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Fetal echocardiography for planning perinatal and delivery room care of neonates with congenital heart disease

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Fetal echocardiography facilitates the prenatal diagnosis of infants with congenital heart disease (CHD) and through sequential examinations, allows assessment of fetal hemodynamics and cardiovascular status from the time of diagnosis to delivery. Fetal cardiologists have created diagnostic protocols aimed at risk stratifying severity and potential postnatal compromise in fetuses with CHD, and identifying those who may require special intervention at birth or within the first days of life. In this article, we review fetal cardiovascular physiology, the progression of CHD in utero and fetal echocardiographic findings used for risk stratification of newborns with CHD, as well as some of the basic principles of planning for the neonatal resuscitation and initial transitional care of these complex newborns.

KEYWORDS
congenital heart disease, delivery management, delivery room care, fetal echocardiography, prenatal diagnosis, prenatal risk factors

1 | INTRODUCTION

Congenital heart disease (CHD) is the most common congenital abnormality. Historically, the diagnosis of CHD mainly occurred after birth. However, in recent years, advances in prenatal diagnosis have led to a significant increase in the prenatal detection of fetuses with CHD, with detection rates reported as high as 95% in tertiary perinatal centers.[1–3] Fetal echocardiography in the current era provides a detailed characterization of cardiac anatomy and through sequential examinations, assessment of the fetal hemodynamic changes that occur during gestation.[4] When CHD is suspected, prenatal diagnosis has 3 main clinical aims that go beyond parental counseling: (1) to diagnose the specific cardiac defect, (2) to plan perinatal management by identifying the fetuses at risk of postnatal hemodynamic instability who may require intervention in the delivery room (DR) or within the first days of life, (3) to identify those fetuses who may benefit from fetal cardiac intervention.[4,5] Fetal medicine specialists now consider the fetus as a patient with prenatal assessment of the severity of the lesion and perinatal management tailored for the specific defect with the goal to improve in utero and postnatal outcome.[6–8] For this reason, pregnancy and delivery management of newborns with a prenatal diagnosis of CHD requires a multidisciplinary team, composed of fetal and pediatric cardiologists, obstetricians and maternal-fetal specialists, neonatologists, as well as other pediatric specialists.[5]

In recent years, classification of CHD using fetal echocardiography findings has been proposed, with the goal of stratifying the severity of the cardiac defect and expected degree of postnatal hemodynamic compromise, and then using this information to specify recommendations for delivery and postnatal care.[9–13] In this article, we aim to review fetal and transitional physiology, the in utero progression of CHD, models of risk stratification and classification of CHD using fetal echocardiography, and strategies for perinatal management of infants with a prenatal diagnosis of CHD.

2 | FETAL AND TRANSITIONAL CIRCULATION: UNDER NORMAL CONDITION AND IN THE PRESENCE OF CHD

A parallel circuit of the left and right heart characterizes the normal fetal circulation. The oxygenated blood flow from the placenta reaches the fetus via the umbilical vein. A system of shunts, including the ductus venosus and the foramen ovale, delivers the most oxygenated blood from the umbilical vein to the left heart, then to the ascending aorta and cerebral circulation, while the remainder of the umbilical vein blood combines with the less oxygenated blood from the fetal body, and reaches the right heart. The right ventricle pumps blood to the pulmonary circulation, and via the ductus arteriosus to the descending aorta, such that it reaches the placenta and lower body.[14] At delivery, cord clamping results in an acute increase in systemic vascular resistance, while spontaneous respiration decreases the pulmonary vascular resistance. This significantly increases pulmonary blood flow and the left atrial pressure, which results in closure of the foramen ovale. The ductus arteriosus closes usually within 12–72 hours of birth,[15] and with this, the fetal circulation changes to a circulation in series.[16]

In some cases of CHD, less oxygenated blood reaches the ascending aorta and the brain and heart instead of perfusing the lower body and returning to the placenta. The presence of the fetal circulatory shunts permits a redistribution of blood flow when there is obstruction to inflow or outflow from the heart, and therefore, most types of CHD are well tolerated in utero.[16] The altered circulation may, however, impair systemic oxygenation and affect fetal growth and brain development.[17,18]

At delivery, the risk of hemodynamic instability depends on the type of CHD and whether patency of the fetal shunt pathways is necessary to deliver blood flow to the systemic or pulmonary circulations after separation from the placental circulation. Hemodynamic instability is also dependent on how the heart responds to the change in systemic resistance that comes with cord clamping as well as the presence of associated abnormalities of the lungs or respiratory system that may impede the normal decrease in pulmonary vascular resistance.

3 | THE IN UTERO PROGRESSION OF CHD

While the majority of congenital cardiovascular defects develop at the time of the cardiac embryogenesis, in the first 6–7 weeks of development, there is evidence that certain types of CHD have the potential to progress in utero, during the second and third trimester of gestation.[19] The exact mechanisms for evolution of CHD in utero are in part unknown and not well quantified. However, progression of cardiac disease has been reported in cases of: (1) worsening of the structural defects, such as worsening of hypoplasia, (2) new onset of foramen ovale restriction, decreasing ventricular inflow or outflow, or worsening arch obstruction, (3) development of a cardiomyopathy, as a primary disease or as a consequence of superimposed pregnancy complication, such as the hypertrophic cardiomyopathy described in the twin recipient in cases of twin to twin transfusion syndrome, (4) new onset or progressive valvular regurgitation, (5) diminution or closure of a ventricular septal defect, and (6) development of congestive heart failure with high risk of poor perinatal outcome such as in Ebstein anomaly, tetralogy of Fallot (TOF) with absent pulmonary valve, or uncontrolled fetal arrhythmias.[19]

While the factors that influence evolution of CHD need further investigation, the potential progression of CHD severity in utero supports sequential evaluation using fetal echocardiography examination. Serial assessment with an understanding of progression creates possibilities for fetal intervention to alter the natural history of CHD in utero, as well as assists clinicians in delivery management planning for specific CHD, which may have a variable clinical presentation during the perinatal transition.[19]

4 | DELIVERY PLANNING OF FETUSES WITH CHD: MULTIDISCIPLINARY APPROACH

The majority of children with prenatal diagnosis of CHD are stable at birth and do not require any specialized care in the perinatal period. In these cases, the delivery plan can be determined by the level of maternal care needs[20] and care of the newborn by the pediatrician. Oftentimes, the postnatal diagnosis can be confirmed by telemedicine or cardiology consultation and the baby followed as an outpatient.[4] In contrast, for newborns at risk of compromise, delivery at the cardiac center or in close proximity may improve neonatal and surgical outcomes in select groups of infants with prenatally diagnosed high-risk CHD.[4] Previous studies have shown that infants with a prenatal diagnosis of high-risk CHD and appropriate postnatal management have a better presurgical outcome compared with those diagnosed postnatally, especially in areas with limited pediatric resources.[21–24] For these infants with high-risk CHD, delivery planning requires multidisciplinary collaboration, involving obstetricians, maternal-fetal specialists, neonatologists, and cardiac specialists. Delivery room management should be determined by the risk of hemodynamic instability at birth, the medical resources available in the region, the distance to the cardiac care center, the type and availability of the transportation to the cardiac center, and any anticipated or known obstetric or maternal complications.[25] When highly specialized care is needed in the DR, strategies to ensure the presence of the necessary care team and avoid delays in treatment are essential. Potential strategies that

should be considered include (1) maternal-fetal transport to the adult hospital closest to the cardiac center, (2) planned delivery in proximity to the cardiac center with rapid transportation of the newborn, and (3) creation of a specialized delivery unit in the cardiac center.[9,26,27] The advantages of in utero transportation vs postnatal transportation of infants with CHD, including maternal and neonatal safety and costs, vary according to the obstetric and pediatric resources of a specific region. Therefore, location of delivery should be discussed with the parents and the cardiology care team such that delivery planning ensures appropriate postnatal care.[24,28,29]

Recent studies have investigated the costs of specialized delivery and early postnatal management in pregnancies complicated by fetal CHD. A recent population-based cohort study showed that prenatal diagnosis of D-transposition of the great arteries (D-TGA) was associated with higher costs for mothers during pregnancy, and infants post delivery compared to those diagnosed postnatally.[30] The higher costs for infants prenatally diagnosed with D-TGA primarily resulted from longer hospital stays; however, after controlling for the reduced costs related to neonatal death events in both groups, the difference in cost was no longer significant. In another retrospective study, prenatally diagnosed infants with CHD admitted to the cardiac intensive care unit (ICU) compared to those admitted to the neonatal ICU had shorter length of stay, less mechanical ventilation, and lower costs of care.[31] Finally, a prospective multicenter study showed that postnatal diagnosis of CHD was associated with higher costs, compared to those with prenatal diagnosis, due to the need for emergency transportation.[32] While these results suggest that prenatal diagnosis of CHD and management in the proper ICU setting can potentially reduce healthcare costs for these conditions, further studies investigating this topic are needed.

It has been shown that infants with CHD delivered at term (39–40 weeks) have a lower mortality and shorter postoperative length of stay compared to those delivered before 39 weeks.[33] Unfortunately, previous studies have found that infants diagnosed with CHD prenatally tend to be born earlier (around 38 weeks of gestation) and with a lower birth weigh compared to newborns who are diagnosed with CHD postnatally (gestational age at birth 39 weeks).[22,34,35] While this is in part related to necessary planned delivery coordination in order to guarantee specialized care at birth, in the absence of fetal or maternal complications, advantages of term delivery should always been considered.

