Seminars in Fetal and Neonatal Medicine 24 (2019) 101034

Contents lists available at ScienceDirect

Seminars in Fetal and Neonatal Medicine

journal homepage: www.elsevier.com/locate/siny

Delivery room emergencies in critical congenital heart diseases

Jay D. Pruetz[a,b], Shuo (Sue) Wang[a], Shahab Noori[c,*]

[a] Heart Institute, Division of Cardiology, Children's Hospital Los Angeles, Department of Pediatrics, Keck School of Medicine, University of Southern California, Los Angeles, CA, United States

[b] Department of Obstetrics & Gynecology, Keck School of Medicine, University of Southern California, Los Angeles, CA, United States

[c] Fetal and Neonatal Institute, Division of Neonatology, Children's Hospital Los Angeles, Department of Pediatrics, Keck School of Medicine, University of Southern California, Los Angeles, CA United States

ARTICLE INFO

Keywords:
Congenital heart disease
Delivery room
Ductus arteriosus
Fetal circulation
Fetal echocardiography
Prenatal diagnosis resuscitation

ABSTRACT

Transition from fetal to postnatal life is a complex process. Even in the absence of congenital heart disease, about 4–10% of newborns require some form of assistance in the delivery room. Neonates with complex congenital heart disease should be expected to require significant intervention and thus the resuscitation team must be well prepared for such a delivery. Prenatal assessment including fetal and maternal health in general and detailed information on fetal heart structure, function and hemodynamics in particular are crucial for planning the delivery and resuscitation. In addition, understanding the impact of cardiac structural anomaly and associated altered blood flow on early postnatal transition is essential for success of resuscitation in the delivery room. In this article, we will briefly review transitional circulation focusing on altered hemodynamics of the complex congenital heart diseases and then discuss the process of preparing for these high-risk deliveries. Finally, we will review the pathophysiology resulting from the cardiac structural anomaly with resultant altered fetal circulation and discuss delivery room management of specific critical congenital heart diseases.

1. Introduction to the hemodynamic effects of critical congenital heart defects at birth

1.1. Fetal and transitional circulation

Knowledge of normal fetal and transitional circulations is essential for understanding the effect of congenital heart disease (CHD) and the associated altered blood flow in the fetus and the newborn. This in turn allows for anticipating the symptomatology and helps in management of these newborns in the delivery room (DR). We will briefly describe the normal fetal and transitional circulations as they have been described in detail elsewhere in this issue of Seminars. The most oxygenated blood coming from the umbilical vein first enters the portal venous system with about 50% of blood bypassing the liver via the ductus venosus flowing medially into the upper portion of inferior vena cava (IVC) [1,2]. This stream of blood flow is directed toward the foramen ovale by the Eustachian valve. In contrast, the poorly oxygenated blood flow from the lower part of the body flows along the lateral portion of IVC and is, in addition to superior vena cava (SVC) flow, directed toward the tricuspid valve. The most oxygenated blood, therefore, enters the left side of the heart and supplies the myocardium and brain. The right ventricle receives most of the systemic venous return; however, about 70–80% of the right ventricular output bypasses the high resistance pulmonary vascular bed via the ductus arteriosus to enter the descending aorta [2,3]. Therefore, both ventricles contribute to systemic blood flow with the right ventricle being the dominant ventricle and contributing about 55–60% of the combined cardiac output. At birth, there is a drop in pulmonary vascular resistance secondary to lung aeration and higher oxygen exposure, an increase in systemic vascular resistance secondary to removal of the low resistance placental circulation, and blood flow starts transitioning to a mature type of circulation. These changes result in a reduction or cessation of ductus venosus flow, reversal of flow through the ductus arteriosus and functional closure of the foramen ovale with no to minimal left-to-right flow.

In cases of CHD, the above described fetal circulation is altered and depending on the structural defect this alteration can be minimal and/or with no observable adverse effect on fetal growth and well-being, or it can severely impact the fetus and result in fetal demise. The changes in blood flow are specific to each CHD and the severity of the defect. Any defect resulting in either increased or decreased flow has both upstream and downstream effects. In addition to affecting the oxygen content of blood and the amount of blood supply to a vascular bed (lungs, brain, other organs), this altered blood flow leads to changes in

* Corresponding author. Division of Neonatology, Children's Hospital Los Angeles, 4650 Sunset Blvd, MS#31, Los Angeles, CA, 90027, United States.
E-mail address: snoori@chla.usc.edu (S. Noori).

