antegrade flow or an alternative source of pulmonary blood flow (e.g. a surgical shunt) can be established.

If there is functional pulmonary atresia with pulmonary regurgitation, a circular shunt may occur. The DA is part of the circular shunt circuit, which results in diastolic steal from the fetal circulation and may even cause absent or reversed flow during diastole in the umbilical artery. This circular shunt physiology can result in fetal hypoxia, acidosis, hydrops and intrauterine death. Some centers have attempted maternal treatment with non-steroidal anti-inflammatory drugs to reduce the circular shunt by means of ductal constriction [56]. This treatment is controversial, given the potential risks, including those of causing fetal renal impairment or oligohydramnios and a strategy to provide pulmonary blood flow in the setting of a restricted or closed duct in the immediate postnatal period would have to be in place. The fetal cardiologist managing a case such as this should consider the risk:benefit ratio, including considering alternative strategies such as early delivery with subsequent ductal closure, if the gestational age is appropriate and the RV is able to generate a sufficient systolic pressure.

5.6. Absent pulmonary valve syndrome

Absent pulmonary valve syndrome is a very rare form of CHD defined by the presence of a rudimentary, dysplastic pulmonary valve. The abnormal pulmonary valve is usually stenotic and incompetent. It is frequently associated with tetralogy of Fallot (> 80%) [57]. The DA (or its absence) plays a fascinating and poorly understood role in this condition.

Tetralogy of Fallot with absent pulmonary valve is characterized by extremely dilated pulmonary arteries. Approximately 80% of cases have agenesis of the DA [57]. It is unclear why this pathology is almost always associated with DA agenesis. Ductal agenesis has been postulated as an either a consequence or a cause of the underdevelopment of the pulmonary valve leaflets [58,59]. It is uncertain whether there is true agenesis of the DA as part of the embryology of the condition, or whether there is early closure of the DA subsequent to the abnormal hemodynamics [60,61]. It has been proposed that cases with a widely patent DA demise in early pregnancy, due to biventricular volume overload secondary to the combination of severe pulmonary regurgitation and a large ventricular septal defect, are incompatible with survival, and there is emerging evidence to support this theory [61,62]. The most frequently associated extracardiac abnormalities are chromosomal anomalies, especially 22q11 deletion, and cases with severely dilated pulmonary arteries often have significant respiratory comorbidities due to bronchomalacia [57].

Less common variants of absent pulmonary valve have an intact ventricular septum or small ventricular septal defect (so-called “isolated absent pulmonary valve”). Some cases have tricuspid atresia or stenosis with right ventricular hypoplasia, left ventricular hypertrabeculation, or aortic valve abnormalities [62,63]. Fetuses with isolated absent pulmonary valve are more likely to have a patent DA and tend to have less-dilated pulmonary arteries than those with tetralogy of Fallot [63].

It has been suggested that the presence of a DA in isolated absent pulmonary valve allows volume offloading of the pulmonary arteries and is responsible for the smaller pulmonary arteries in this condition compared with tetralogy of Fallot with absent pulmonary valve syndrome [63].

5.7. Truncus arteriosus

Truncus arteriosus is defined by the presence of a single arterial trunk that gives origin to the systemic, coronary, and pulmonary arteries. This pathology is almost always associated with ductal agenesis [64]. In the setting of truncus arteriosus with interrupted aortic arch, all cases have a DA supplying flow to the descending aorta [65]. Very rarely, there are cases of truncus arteriosus with one of the pulmonary arteries supplied only by a DA.

6. Summary

Abnormalities of the DA can occur in isolation or in combination with CHD. The DA can both help and hinder depending on the nature of the CHD studied. A good understanding of the DA is vital for the practice of fetal cardiology. Fetal cardiologists can use information obtained prenatally to predict the need for postnatal intervention and ensure optimum perinatal case management.

6.1. Practice points

- The DA can be interrogated by fetal echocardiography using the ductal arch view and the three-vessel view.
- The use of colour and pulsed-wave Doppler in addition to two-dimensional imaging enable detailed assessment of size, shape, location and flow patterns within DA.
- Ductal constriction and ductal aneurysm are likely under-recognized prenatally.
- DA constriction may result in persistent pulmonary hypertension of the newborn.
- In CHD with pulmonary outflow tract obstruction, retrograde flow in the DA suggests that the condition is duct dependent.
- The presence of a patent DA in utero may conceal the presence of a significant coarctation of the aorta.
- In TGA, a small DA or retrograde flow in the DA may be associated with postnatal restrictive atrial septum.
- In Ebstein anomaly, retrograde flow occurs in the setting of anatomical or functional pulmonary atresia.
- Absence of the DA occurs frequently in tetralogy with absent pulmonary valve syndrome and common arterial trunk (without interrupted aortic arch).

Conflicts of interest

None declared.

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