5 | MODELS FOR RISK-STRATIFIED DELIVERY AND POSTNATAL CARE OF NEWBORNS WITH CHD

Over the past 15 years, several authors[9–13] have proposed methodology for the prenatal classification of CHD to stratify the severity of disease and type of postnatal care required based on fetal echocardiography parameters. Recently, the American Heart Association Statement on Fetal Cardiology included a comprehensive protocol, based on evidence from the literature and expert opinion, for perinatal and DR risk stratification of CHD using fetal echocardiographic criteria.[4] The levels of care were based on disease severity and linked to specific management strategies. While these various classification systems were designed independently at different centers across the world and reflect the local resources of their specific region, they do share many similarities and common pathways for care (Table 1). All reported classification systems consist of 4 diagnostic categories corresponding to level of severity and anticipated postnatal care required, ranging from CHD for which the risk of hemodynamic instability at birth is not anticipated to those with minimal or a high-risk of compromise, requiring specialized care or intervention for stabilization. While these categories have been named differently (level of care or LOC 1–4[9,13]; planned CHD to severe-severest CHD[10]; Care Plan 2–5[11]; and emergent neonatal cardiac intervention or ENCI 1–4[12]), they all describe very similar methods and ranking strategies. In addition, in 1 classification system,[11] comfort care is also included as an additional fifth category (not included in Table 1), when palliative care is planned. The following text summarizes the conceptual framework for risk stratification of CHD and the levels of severity of different CHD.

5.1 | Low-risk CHD

Cardiovascular defects that are expected to be hemodynamically stable at birth include left-to-right shunt lesions such as atrial or ventricular septal defects or endocardial cushion defects, mild valve abnormalities, and benign arrhythmias (ie, premature atrial contractions) with normal cardiac function. In the absence of additional fetal abnormalities, the delivery plan for fetuses diagnosed with these CHDs using fetal echocardiography should be determined according to the presence or absence of maternal or obstetric complications, or levels of maternal care (LMC).[20] Newborns with a low-risk CHD usually can be delivered at or near term via a normal mode of delivery (MOD). They require inpatient consult or telemedicine confirmation of the diagnosis with outpatient cardiology follow-up within the first weeks of life.[4] (See Table 1 for different low-risk classification systems).

5.2 | Minimal-risk CHD

Congenital heart disease with minimal risk of hemodynamic instability at birth mainly consists of structural defects with severe pulmonary or systemic outflow tract obstruction that requires administration of prostaglandin E1 (PGE1) to maintain patency of the ductus arteriosus after birth to sustain the pulmonary or systemic circulation.[4] Although newborns with these diagnoses are usually stable in the DR, instability can occur if the ductus arteriosus closes. The delivery plan for these babies includes assuring that a neonatologist is present in the DR, administration of PGE1 if required, establishment of intravenous access (IV), either peripheral or umbilical, and transport to the cardiac center to evaluate the need for intervention, either catheterization or surgery. Delivery recommendations will vary based on the following factors: (1) presence of additional fetal factors such as arrhythmias that may impact MOD, (2) presence of maternal and obstetric conditions, (3) pediatric resources available at the delivery hospital,

TABLE 1 Risk-stratified classification of postnatal care of newborns with CHD proposed by different authors

Predicted risk of hemodynamic instability at birth	Reported classification system				Suggested delivery plan[a]	DR Recommendations	Example CHD
	Donofrio, 2013[9]	Respondek-Liberska & Slodki, 2012[10]	Berkley, 2009[11]	Pruetz, 2014[12]			
Low/not expected	LOC 1	Planned CHD	Care Plan 2	ENCI 1	Mode and time of delivery: based on LMC	No specialized care in the DR Cardiology consult, telemedicine, with outpatient cardiology evaluation	Shunt lesions (VSD, ASD, AVSD) Mild valve disease Benign arrhythmias
Minimal	LOC 2	Severe planned CHD	Care Plan 3	ENCI 2	Mode and time of delivery: based on LMC Planned delivery ≥39 wk can be considered to coordinate service	Neonatologist in the DR; PGE if indicated transport to the cardiac center for catheterization/surgery	Ductal-dependent lesions including HLHS, PA/IVS, severe TOF Nonsustained or controlled tachyarrhythmias or bradyarrhythmias with adequate ventricular rate
High	LOC 3	Severe urgent CHD	Care Plan 3 or 4	ENCI 3	Mode and time of delivery: Planned delivery ≥39 wk should be arranged to coordinate service	Neonatologist and cardiologist in the DR and cardiac services alerted Plan for intervention or urgent transport if indicated	HLHS at risk for RAS D-TGA at risk for RAS CHD or arrhythmia with decreased heart function
High	LOC 4	Severest heart defect	Care Plan 5	ENCI 4	Mode and time of delivery: Planned delivery ≥39 wk (or earlier if fetal cardiac dysfunction or hydrops suspected and GA appropriate) at the cardiac center should be arranged	Neonatologist, cardiologist and surgery team in the DR Plan for intervention (catheterization, surgery or ECMO)	HLHS with severe RAS or IAS TGA with severe RAS or IAS, abnormal DA shunt Obstructed TAPVR Tachy or brady arrhythmia with hydrops Severe Ebstein anomaly or TOF/APV with hydrops

ASD = atrial septal defect; AVSD = atrioventricular septal defect; CHD = congenital heart disease; DA = ductus arteriosus; DR = delivery room; D-TGA = transposition of the great arteries; ECMO = extracorporeal membrane oxygenation; ENCI = emergent neonatal cardiac intervention; GA = gestational age; HLHS = hypoplastic left heart syndrome; IAS = intact atrial septum; LMC = level of maternal care; LOC = level of care; PA/IVS = pulmonary atresia with intact ventricular septum; PGE = prostaglandin E; RAS = restrictive atrial septum; TAPVR = total pulmonary venous return; TOF = tetralogy of Fallot; TOF/APV = tetralogy of Fallot with absent pulmonary valve; VSD=ventricular septal defect.

[a]The delivery plan may vary according to: LMC; the pediatric resources of the delivery hospital; distance to the cardiac care center; type and availability of the transportation to the cardiac center. The delivery plan should ensure the appropriate DR recommendations.

including a nursery that can support short-term mechanical ventilation, administration of medications including PGE1, and treatment of arrhythmias including cardioversion and medical therapy, and (4) distance to the cardiac care center; in that in some rural or remote areas, it may be prudent to deliver these babies near the cardiac center to avoid long transport times. (See Table 1 for different minimal-risk classification systems).

Historically ductal-dependent cardiac lesions were considered to be critical CHD,[36] as newborns with these defects often presented in extremis during the first few days of life coincident with closure of the ductus arteriosus, which occurs in most newborns within 12–72 hours after birth.[15] A prenatal diagnosis of such defects now enables institution of PGE1 infusion at delivery, therefore eliminating postnatal compromise. A prospective evaluation has shown that fetal echocardiography can accurately predict a postnatal ductal-dependent circulation.[13] Newborns identified prenatally with ductal-dependent CHD can now be stabilized with a PGE1 infusion through a peripheral or umbilical line and therefore, as long as resources are available, be considered as minimal risk of DR management.

The following features identified during serial assessment of CHD have been shown to be useful to predict a ductal-dependent pulmonary circulation at delivery in cases of critical pulmonary stenosis or atresia, severe TOF, tricuspid valve (TV) stenosis, or atresia with or without a small ventricular septal defect (Table 2):

- Reversed flow in the ductus arteriosus.[37,38] (Figure 1, Movie S1)
- Reversed orientation of the ductus arteriosus, defined by the angle between the ductus arteriosus and the aorta measuring less than 90°[39]
- Pulmonary valve *z*-score value less than −3, after 16 weeks of gestation in case of TOF.[40]

The following features identified during serial assessment of CHD can be used to predict a ductal-dependent systemic circulation at delivery in cases of CHD with obstruction to the systemic circulation such as hypoplastic left heart syndrome (HLHS) or aortic/mitral stenosis (Table 2):

- Reversed blood flow across the foramen ovale, defined as blood flow from the left to the right atrium.[37,41]
- Reversed systolic flow in the distal transverse aortic arch, indicating perfusion of the aortic arch via the ductus arteriosus.[37,41] (Figure 2; Movie S2)

5.3 | High-risk CHD

This group of CHD includes cardiovascular defects that require immediate stabilization in the DR, including lifesaving procedures and urgent cardiac intervention within the first hours of life, such as cardiac catheterization (balloon valvotomy, balloon atrial septostomy [BAS]), cardioversion of unstable arrhythmias, urgent pediatric cardiothoracic surgery or initiation of extracorporeal membrane oxygenation (ECMO). For infants with prenatal diagnosis of these high-risk CHD, delivery should be planned at tertiary hospitals with availability of neonatology and cardiology services in the DR or with planned and coordinated initial stabilization in the DR with urgent transportation to a nearby pediatric hospital with neonatal cardiac services available. Mode and timing of delivery is determined by the multidisciplinary care team including obstetrician, maternal-fetal specialist, neonatologist, cardiologist, and other pediatric specialists and surgeons. Planned induction of labor or cesarean section prior to 40 weeks of gestation is often proposed to ensure a successful postnatal care plan.[9] (See Table 1 for different high-risk classification systems).