https://doi.org/10.1016/j.siny.2019.101034

Abbreviations

ACOG	American College of Obstetricians and Gynecologists
ASD	atrial septal defect
BAS	balloon atrial septostomy
CHB	complete heart block
DCC	delayed cord clamping
DR	delivery room
D-TGA	dextro-transposition of the great arteries
ECMO	extracorporeal membrane oxygenation
EXIT	ex utero intrapartum treatment
HLHS	hypoplastic left heart syndrome
ICU	intensive care unit
LOC	level of care
MOD	mode of delivery
PFO	Patent foramen ovale
PGE	prostaglandin E1
PR	pulmonary regurgitation
RAS	restrictive atrial septum
RV	right ventricle
TAPVR	total anomalous pulmonary venous return
TR	tricuspid regurgitation
TOF	tetralogy of Fallot
UVC	umbilical venous catheter
VSD	ventricular septal defect

growth of the heart chambers and vessels with further impact on hemodynamics. For example, in hypoplastic left heart syndrome (HLHS), hypoplasia of the aortic and/or mitral valve decreases forward flow through the left heart resulting in left ventricular hypoplasia and dysfunction as a result of coronary ischemia and endocardial fibroelastosis. The result is decreased LV compliance with increased ventricular filling pressure that in turn increases the left atrial pressure which reduces right-to-left shunt at the patent foramen ovale (PFO). In severe cases, the PFO shunt reverses (becoming left-to-right) leading to maldevelopment of the foramen. The reduction or cessation of blood flow through the aortic valve leads to hypoplasia of the ascending aorta and the aortic arch with brain oxygenation being compromised due to retrograde supply of less saturated blood from the patent ductus arteriosus (PDA).

The alteration of blood flow associated with CHD becomes a bigger challenge after birth. In addition, the normal increase in metabolism and oxygen consumption (breathing, thermoregulation, etc) after birth potentiate the effects of low oxygen saturation and blood flow in neonates that may be present in CHD. The timing and degree of cardiorespiratory compromise depends on the type and severity of the defect. For example, in HLHS, the low or absent flow through the aortic valve means that ductal patency must be maintained to ensure adequate systemic blood flow. More importantly, the already elevated left atrial pressure is further increased by the natural postnatal increase in pulmonary blood flow. This in turn can result in pulmonary congestion, respiratory distress and need for respiratory support. The severity of presentation in the DR in large part depends on the PFO flow. The more restrictive the PFO, the more severe the presentation will be at birth. This example highlights the importance of detailed assessment of the heart and fetal circulation for successful planning of delivery.

1.2. Definition of critical congenital heart disease

Complex forms of CHD often require early and/or emergent medical, surgical, or catheterization-based interventions in the first days to weeks of postnatal life. CHD lesions with inadequate aortic or pulmonary outflow can usually be stabilized in the neonatal period with medical therapy, using prostaglandin E1 (PGE) to maintain ductal patency, prior to cardiac intervention. However, critical forms of CHD have an additional element of instability during the perinatal transition period and often require emergent cardiac intervention in the first hours after delivery for stabilization and survival. These include lesions such as obstructed total anomalous pulmonary venous return (TAPVR) and HLHS with restrictive atrial septum (RAS) which lack adequate pulmonary egress, D-transposition of the great arteries (D-TGA) with RAS that limits intra-cardiac mixing, severe Ebstein anomaly and tetralogy of Fallot (TOF) absent pulmonary valve which are associated with airway anomalies that compromise the caregivers' ability to ventilate, and tachyarrhythmias or congenital complete heart block that result in inadequate cardiac output due to severe fetal tachycardia or bradycardia respectively. Most of these critical forms of CHD can be diagnosed with fetal echocardiography, which then allows for careful planning of maternal care to optimize the delivery and provide targeted postnatal care [4]. Furthermore, prenatal diagnosis can decrease perinatal morbidity and improve stabilization of patients prior to cardiac surgery [5,6]. Critical CHD diagnoses can be triaged using a combination of anatomic and physiologic fetal echocardiography findings to assign the appropriate risk level predicted postnatally [4,6,7]. This allows both the maternal and neonatal care providers the opportunity to carefully plan the perinatal care in order to optimize the delivery and provide targeted postnatal care.