The following fetal echocardiography parameters can be used as predictors for need of urgent cardiac intervention at birth in cases of HLHS with restrictive or intact atrial septum (RAS/IAS) (Figure 3; Movie S3), which at delivery leads to rapid deterioration due to obstruction of pulmonary venous flow (Table 2):

- Pulmonary vein Doppler flow patterns with ratio of forward pulmonary vein flow to reversed pulmonary vein flow (PV f/r) <3 signifying high risk of urgent intervention[4,42,43] (Figure 4).
- Lack of pulmonary vasoreactivity during third-trimester maternal hyperoxygenation (MH) testing.[44]

In fetuses with D-TGA, the following parameters have been associated with a higher risk of developing DR compromise due to a RAS, which prevents oxygenated blood from reaching the systemic circulation. Of note, the predictive value for urgent cardiac intervention to open the atrial septum is overall low[4,13] (Table 2):

- Presence of an abnormal atrial septal anatomy defined as hypermobile or tethered septum primum or bowing or intact atrial septum.[45,46]
- Presence of an abnormal ductus arteriosus (usually associated with abnormal atrial septum) defined as small (z-score <−2) or absent, or with abnormal (bidirectional or reversed) flow.[47] (Figure 5). A small or absent ductus arteriosus may also be associated with pulmonary hypertension[47,48]
- Increased pulmonary venous blood flow with an increased "s" wave peak velocity.[49]

In total anomalous pulmonary venous return (TAPVR), obstruction can be predicted by the following:

- Pulmonary vein flow pattern with nonpulsatile, low velocity, monophasic flow[50]

6 | ACCURACY OF FETAL ECHO FOR DIAGNOSIS AND PREDICTION OF POSTNATAL CARE

Fetal echocardiography has a high diagnostic accuracy, ranging between 84% and 95% in recent studies.[1–3,11,13] Accuracy varies depending on the type of defect, being higher (86%) in cases with single

TABLE 2 Prenatal predictors of delivery room care

CHD diagnosis	Fetal echocardiogram findings	Delivery room (DR) recommendations
ASD, VSD or AVSD (shunt lesions); Mild valve abnormalities	Isolated ASD or VSD with normal FO and DA flow, normal or minimal flow disturbances at valves, and normal heart function (LOC 1)	Routine care, hospital or telemedicine consult Outpatient cardiology follow-up
Coarctation, critical (ductal dependent lesion)	Ductal dependent coarctation (LOC 2): 1. Left/right heart size discrepancy with MV/TV and AoV/PV ratios <0.6[52] 2. Distal arch in 3rd trimester <3 mm [52] 3. AoI/DA in 3VV <0.75[53] 4. Abnormal Doppler flow in isthmus[13,54] 5. Posterior shelf[56]	Initiation of prostaglandin infusion through peripheral IV or umbilical line Intubation with mechanical ventilation only if clinically indicated Transfer to cardiac center
Pulmonary atresia, HLHS, other single ventricles, or cyanotic TOF (ductal dependent lesions)	Ductal dependent pulmonary circulation (LOC 2): 1. Aorta to pulmonary flow in the DA[37,38] 2. Reversed orientation of the DA (inferior angle <90°) [39] 3. Pulmonary valve z-score value less than 3, after 16 weeks[40] Ductal dependent systemic circulation (LOC 2): 1. Left to right atrial flow across the foramen ovale and distal aortic arch[37,41]	Initiation of prostaglandin infusion through peripheral IV or umbilical line Intubation with mechanical ventilation only if clinically indicated Transfer to cardiac center
HLHS and variants with severely restrictive or intact atrial septum	Pulmonary vein Doppler[42,43]: 1. Moderate obstruction: PV f/r <5 and >3 (LOC 3) 2. Severe obstruction: PV f/r <3; (LOC 4)	Initiation of prostaglandin infusion through peripheral IV or umbilical line Intubation with mechanical ventilation OR or cath lab on standby Plan for immediate intervention to decompress left atrium ECMO available
TAPVR Obstructed	Pulmonary vein Doppler[50]: 1. Monophasic nonpulsatile pulmonary (LOC 4) 2. Infradiaphragmatic TAPVR (LOC 3 or 4)	Intubation with mechanical ventilation Peripheral IV and/or umbilical line OR team on standby Initiation of prostaglandin infusion (may relax the ductus venosus smooth muscle for infradiaphragmatic TAPVR) Plan for immediate surgical intervention
D-TGA and variants with restrictive atrial septum	Foramen ovale findings[45,46]: 1. Hypermobile septum (LOC 3) 2. Angle of septum primum <30° (LOC 3) 3. Lack of swinging motion of septum or "tethered" septum (LOC 3) 4. Bowing of atrial septum >50% (LOC 3 or 4) 5. intact (LOC 4) Abnormal ductus arteriosus[47-48]: 1. With additional RFO (LOC 4) 2. Small with moderate/severe restriction (LOC 3 or 4) 3. Reversed, bidirectional or accelerated flow (LOC 3 or 4) Pulmonary vein Doppler, proximal to the left atrium[49]: 1. Max velocity "s" wave >41 cm/s (LOC 3 or 4)	Initiation of prostaglandin infusion through peripheral IV or umbilical line Intubation with mechanical ventilation Cath lab on standby Plan for immediate balloon atrial septostomy If ductal flow abnormal, consider pulmonary hypertension therapy including intubation, 100% oxygen, inhaled nitric oxide
TOF/APV	1. With associated cardiac dysfunction (LOC 3) 2. With associated hydrops fetalis (LOC 4) 3. Lung findings suggestive of compression or fluid trapping (LOC 4)	Specialized cardiac care team in the DR Specialized ventilation (prone) Peripheral IV or umbilical access Intubation with mechanical ventilation if needed Consider 100% oxygen and inhaled nitric oxide to decrease pulmonary resistance Consider ECMO

(Continued)

TABLE 2 *Continued*

CHD diagnosis	Fetal echocardiogram findings	Delivery room (DR) recommendations
Severe Ebstein's anomaly	1. With associated cardiac dysfunction (LOC 3) 2. With associated hydrops fetalis (LOC 4)	Specialized cardiac care team in the DR Specialized ventilation (prone) Peripheral IV or umbilical access Intubation with mechanical ventilation if needed Consider 100% oxygen and inhaled nitric oxide to decrease pulmonary resistance Consider ECMO cardioversion or medical therapy in DR as indicated for arrhythmia
Unstable tachyarrhythmias	1. With associated heart failure (LOC 3) 2. With associated hydrops fetalis (LOC 4)	Consider early delivery if gestational age appropriate Cardioversion and/or medical therapy in DR
Complete heart block with low ventricular rate and/or cardiac dysfunction	1. With associated heart failure (LOC 3) 2. With associated hydrops fetalis (LOC 4)	Consider early delivery if gestational age appropriate Consider chronotropic agents vs. temporary pacing in DR

ASD = atrial septal defect; AoI = aortic isthmus; AoV = aortic valve; APV = absent pulmonary valve; AVSD = atrioventricular septal defect; DA = ductus arteriosus; D-TGA = D-transposition of the great arteries; DR = delivery room; ECMO = extracorporeal membrane oxygenation; FO = foramen ovale; HLHS = hypoplastic left heart syndrome; IV = intravenous; LOC = level of care; MV = mitral valve; OR = operating room; PV f/r = pulmonary vein forward/reversed flow integral; PV = pulmonary valve; TAPVR = total abnormal pulmonary venous return; TOF = tetralogy of Fallot; TV = tricuspid valve; VSD = ventricular septal defect; 3VV = three vessel view. Modified with permission from "Risk-stratified postnatal care of newborns with congenital heart disease determined by fetal echocardiography". Donofrio MT, Skurow-Todd K, Berger JT, McCarter R, Fulgium A, Krishnan A, Sable CA. J Am Soc Echocardiogr 2015:28:1339-49, from Elsevier.

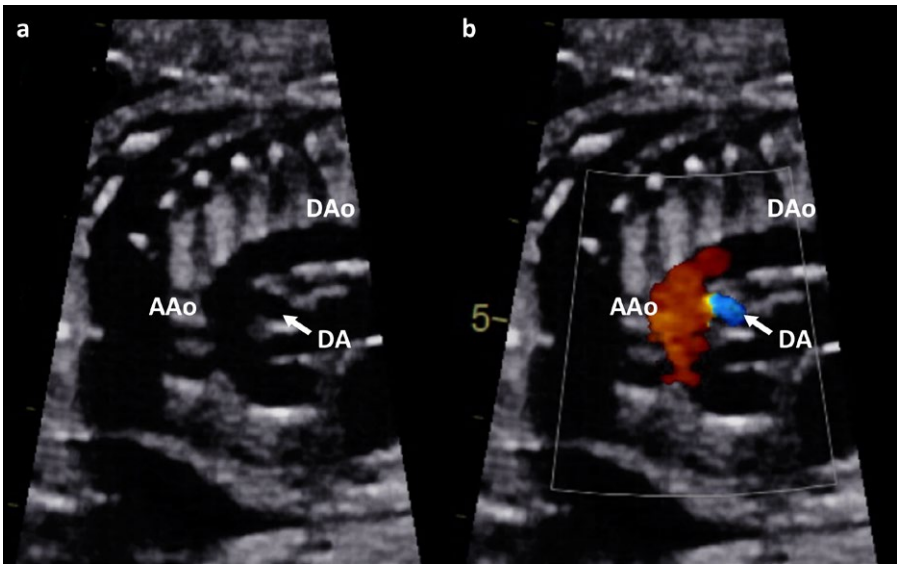

FIGURE 1 A. Sagittal two-dimensional view of the aortic and ductal arch in a fetus with tetralogy of Fallot. B. Color Doppler shows reversed flow (blue) in the ductus arteriosus. AAo = ascending aorta; DA = ductus arteriosus; and DAo = descending aorta

ventricle defects such as HLHS and lower for D-TGA (28%) and obstructed total anomalous pulmonary venous return (TAPVR) (13%).[12] Accuracy for prediction of postnatal care is less consistent, ranging from 20% to 96% depending on the specific CHD.[11–13] Donofrio et al., in a prospective study over 8 years, reported a sensitivity of 90%–97% and positive predictive value (PPV) of 87%–99% for prediction of low or minimal-risk CHD (LOC 1 and 2), while sensitivity and PPV for high-risk CHD (LOC 3 and 4) were 83% and 87%, respectively.[13] According to the same study, the accuracy to predict those newborns requiring standard DR care (low risk or LOC 1) vs those requiring special intervention at birth, including need for a pediatric cardiac center (minimal to high-risk CHD or LOC 2–4), was overall high with a sensitivity of 99% and specificity of 90%. These classifications are of particular importance for the perinatal management of newborns with CHD in areas with limited pediatric resources, where the delivery plan may changes according to the distance to the cardiac center.

Predicting postnatal risk of hemodynamic instability and the specialized care required is dependent not only on an accurate diagnosis of the specific CHD, but also on the additional hemodynamic findings unique to each patient. The following section provides a discussion of specific cardiac lesions at risk of hemodynamic compromise, highlighting the fetal echocardiographic findings that are predictive of individualized DR care.

7 | COARCTATION OF THE AORTA

In its severest form, coarctation (CoA) is a ductal-dependent lesion, and in these patients, prenatal detection has been associated with

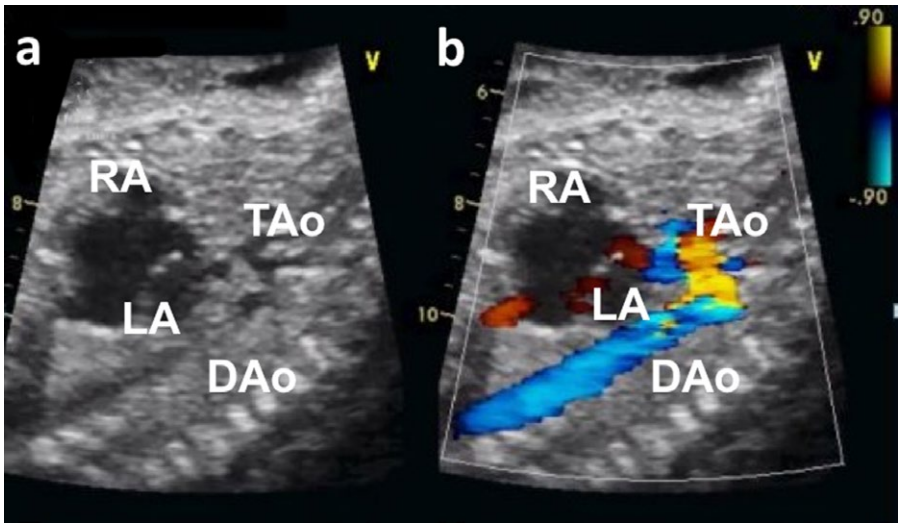

FIGURE 2 A. Sagittal two-dimensional view of the aortic arch in a fetus with hypoplastic left heart syndrome. B. Color Doppler shows reversed flow (red) in the transverse aortic arch. DAo = descending aorta; LA = left atrium: RA = right atrium; and TAo = transverse aortic arch

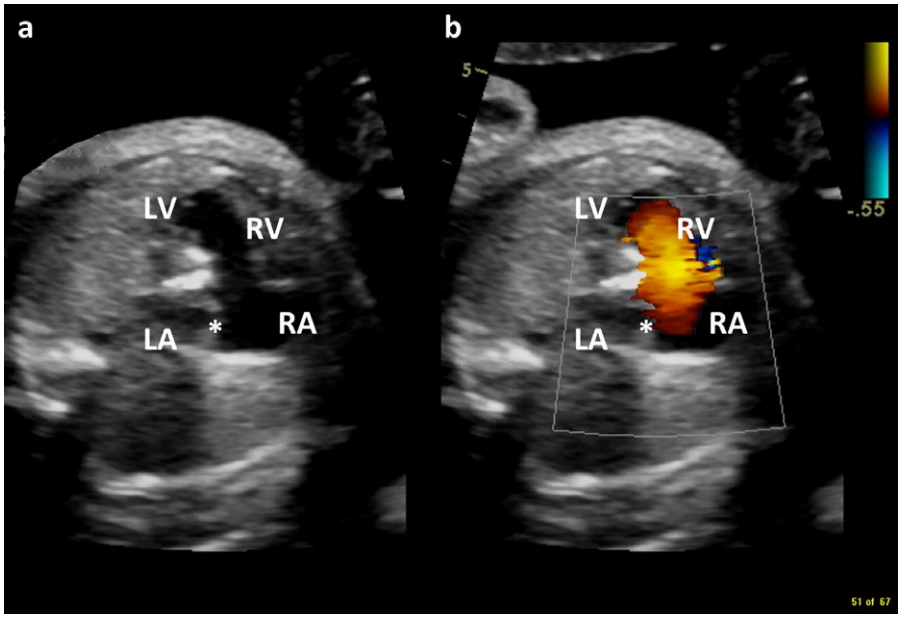

FIGURE 3 A. Axial four-chamber view of a fetus with hypoplastic left heart syndrome and intact atrial septum. B. Color Doppler shows the absence of blood flow across the foramen ovale (the foramen ovale is indicated by the asterisk). RA = right atrium; RV = right ventricle; LA = left atrium; and LV = left ventricle

decrease in mortality and morbidity.[51] Unfortunately, current strategies for prenatal and early postnatal detection are limited in their ability to accurately diagnose those in need. In recent studies, various fetal echocardiography parameters have been proposed to diagnose CoA, and diagnostic accuracy varies with the criteria used.[52,53] In a recent study, the persistence of diastolic flow at the aortic isthmus in addition to an aorta/pulmonary artery ratio (Ao:PA) ratio <0.65 in the 3 vessels with trachea view had a sensitivity of 87% for detection of CoA; however, specificity was lower at 53%, due to a higher false-positive rate.[54] In another study, a PA:Ao ratio of 1.60 had a sensitivity of 83.0% and specificity of 85.0% for predicting CoA.[55]

In a recent meta-analysis of 922 fetuses from studies published after 2000, prenatal detection of CoA using fetal echocardiography was 31%.[56] The parameters with the highest detection rate of CoA were: (1) hypoplastic aortic arch in fetuses with ventricular disproportion (sensitivity 90%; specificity 87%) (Figure 6A–B) and (2) presence of CoA shelf, defined as a prominent posterior fold (Figure 6C–D) (sensitivity 48.4%; specificity 97.7%). In this study, the use of multiparametric models integrating different fetal echocardiography variables had a higher diagnostic accuracy compared to the use of a single parameter. Four different algorithms were analyzed; 3 from the retrospective studies[57–59] and 1 from a prospective study.[60] Although a

comparison between models was limited, the model using the angles between the (1) ascending and descending aorta and (2) transverse and descending aorta had the highest sensitivity (95% and 100%, respectively) for predicting CoA of the aorta.[57] In the prospective study using fetal echocardiography for postnatal planning by Donofrio et al., fetuses suspected of having CoA that had a mildly dilated right heart and small aortic isthmus but with normal Doppler flow pattern were assigned to be low risk of CoA (LOC 1) and were delivered in the local hospital, utilizing standard postnatal care protocols with consult or telemedicine if the pediatrician was concerned, while those with a dilated right heart and a small distal arch with juxtaductal narrowing and reversed isthmus flow were assigned to be at higher risk (LOC 2) with recommendations to initiate PGE1 at the time of delivery and transfer to the cardiac center.[13] In the 17 fetuses thought to be at low risk of CoA, 3 (18%) had mild CoA, although only one required transfer. For those thought to have significant CoA requiring PGE1 with a plan for transfer (n = 19), 15 (79%) had CoA requiring surgery.[13]

For infants presenting with prenatal findings suggestive of CoA, delivery at a medical center with telemedicine services to confirm the diagnosis is useful. Resources should be available to initiate PGE1, and although often not necessary, the capability for mechanical ventilation is recommended. Unless there are additional maternal or fetal concerns, these babies do not need to be delivered early and the MOD is dependent on the obstetrical history (Table 2).

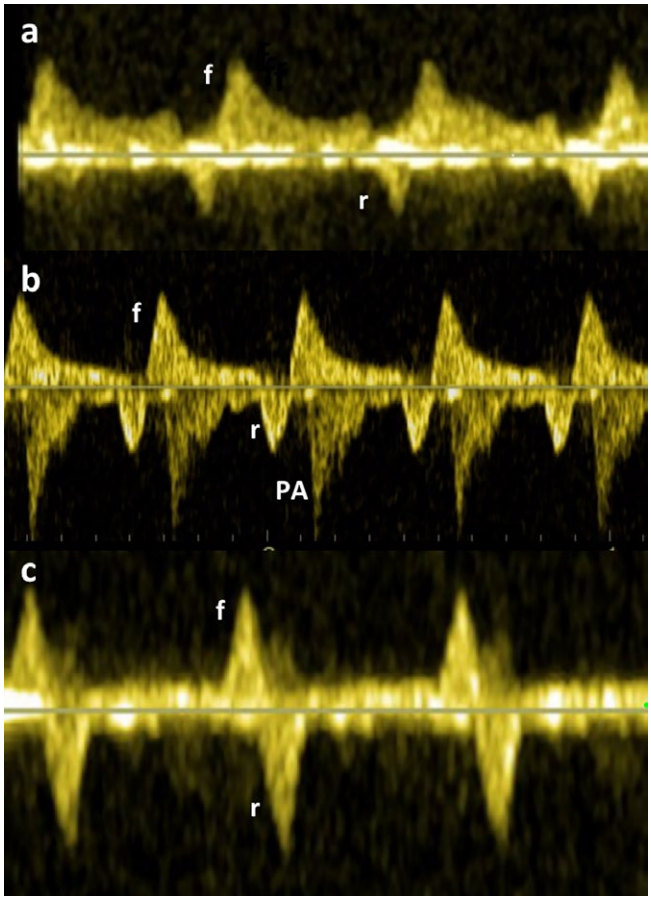

FIGURE 4 Color Doppler of the pulmonary vein flow in fetus with HLHS. A. PV flow with f/r >5. B. PV flow with f/r <5 and >3. Color Doppler of the pulmonary artery is seen below the baseline. C. PV flow with f/r <3. PV f/r, velocity-time integral forward/reversed flow ratio of the pulmonary vein flow. f = forward; r = reversed; and PA = pulmonary artery