1.3. Preparation for resuscitation of neonates with critical CHD

As preparation is made for resuscitation of a neonate with critical CHD, a careful review of the prenatal findings including fetal echocardiogram is crucial. A clear communication among the neonatologist, fetal cardiologist and the delivering obstetrician is paramount for the success of resuscitation. Categorizing patients into severity groups (see below) and understanding the severity of lesion are helpful in anticipating the interventions needed in the DR. Decisions regarding the use of delayed cord clamping should be made ahead of time and reviewed before delivery with the obstetrician.

The team should be assembled far in advance and briefed on the details of the case, the anticipated clinical status of the newborn, and any interventions that might be needed. Each team member should have a clear instruction on his/her role and understand how the role might change depending on the scenario encountered. All critical CHD deliveries should be attended by a neonatologist. As these patients often require respiratory support and intubation, a respiratory therapist should also be in attendance. In addition, at least 2 nurses are needed to assist with stabilization including emergency vascular access and chest compression. Other specialists may also be needed depending on the case. Transport team should be ready and on site for the delivery in the highest risk cases, those requiring emergent neonatal cardiac intervention, in order to facilitate immediate transfer to cardiac care and minimize time to intervention.

Although all supplies and equipment needed for a full resuscitation should be available for every delivery, in cases of critical CHD, additional steps need to be taken. An umbilical venous catheterization (UVC) insertion kit with the line flushed and ready for insertion and normal saline syringes for a total of 20–30 ml/kg bolus should be prepared in advance. Depending on the case, thoracentesis and pericardiocentesis set-ups, and prefilled epinephrine syringes should also be available prior to the delivery.

1.4. Perinatal management strategies to optimize postnatal transition

Active prenatal planning and perinatal management for neonates with CHD allow for a well-coordinated transition from fetal life to

postnatal care, minimization of mortality and morbidity, and a stable pre-operative clinical status. Perinatal management action plans for critical CHD are now utilized by many centers across the United States and Europe using similar risk stratifying schemes with recommended care plans [6–9]. These classification systems are based on regional practice patterns and designed to identify patients that require specialized treatment in the DR and cardiac intervention in the first hours after delivery [10,11]. Cardiovascular disease severity scales are based on the anatomic severity of CHD, need for postnatal intervention, complexity of intervention and overall prognosis. The level of care (LOC) is typically assigned first by the cardiologist, according to the CHD diagnosis, and is then reviewed and agreed upon by the entire maternal fetal medicine team. Each LOC is linked with a specific coordinated action plan and detailed perinatal recommendations for delivery and DR management such as need for PGE, transport, and intervention. Risk stratification systems are designed for multiple levels of CHD severity and are used to select the appropriate medical center for delivery, mode of delivery (MOD), level of perinatology and neonatology services available, and capability for immediate access to cardiology and cardiothoracic surgery care. These risk stratification and LOC management plans for prenatally diagnosed CHD are highly accurate at predicting the postnatal care required and need for emergent intervention at birth [8]. These classification strategies have been highly reproducible with the exception of D-TGA due to the difficulty determining the risk for postnatal atrial level restriction. At our institution we developed a similar method of risk stratification of prenatally diagnosed cases of CHD that require emergent neonatal cardiac intervention, incorporating a four tier classification system, which we have termed “Emergent Neonatal Cardiac Intervention” (ENCI) risk categories (Table 1) [6]. A recent evaluation of this system at our institution showed an overall predictive ability of 89% with high adherence to recommendations, but not in all areas (unpublished data). This review led us to make additional improvements in LOC plans including standardizing communications, better prenatal coordination of the transport team and the addition of prenatal consenting for transport/procedures. Here is a review of the ENCI Risk Categories:

1.4.1. Level 1 (low risk)

CHD that does not cause hemodynamic instability and is not expected to require specialized care or intervention in the newborn period. Mothers can deliver at a hospital capable of providing care for babies with mild forms of CHD. MOD is not an issue and no special DR care is anticipated. Examples: atrial septal defect (ASD), ventricular septal defect (VSD), and mild valve abnormalities.

1.4.2. Level 2 (intermediate risk)

CHD with potential for hemodynamic instability and possible need for postnatal evaluation by subspecialists, but low risk for neonatal intervention. Mothers should deliver at a facility with access to neonatology and subspecialty consultation as needed. Delivery should occur in a facility with a Level III neonatal intensive care unit, in close proximity to a pediatric heart center. MOD is usually not an issue but must take into account any evidence of congestive heart failure or hydrops. Examples include complete atrioventricular septal defect, aortic arch obstruction, moderate valve abnormality and TOF with mild to moderate level of pulmonary stenosis.