8 | TETRALOGY OF FALLOT

Tetralogy of Fallot is the most common cyanotic CHD, with the prenatal detection of 90% using fetal echocardiography in experienced hands.[61] Among those with a patent pulmonary valve, the delivery plan is based on prediction of those infants with TOF who will be cyanotic after ductal closure and therefore require continued patency of the ductus arteriosus at birth to sustain the pulmonary circulation. In 1 retrospective study, a small pulmonary valve (*z*-score <−3) had a 100% sensitivity although only 34% specificity for prediction of a ductal-dependent circulation, while reversed flow at the ductus arteriosus had a sensitivity of 80% and a specificity of 100%.[40] In the prospective study by Donofrio et al., among fetuses with TOF, the presence of reversed flow in the ductus arteriosus had a sensitivity of 100% and specificity of 97% for prediction of the need for PGE1 at birth and subsequent neonatal surgery (LOC 2).[13]

Given these findings, ductal dependency and need for neonatal surgery vs a plan that includes postnatal confirmation of the diagnosis with outpatient follow-up and elective repair in fetuses diagnosed with TOF can be determined by fetal echocardiography (Table 2).Those at low risk can be delivered in a medical center with resources available such that postnatal cardiology consult or telemedicine confirmation of the diagnosis can be made. Otherwise, plans should be made

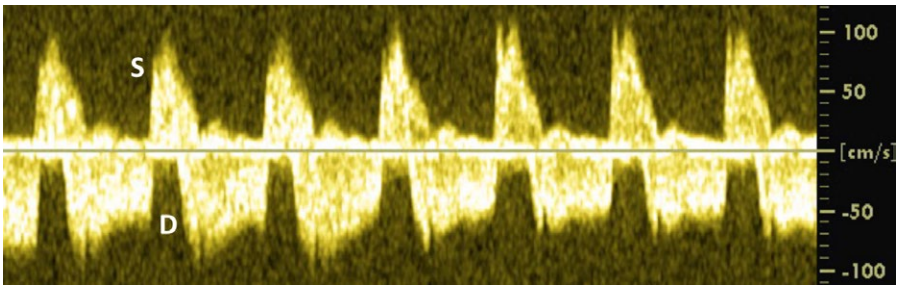

FIGURE 5 Bidirectional pulsed-Doppler blood flow in the ductus arteriosus in a fetus with D-transposition of the great arteries. S = systole; and D = diastole

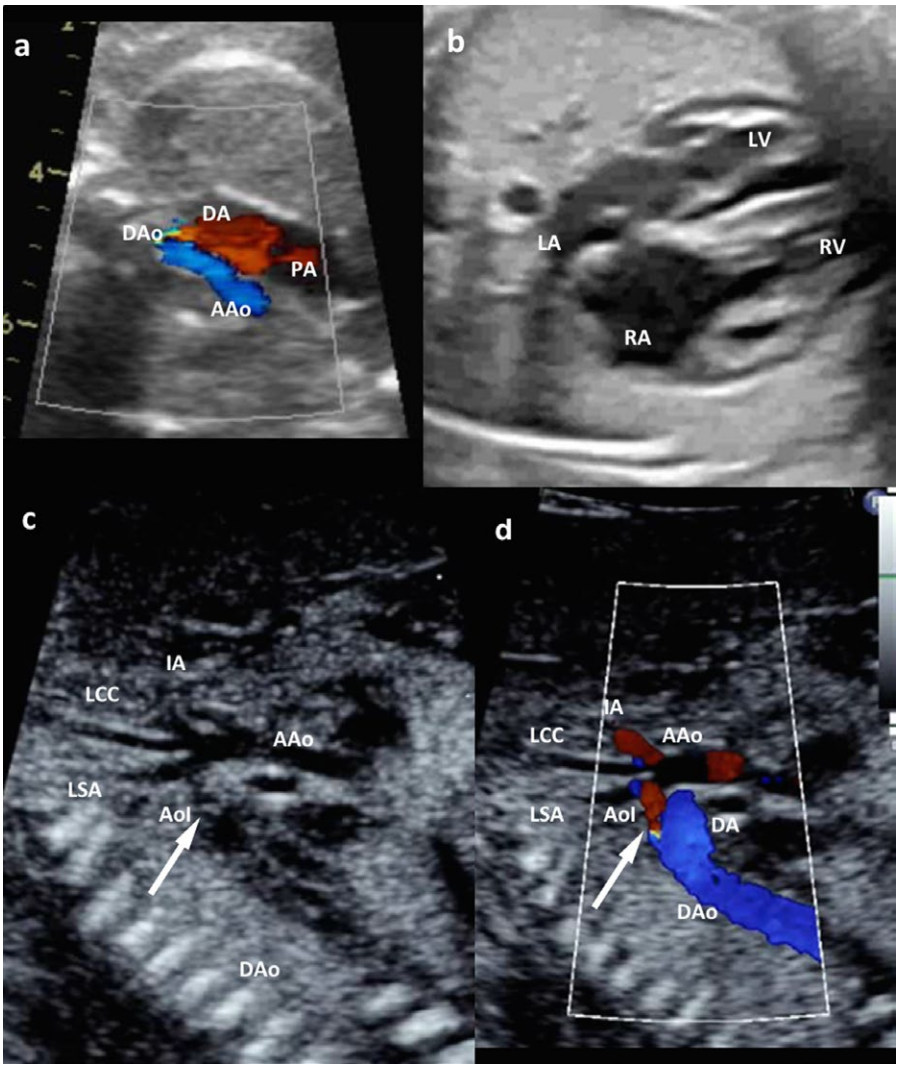

FIGURE 6 Multiple views of findings representative of coarctation of the aorta. A. Color Doppler at the level of the three-vessel view. The aortic arch is significantly smaller than the ductus arteriosus. Flow in the transverse arch is retrograde (blue). B. Four-chamber view with ventricular disproportion with the right ventricle appearing larger than the left ventricle. C. Grayscale and D. Color Doppler in a sagittal view of the aortic arch. Posterior shelf (arrow) is noted at junction of the isthmus with the ductus arteriosus. Flow in the isthmus and distal arch is retrograde (red). AAo = ascending aorta; AoI = aortic isthmus; DA = ductus arteriosus; DAo = descending aorta; IA = innominate artery; LA = left atrium; LCC = left common carotid artery; LSA = left subclavian artery; LV = left ventricle; PA = pulmonary artery; RA = right atrium; and RV = right ventricle

for delivery close to the cardiac center. Unless there are additional maternal or fetal concerns, these babies do not need to be delivered early and the MOD is dependent on the obstetrical history.

9 | HYPOPLASTIC LEFT HEART SYNDROME

Hemodynamic stability in newborns with HLHS depends on patency of ductus arteriosus and an adequate interatrial communication. Patency of the ductus arteriosus is needed to supply the systemic circulation, and therefore, initiation of PGE1 is recommended for all babies with this diagnosis. In contrast, 6%–20% of newborns with HLHS also have a severely RAS or IAS.[10,62,63] The presence of a RAS or IAS at birth significantly affects outcome after delivery, by impairing pulmonary venous egress, leading to pulmonary edema, severe hypoxemia, and poor cardiac output. Newborns with HLHS and a severely RAS or IAS require urgent cardiac intervention to open the atrial septum and allow left atrial egress of pulmonary venous blood flow.[63] Surgical survival for newborns with HLHS is lower for those with a RAS or IAS, and survival may be higher for those diagnosed during the fetal period compared to those diagnosed postnatally. [63]

The identification of fetuses with HLHS and a RAS or IAS in utero allows coordination between the obstetrician and the pediatric specialists needed at birth.[9,10,12,63] Detailed planning allows immediate cardiac intervention with improvement in the cardiovascular status. In retrospective studies, the antenatal prediction of RAS or IAS in case of HLHS ranges from 67% to 99%.[12,63] In a prospective study, using pulmonary vein Doppler assessment in fetuses with HLHS, Donofrio et al. reported a sensitivity of 100% and specificity of 97% for prediction of need for urgent intervention in newborns with HLHS and RAS or IAS.[13] Given that foramen ovale restriction can become more severe in the third trimester, it has been recommended that serial assessment during pregnancy until delivery be performed.[64]

An additional advantage of serial evaluation of the foramen ovale in fetuses with HLHS may lie in the potential for fetal cardiac intervention for select patients to open the atrial septum prior to delivery.[65,66] In fetuses with HLHS and RAS or IAS, different techniques of fetal intervention have been proposed, all aimed to open the atrial septum and decrease the postnatal risk of pulmonary venous congestion and associated lung injury.[4]

All newborns diagnosed with HLHS by fetal echocardiography require specialized postnatal care. In those with an open atrial septum and

pulmonary vein flow that is not concerning, delivery should occur in a medical center with resources to care for critically ill neonates. A neonatologist on site is imperative to initiate PGE1. Mechanical ventilation may be necessary. Supplemental oxygen should be used with caution given that this may decrease the pulmonary resistance and compromise the systemic perfusion. Transport to the cardiac center should be arranged and in instances where the local hospital is remote or a long distance away from the cardiac center, consideration for delivery closer to the cardiac center is indicated.[27] Delivery in these instances can be at or near term, and the timing and MOD depend on the obstetrical history. In fetuses with HLHS and a RAS or IAS, the delivery should be coordinated such that the necessary team is readily available to care for the newborn, including neonatologist, pediatric cardiologist, interventionalist, and cardiothoracic surgeon. To facilitate rapid postnatal intervention, the delivery should be planned to occur in the cardiac center or in close proximity with a plan in place for rapid transport for care. Delivery earlier than 39 weeks should be avoided unless there are additional fetal or maternal conditions. In some instances, to facilitate coordination of multispecialty care, cesarean section may be considered. (Table 1)

10 | OBSTRUCTED TOTAL ABNORMAL PULMONARY VENOUS RETURN

Total abnormal pulmonary venous return is a rare CHD, with a high mortality rate, up to 27%.[67] An important risk factor for poor outcome is coexistence of pulmonary vein obstruction, occurring in about 45% of cases and leading to pulmonary venous congestion, pulmonary hypertension, and severe hypoxia soon after birth.[67] Prenatal detection of obstructed TAPVR allows appropriate delivery planning, stabilization, and early surgery.[12,50] However, the prenatal detection rate of TAPVR is overall low. Seale et al., in a retrospective European multicenter study, reported that prenatal diagnosis identified only 1.9% of the newborns born between 1988 and 2004 with obstructed or nonobstructed TAPVR.[68] A more recent study reported that 13% of newborns with obstructed TAPVR were identified prenatally by experienced fetal cardiologists.[12] In both of these studies, the mortality rate was higher among the group of infants who were diagnosed postnatally, compared to those for which TAPVR was diagnosed after birth. Ganesan et al.[50] recently proposed an algorithm, based on 26 fetuses, to improve prenatal detection of TAPVR using the following findings to suggest a risk of TAPVR: (1) lack of identification of at least 2 pulmonary veins connecting to the left atrium, (2) right-left heart size discrepancy, (3) presence of the "twig" sign on the four-chamber view, defined as an abnormally wide space in the retro-atrial area, (4) abnormal three-vessel view, with the presence of either an enlarged superior vena cava, or abnormal ascending vessel, and (5) abnormal pulmonary vein Doppler waveform.

Once TAPVR is detected prenatally, determination of risk of obstruction should be attempted. If the venous pathway is supracardiac with a flow pattern not suggestive of obstruction, then delivery at a hospital with resources to confirm the diagnosis either with cardiology consultation or telemedicine can be considered. If the Doppler pattern suggests obstruction or the venous pathway is infradiaphragmatic (Figure 7A–D), delivery at the cardiac center or a hospital in close

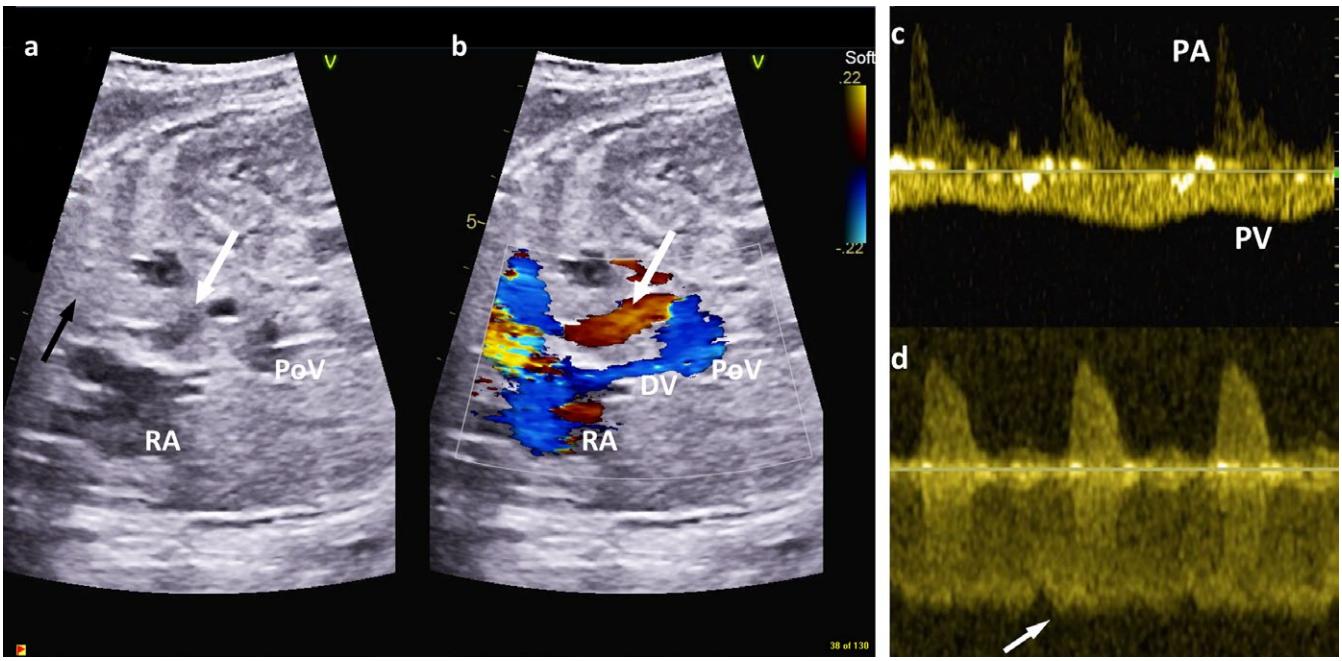

FIGURE 7 A-B. Coronal two-dimensional view (A) and with color Doppler (B) of a fetus with total anomalous pulmonary venous return, infradiaphragmatic type. The pulmonary veins drain into a descending vertical vein (white arrow), which passes below the diaphragm (black arrow) and drains into the right atrium via the portal vein and ductus venosus, C. Spectral Doppler waveform of the pulmonary vein flow in a fetus with infradiaphragmatic TAPVR. D. Spectral Doppler of the descending vertical vein draining into the portal vein/ductus venosus. Flow is of high velocity and continuous suggesting obstruction. This fetus presented with obstructed TAPVR at birth. DV = ductus venosus; PA = pulmonary artery; PoV = portal vein; PV = pulmonary vein; and RA = right atrium

proximity is recommended. To facilitate rapid postnatal care, the delivery should be planned with a plan for urgent cardiac surgery. Delivery earlier than 39 weeks should be avoided unless there are additional fetal or maternal conditions. In some instances, to facilitate coordination of multispecialty care, cesarean section may be considered.

11 | D-TRANSPOSITION OF THE GREAT ARTERIES WITH RESTRICTIVE ATRIAL SEPTUM

Postnatal compromise in newborns diagnosed with D-TGA depends on whether the foramen ovale and/or ductus arteriosus will be restrictive or closed at birth. Infants diagnosed with D-TGA are at risk of developing RAS during the fetal period, with reduced or absent blood flow through the foramen ovale, postnatally resulting in progressive hypoxemia and acidosis. The presence of a severe RAS requires cardiac intervention soon after birth to open the atrial septum. This is done by catheter BAS. Failure to open the atrial septum may result in rapid hemodynamic decompensation and poor outcome, including death.[10,45] Pruetz et al.[12] in their retrospective review reported low antenatal prediction of postnatal care in cases of D-TGA. Among the 18 newborns with D-TGA who underwent emergent BAS, only in 5 cases (28%), the postnatal care was correctly predicted prenatally.

In a prospective study by Donofrio et al.,[13] fetal echocardiography evaluation of the atrial septum predicted the need for urgent BAS in 15 of 17 (88%) newborns diagnosed prenatally with D-TGA and who were assigned as high risk (LOC 3 and 4). However, using the published criteria,[45–47] 10 fetuses were considered to have a lower risk of foramen ovale closure (LOC 2). Among these, 3 (30%) did not require urgent intervention at birth; however fetal echocardiography failed to predict the need for BAS in 7 (70%). In 6, mild persistent cyanosis prompted intervention. In 1, severe hypoxia and acidosis occurred, requiring urgent intervention. This case resulted in a change to the protocol, with all babies being considered high risk (assigned LOC 3 or 4). Overall, in this prospective study, the prenatal prediction of need for atrial septostomy at birth in newborns with D-TGA had a sensitivity of 68% and specificity of 60%.[13] In addition to assessment of the atrial septum and ductus arteriosus, pulmonary vein Doppler may be useful to predict need for BAS. In a recent study, urgent BAS was predicted with a sensitivity of 82% and specificity of 100%.[49] Of note is that changes in the foramen ovale in fetuses with D-TGA may occur late in pregnancy.[10,48] (Figure 8; Movies S4–S5). Therefore, sequential fetal echocardiography to investigate the atrial septum has been recommended from the time of diagnosis to the time of delivery[10,45,46,48] (Table 2).

Given the current limitations of fetal echocardiography to predict postnatal need for BAS, it is recommended that all babies with D-TGA be considered high risk.[4] Delivery at or near a cardiac center is recommended for all babies diagnosed prenatally. To facilitate rapid postnatal care, the delivery should be planned. Delivery earlier than 39 weeks should be avoided unless there are additional fetal or maternal conditions. In some instances, to facilitate coordination of multispecialty care particularly if the foramen ovale is closed and the ductus arteriosus is severely restrictive, cesarean section may be considered. Delivery room care should include resuscitation to maintain oxygenation and systemic perfusion until the procedure can be undertaken. Ideally, the BAS should occur in the DR or in the ICU as soon as possible after delivery when there is compromise. Resources should be available to initiate PGE1 and mechanical ventilation using supplemental oxygen if needed. In babies who are noted to have a restrictive or closed ductus arteriosus, pulmonary hypertension may occur. In these instances, 100% oxygen and inspired nitric oxide may be beneficial.