1.4.3. Level 3 (moderate risk)

CHD that requires neonatal intervention in the first days to weeks after delivery, which includes all ductal dependent lesions. These deliveries should be highly coordinated and occur at or nearby tertiary care centers with a high level of neonatal and cardiac expertise. If early intervention is likely or there is increased risk for high acuity at birth, delivery by induction or scheduled C-section should be considered to provide a window of anticipated delivery. MOD must also take into account if there is any evidence of congestive heart failure or hydrops. Cardiac intensive care unit (ICU), cardiology, and cardiothoracic surgery should be notified well in advance of the delivery. Transport team should be notified and on standby, to expedite the transfer. Examples include D-TGA with VSD, HLHS without RAS, severe aortic or pulmonary valve abnormalities (including single ventricles), unobstructed TAPVR, TOF absent pulmonary valve without lobar emphysema, Ebstein anomaly without hydrops and complete heart block (CHB) with normal heart function and adequate HR ($\geq$55 beats per minute).

1.4.4. Level 4 (high risk)

CHD requiring immediate or emergent intervention, within hours after birth, and in whom severe instability is anticipated. The perinatal care should be highly coordinated in order for all resources to be available at the time of birth. Mothers should deliver via scheduled C-section to minimize time to treatment with the necessary subspecialists on standby to care for the newborn. Ideally the delivery could occur in a highly specialized labor and delivery unit in a children's hospital for immediate intervention [8]. If transfer is needed the transport team should be on standby and present at the delivery institution. The baby must be adequately stabilized and monitored for transport, but performance of procedures in the DR must be balanced with the need to get the baby to intervention with minimal delay. Cardiac ICU, cardiology, and cardiothoracic surgery should be notified again immediately upon confirmation of birth. The operating room and/or cardiac catheterization laboratory should be on standby.

Examples include obstructed TAPVR, HLHS with RAS, D-TGA with RAS, TOF absent pulmonary valve with lobar emphysema, severe Ebstein anomaly with hydrops or uncontrolled arrhythmia and unstable

Table 1
Emergent neonatal cardiac intervention (ENCI) classification system.

ENCI Risk Level	Emergent Neonatal Cardiac Intervention	PGE Dependent	Mode of Delivery an Issue	NICU Acuity Level	Neonatologist present in DR	Critical Care Transport Needed	Cardiology, CT Surgery, CTICU, OR/Cath lab on Standby	Examples of CHD
I Low Risk	No	No	No	Low	No	No	No	ASD, VSD, mild PS
II Intermediate Risk	No	No	No	Mid	Possibly	Possibly	No	CAVC, TOF/PS, Truncus Arteriosus
III Moderate Risk	Possibly	Likely	Possibly	High	Yes	Yes	Possibly	HLHS, TOF/PA, PA/IVS
IV High Risk	Likely	Likely	Yes	High	Yes	Yes	Yes	D-TGA/RAS, HLHS/RAS, obstructed TAPVR

ASD, Atrial Septal Defect; CAVC, complete atrioventricular canal defect; Cath, catheterization; CT, Cardiothoracic; CTICU, Cardiac Intensive Care Unit; DR, Delivery Room; D-TGA, D-transposition of the great arteries; HLHS, hypoplastic left heart syndrome; NICU, Neonatal Intensive Care Unit; OR, Operating room; PA/IVS, pulmonary atresia with intact ventricular septum; PGE, Prostaglandin E1; PS, pulmonary stenosis; RAS. restrictive atrial septum; TAPVR, Total Anomalous Pulmonary Venous Return; TOF, tetralogy of Fallot; VSD, Ventricular Septal Defect.

CHB with slow ventricular rate (< 55bpm), decreased heart function, or hydrops fetalis.

2. Overview of critical CHD requiring emergent intervention in the DR

Critical CHD lesions can be grouped into four categories, by (1) inadequate flow of oxygenated blood to the systemic circulation, D-TGA with RAS; (2) inadequate pulmonary venous egress, TAPVR and HLHS with RAS; (3) associated lung or airway anomaly that compromises oxygenation and ventilation, severe Ebstein anomaly and TOF absent pulmonary valve; and (4) inadequate cardiac output, severe fetal arrhythmias and depressed cardiac function either in isolation or in combination with CHD. Here we will present one hypothetical case scenario to highlight the recommended perinatal care plan and DR management from each of the four categories of critical CHD (Table 2).