12 | CHD AT RISK OF HEART FAILURE AND HYDROPS

Cases of severe Ebstein anomaly, TOF with absent pulmonary valve, primary or secondary cardiomyopathy, uncontrolled tachyarrhythmia, and complete atrioventricular block are all at increased risk of the development of hydrops and fetal demise. Even if born at term, there is an increased risk of poor neonatal outcome due to complications

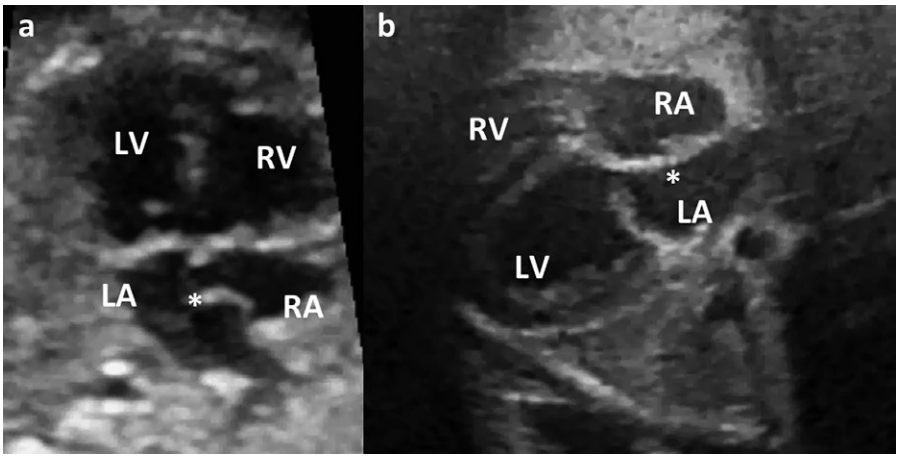

FIGURE 8 Four-chamber view of a fetus with D-transposition of the great artery. At 22 weeks, the atrial septum is mobile (A), while it appears closed at 38 weeks (B). LA = left atrium; LV = left ventricle; RV = right ventricle; and RA = right atrium. The asterisk indicates the atrial septum

from low cardiac output, airway obstruction or pulmonary hypoplasia, arrhythmias, and heart failure. Currently, there is limited information regarding delivery management for these severe forms of CHD.[4] Prenatal assessment and close follow-up of cardiac function are indicated, and premature/early delivery may be considered for signs of heart failure or fetal distress[4,69] (Table 2).

12.1 | Tetralogy of Fallot with absent pulmonary valve (TOF/APV)

The absence of a functioning pulmonary valve occurs in up to 6% of fetuses diagnosed with TOF.[70] The absence of a pulmonary valve results in severe pulmonary artery dilation, ventricular volume overload, and right-side heart failure. Airway and lung abnormalities are often associated with TOF/APV due to extrinsic compression by the dilated pulmonary vessels including tracheobronchial obstruction, congenital lobar emphysema, and pulmonary hypoplasia. These fetuses are at increased risk of cardiac failure, hydrops, and in utero demise (up to 50%). Severe hypoxia can develop at birth with a high overall perinatal morbidity and mortality, with rate of death in infancy up to 42%.[70–72] The ductus arteriosus in fetuses with TOF/APV is often absent, and although the exact pathophysiology is unknown, this additional finding has been associated with more severe right ventricular volume overload.[73]

Despite advances in prenatal imaging, prenatal prediction of outcomes among fetuses with TOF/APV remains challenging. Fetal echocardiography parameters, such as measurements of the pulmonary valve annulus, pulmonary artery sizes, and pulmonary to aortic annular ratio have failed to predict outcome.[72] Recently, lung parenchymal abnormalities identified by fetal MRI in fetuses with TOF/APV have shown to correlate with poor neonatal outcome. For this reason, fetal MRI has been proposed to be used in addition to fetal echocardiography to identify those newborns at risk of compromise.[74,75] Information regarding prediction of delivery management for TOF/APV remains limited.[4] Given the high risk of poor perinatal outcome, close prenatal evaluation is indicated, with early delivery considered in cases with signs of fetal cardiac failure or hydrops[4,69] (Table 2). A multidisciplinary team in the DR is recommended, including neonatologist, cardiologist, and cardiothoracic surgeon, to ensure appropriate cardiopulmonary support.[4] The recommended timing and MOD depend on the severity, but in general, early delivery should be avoided unless compromise is present in which delivery by cesarean may be indicated. In some instances, respiratory status may be improved by placing the infant in the prone position. If lung abnormalities are severe, mechanical ventilation may be needed. Given the absence of the ductus arteriosus, a PGE1 infusion is not typically helpful. Inhaled nitric oxide and 100% oxygen may be useful to decrease pulmonary vascular resistance and promote forward flow. In some instances, ECMO is required to stabilize the circulation prior to surgical intervention.

12.2 | Ebstein anomaly and TV dysplasia

Ebstein anomaly and tricuspid valve dysplasia (EA/TVD) represent a spectrum of rare CHD of the TV that can result in severe tricuspid regurgitation (TR), massive cardiomegaly, heart failure, hydrops, and fetal arrhythmia.[76] Mortality is high, with a reported risk of perinatal mortality up to 45%.[77]

According to a recent multicenter study of 243 fetuses with EA/TVD,[77] prenatal predictors of perinatal mortality include early gestational age at diagnosis <32 weeks; presence of pulmonary valve regurgitation; large TV annulus; pericardial effusion; larger cardiothoracic ratio; lower TR velocity; absence of anterograde flow across the pulmonary valve; and decreased left ventricular function. As recently reported,[78] the absence of these predictors at a second-trimester fetal echocardiography (<24 weeks) may not be reassuring for good outcome, as some of these abnormalities can develop and progress up to the time of delivery. Serial evaluation of the fetus with EA/TVD is suggested to identify those with high risk of poor perinatal outcome.[77]

Data regarding time and MOD for these fetuses are limited due to a paucity of prospective studies investigating outcomes with specific delivery management strategies. Thus, perinatal management often varies between different institutions.[77] Despite these limitations, delivery should be delayed until near term unless there is evidence of fetal compromise including hydrops fetalis, severe cardiac dysfunction, or uncontrolled arrhythmia[4] (Table 2).

12.3 | Congenital complete heart block

Bradycardia caused by complete heart block (CHB) puts the fetus at increased risk of development of fetal hydrops and heart failure, with overall high perinatal mortality rate.[4] CHB is a rare arrhythmia with an incidence of fetal demise up to 13% when associated with major CHD.[79] A recent retrospective study[79] investigating the postnatal outcome of fetuses diagnosed with CHB, idiopathic or associated with maternal anti-Ro or anti-La antibodies, showed that fetal hydrops was the most significant risk factor for fetal or postnatal demise. The gestational age at birth of those who died postnatally was significantly lower (34.3 weeks) compared to those who survived (36.8 weeks, $P = .02$). In this study, the etiology of CHB (ie, the presence of SSA antibodies), the postnatal ventricular rate, and history of antenatal treatment did not predict outcome.

Despite limited data regarding delivery planning in cases of newborn with prenatal diagnosis of CHB, close fetal surveillance is recommended, and early delivery should be considered in cases with signs of fetal hydrops and severe heart failure.[13] Delivery is recommended at the cardiac center or in close proximity, with neonatologist and cardiologist in the DR and availability for urgent therapy, including chronotropic and inotropic agents and temporary pacing[13] (Table 2).

13 | IN UTERO ASSESSMENT OF FETUSES WITH CHD: CURRENT AND FUTURE PERSPECTIVES

13.1 | Maternal hyperoxygenation testing

Several authors have proposed using administration of oxygen through a nonrebreathing face mask to the expectant mother during the third trimester either as a diagnostic tool that simulates postnatal

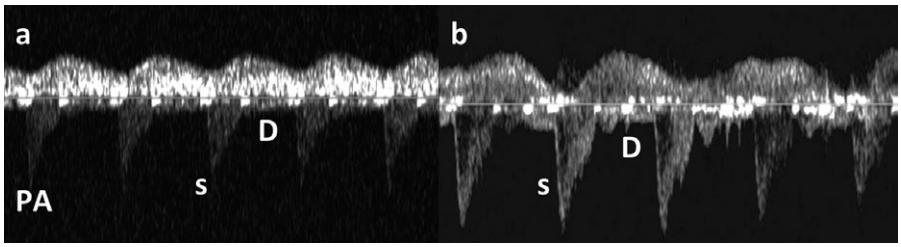

FIGURE 9 Maternal hyperoxygenation testing in a third-trimester fetus. A. Pulsed Doppler of the proximal branch pulmonary artery (below the baseline), while the mother breaths regular room air. B. Pulsed Doppler of the same branch pulmonary artery during maternal administration of oxygen via a nonrebreathing face mask. The diastolic flow is increased with maternal hyperoxygenation compared to the baseline. D = diastole; PA = pulmonary artery; and S = systole

physiology in the fetus[44,80,81] or as in utero chronic therapy to change fetal blood flow and oxygenation[82] in fetuses diagnosed with specific CHD. Invasive and noninvasive methods have proven that maternal hyperoxygenation (MH) increases fetal pO_2, and no maternal, fetal, or neonatal side effects have been reported.[83–86] MH in the third trimester elicits a physiologic response in the fetus characterized by a temporary increase in pulmonary blood flow.[85] In practice, pulmonary vasoreactivity in response to MH is defined by a ≥10% decrease in the Doppler pulsatility indices [(peak systolic velocity−end-diastolic velocity)/mean velocity] in the branch pulmonary arteries[44,85] (Figure 9).