2.1. D-transposition of the great arteries with restrictive atrial septum

D-TGA is the most common cyanotic CHD in the neonatal period. Unlike cyanotic CHD with decreased pulmonary blood flow, neonates with D-TGA often present with severe cyanosis within minutes of birth. Neonates with D-TGA have pulmonary and systemic circulations in parallel rather than in series. Thus, to survive they must have adequate sites for mixing of blood between the two circulations to achieve adequate systemic oxygen delivery. While the presence of an associated VSD and PDA may allow for some mixing, these alone may be inadequate to provide effective oxygenated blood flow to the body. The most reliable strategy to achieve adequate systemic oxygen delivery is to establish an atrial level shunt, which often requires urgent balloon atrial septostomy (BAS), also known as the Rashkind procedure, within the first few hours of life. A balloon-tipped catheter is advanced from the femoral or umbilical vein through the IVC and right atrium, across the foramen ovale and into the left atrium where the balloon is inflated and rapidly pulled back across the atrial septum. By tearing across the

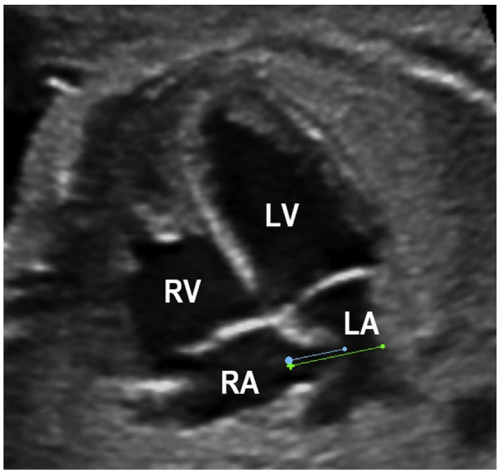

Fig. 1. Fetal echocardiogram four chamber view of D-Transposition of the Great Arteries case at 26 5/7 weeks' gestation demonstrating features of a restrictive atrial septum including hypermobile atrial septum primum with increased bowing into the left atrium (LA) with an atrial excursion ratio of 60% (blue line represents deviation of the septum primum by 5.2 mm, green line represents left atrial length of 8.7 mm). *RA, right atrium. RV, right ventricle. LV, left ventricle.*

Table 2
Delivery Room Management recommendations for ENCI Level 4 Cardiac Lesions.

Cardiac Lesion	DR Preparation	DR Resuscitation
D-TGA with restrictive/intact atrial septum	PGE available	Initiate PGE via umbilical or peripheral line
	IV and UV catheter setup	Intubation, mechanical ventilation (SPO_2 goal 75–85%)
	Inhaled nitric oxide if ductal flow abnormal	Consider inhaled nitric oxide if ductal flow abnormal
	Notify cardiology, cath lab	Immediate transfer to cath lab for balloon atrial septostomy
HLHS with restrictive/intact atrial septum	PGE available	Initiate PGE via umbilical or peripheral line
	IV and UV catheter setup	Intubation, mechanical ventilation (SPO_2 goal 75–85%)
	Notify cardiology, cath lab and/or CT surgery	Immediate transfer to cath lab or OR for intervention to open atrial septum
Severe Ebstein anomaly	PGE available	Initiate PGE via umbilical or peripheral line
	IV and UV catheter setup	Intubation, mechanical ventilation (SPO_2 goal > 90%)
	Antiarrhythmics if concern for tachyarrhythmia	Consider 100% FiO_2 and inhaled nitric oxide to lower PVR
		Transfer to ICU when stabilized
TOF/APV	IV and UV catheter setup	Consider 100% FiO_2
	Notify cardiology	Prone positioning, try to avoid intubation if possible (risk of air trapping)
		Intubation and mechanical ventilation if necessary, consider higher PEEP (SPO_2 goal > 90%)
		Transfer to ICU when stabilized
Obstructed TAPVR	PGE available	Initiate PGE via umbilical or peripheral line
	IV and UV catheter setup	Intubation, mechanical ventilation (SPO_2 goal 75–85%)
	Notify cardiology, CT surgery	Consider ECMO
		Immediate transfer to OR for surgical repair
Tachyarrhythmias	Cardiac Monitor available for rhythm analysis	Cardioversion if unstable
	IV and UV catheter setup	Rapid administration of adenosine via umbilical or peripheral line, if concern for SVT
	Adenosine and antiarrhythmics available	
	Defibrillator and neonatal pads available	Transfer to cardiac center with electrophysiology when stable ECG, initiation of antiarrhythmic
	Notify cardiology	
CHB with HR < 55 bpm	Cardiac Monitor available for rhythm analysis	Initiate chronotropic agent via umbilical or peripheral line, if HR < 55 bpm
	IV and UV catheter setup	Transcutaneous pacing, if HR < 55 bpm
	Isoproterenol and/or epinephrine	Intubation, mechanical ventilation, if hydrops or myocardial dysfunction (SPO_2 goal > 90%)
	Pacer/defibrillator available (set to pacing mode)	Immediate transfer to ICU, possibly to OR for temporary vs permanent pacing wires
	Temporary pacing pads	
	Notify cardiology, CT surgery	