In fetuses with HLHS and a RAS or IAS, lack of pulmonary vasoreactivity has been associated with need for urgent cardiac intervention at birth to decompress the left atrium in a single small series.[44] In addition, in a recent report, MH was shown to be useful for evaluating fetal cardiovascular physiology and predicted transitional changes in specific high-risk CHD including HLHS with RAS, TAPVR, TGA, and Ebstein anomaly.[81] Further studies are needed to define its predictive accuracy for postnatal outcome.

13.2 | Fetal magnetic resonance imaging (MRI)

Fetal MRI provides high-resolution imaging of the fetal anatomy and is used as an additional imaging modality when anomalies are suspected by obstetric ultrasound.[87] Several studies have shown that fetal MRI provides information regarding cerebral structural findings and changes in brain metabolism in fetuses with specific CHD that may affect the postnatal prognosis.[18,88,89] Recently, fetal MRI has also been proposed to assess the lung parenchyma in fetuses diagnosed with complex CHD such as HLHS or TOF with absent pulmonary valve.[74,75,90] In fetuses with HLHS, abnormal lung parenchyma described as "nutmeg lung" was found to be representative of abnormal pulmonary lymphatics[91] (Figure 10). Dilated lymphatics can be primary, due to abnormal development of the pulmonary lymphatic system or can be secondary to obstruction to pulmonary venous flow due to CHD such as HLHS or TAPVR.[91,92] In a recent study, fetuses with HLHS and MRI findings suggesting "nutmeg lung" in the third trimester had higher mortality and higher incidence of RAS or IAS compared to the group of HLHS without these findings.[90]

Tetralogy of Fallot with APV fetuses with significant airway obstruction and congenital lobar emphysema is at increased risk of severe hypoxia at birth[71] (Figure 11). Third-trimester fetal MRI can detect abnormal pulmonary findings in these fetuses.[74,75] In addition, fetal MRI has also shown to add important information among the fetuses with cardiac malposition suspected by fetal echocardiography.[93] In up to 30% of these fetuses, fetal MRI: (1) identified the etiology of abnormal cardiac axis, such as congenital diaphragmatic hernia or primary congenital lung abnormalities, (2) revealed the presence of extracardiac abnormalities, and (3) defined the type of heterotaxy syndrome. Thus, fetal MRI findings may provide important additional details to a prenatal diagnosis of CHD, improving prenatal counseling and perinatal planning.

13.3 | Cardiac function assessment

Some CHD is at significant risk of cardiac dysfunction, which may affect delivery management. The cardiovascular profile (CVP) score has been used to predict risk of perinatal mortality and poor outcome in fetuses with CHD.[94] It consists of 5 parameters: signs of hydrops,

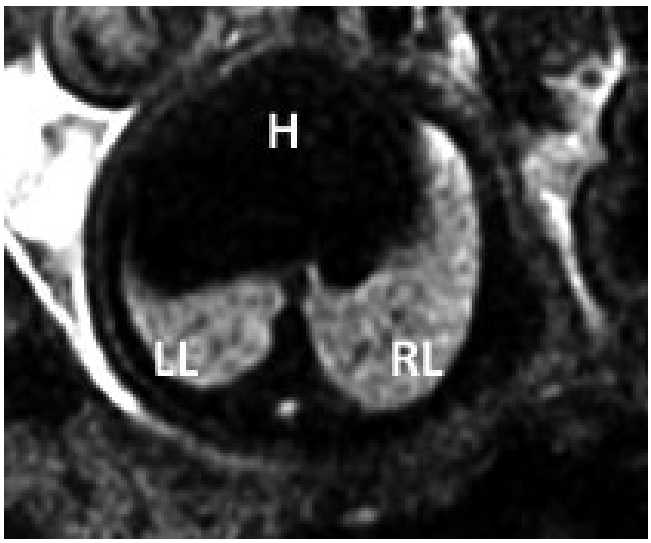

FIGURE 10 T_2-weighted fetal magnetic resonance image of the chest of a fetus with hypoplastic left heart syndrome and intact atrial septum. The lung parenchyma is heterogeneous, with a characteristic linear pattern or "nutmeg lung". H = heart; RL = right lung; and LL = left lung. Image courtesy of Dr. Dorothy I. Bulas

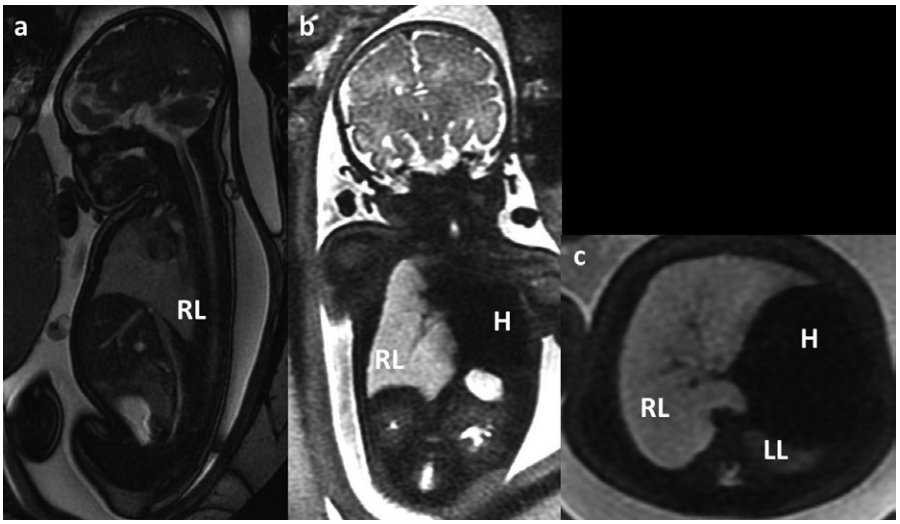

FIGURE 11 T_2-weighted fetal magnetic resonance images of a fetus with tetralogy of Fallot and absent pulmonary valve with over inflation of the right lung due to bronchial compression. This results in deviation of the heart to the left compressing the left lung. A. Sagittal view showing the overinflated right lung. B. Coronal and (C) axial view. H = heart; RL = right lung; and LL = left lung. Image courtesy of Dr. Dorothy I. Bulas

heart size, cardiac function, umbilical artery, and venous Doppler. Any parameter may be rated from 0 to 2, with the final score ranging from 0 to 10. Previous studies found that fetuses with CHD and CVP less than or equal to 7 at last study prior to delivery had a higher risk of perinatal mortality (ranging from 67% to 100%) and worse postnatal outcome compared to those with CPV of 8 or higher (mortality rate ranging from 12% to 16%).[95,96]

While the presence of hydrops and severe cardiomegaly has been shown to have the highest risk of mortality in fetuses with CHD, the utility of umbilical or cerebral artery Doppler indices to predict poor perinatal outcome is unclear.[95,97,98] In these fetuses, abnormal cerebral artery Doppler, with associated normal or high resistance umbilical artery, has been described as independent risk factors for impaired neurodevelopment in cases of CHD.[99,100] However, studies have failed to show that fetuses with CHD and third-trimester abnormal umbilical and cerebral artery Doppler parameters, in the absence of superimposed placenta insufficiency, have a higher risk of perinatal mortality or abnormal artery pH at birth compared to those fetuses with CHD and normal umbilical and cerebral Doppler.[97,98]

14 | CONCLUSION

Fetal echocardiography can accurately diagnose CHD, can be used for prediction of postnatal severity of disease, and can guide the care needed for newborns with different forms of CHD. Antenatal identification of newborns with CHD requiring fetal intervention or special care in the DR or shortly after birth allows creation of detailed fetal, perinatal, and delivery recommendations, tailored for the specific lesions. Fetal echocardiography therefore has the potential to improve perinatal and perioperative outcome of newborns with specific CHD. Despite advances, prediction of postnatal compromise remains difficult for some defects. For these, multiparametric diagnostic models integrating different fetal echocardiography variables and the use of other diagnostic tools, such as MH testing and fetal MRI, may be beneficial.

The prenatal diagnosis of CHD has shown important benefits to care including earlier age at treatment, decreased perioperative morbidity, and improved neurologic outcome in specific CHD.[21–23] Only by expanding efforts to design strategies for improving detection of CHD, identifying risk factors that determine risk of postnatal compromise, investigating diagnoses that may benefit from fetal intervention, and creating coordinated multidisciplinary DR care plans, we will move forward in our goal to improve outcome beyond current practice.

CONFLICT OF INTEREST

The authors report no conflict of interest.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

Movie S1. Color Doppler reversed flow (blue) in the ductus arteriosus (arrow) in a fetus with tetralogy of Fallot.

Movie S2. Color Doppler shows reversed flow (red) in the transverse aortic arch (arrow) in a fetus with hypoplastic left heart syndrome.

Movie S3. Color Doppler shows the absence of blood flow across the foramen ovale (the foramen ovale is indicated by the asterisk) in a fetus with HLHS. Blue flow in the right atrium represents mild tricuspid valve regurgitation.

Movie S4. Freely mobile atrial septum in a 22 weeks of fetus with D-TGA.

Movie S5. Intact atrial septum in the same fetus (of Movie S4) with D-TGA at 38 weeks.

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