CHB = complete heart block; CT = cardiothoracic; DR = delivery room; D-TGA = transposition of the great arteries; ECG = electrocardiogram; ECMO = extracorporeal membrane oxygenation; HLHS = hypoplastic left heart syndrome; HR = heart rate; ICU = intensive care unit; OR = operating room; PGE = prostaglandin E1; PVR = pulmonary vascular resistance; SPO_2 = arterial oxygen saturation; TAPVR = total anomalous pulmonary venous return; TOF/APV = tetralogy of Fallot absent pulmonary valve.

septum primum, a larger atrial communication is created which allows for adequate mixing of deoxygenated and oxygenated blood for stabilization.

Despite advances in prenatal diagnostic evaluation for prediction of the need for urgent BAS, there remains a high false negative predictive rate. Such predictive factors have included hypermobility of the septum primum, bowing of the septum primum into the left atrium by > 50% (Fig. 1), diminished mobility with an angle < 30° between the atrial septum and the septum primum [12–14]. Size and shunting pattern of the ductus arteriosus (reversed diastolic flow) and pulmonary vein peak systolic velocity > 41 cm/s have also been used with some degree of accuracy [13,15]. While delivery of fetuses with D-TGA is often classified as ENCI 3, when fetuses demonstrate any of the above findings concerning for postnatal atrial septal restriction, the delivery category elevates to ENCI 4. Given that the predictive value of these factors remains limited, one should consider all fetuses with D-TGA to be at risk for restriction of the atrial septum postnatally with associated hemodynamic instability.

2.2. Delivery room preparation

Due to the increased potential for requiring emergent neonatal intervention these mothers should deliver at a specialized labor and delivery unit equipped with facilities and staff capable of handling postnatal hemodynamic instability, with a plan for immediate postnatal evaluation by neonatology and cardiology. Given the possible need for an emergent BAS, these neonates should have immediate access to interventional cardiology that can perform a BAS procedure either at bedside with echocardiographic guidance or in a cardiac catheterization lab. If delivery cannot be performed at a children's hospital, transport should be arranged prior to delivery to ensure immediate transport to a hospital with access to cardiac care. If there is a high concern for intact or restrictive atrial septum on the prenatal echocardiogram, delivery by cesarean section is recommended.

Upon birth, cardiac ICU, interventional cardiology, and cardiothoracic surgery should be notified immediately. The latter should be on standby in case extracorporeal membrane oxygenation (ECMO) or surgical intervention is necessary. The cardiac catheterization laboratory and/or the operating room should be on standby for possible intervention.

2.3. Respiratory and cardiovascular support at birth

Initial DR management consists of assessment of respiratory effort, heart rate, circulation and color by the neonatology team. Target preductal oxygen saturation is in the range of 75%–85% after the first few minutes of transition and if supplemental oxygen is used, it should be adjusted to achieve this goal. Early elective intubation is recommended, as these patients have a high risk of respiratory decompensation. With intact atrial septum or severely RAS these patients show signs of cardiorespiratory failure in the DR shortly after birth. In rare circumstances there can be associated severe pulmonary hypertension which would necessitate iNO therapy and possible ECMO support [16]. Although opening the atrial septum by BAS is the main palliative treatment, administration of cardiac medications and judicious use of volume expanders via a low UVC made be necessary in the DR.

Soon after delivery and initial stabilization in the DR, venous access is obtained either by peripheral or standard umbilical venous line in order to administer PGE. This maintains ductal patency, thereby increasing pulmonary blood flow which in turn increases left to right shunting at the atrial level to improve systemic oxygen saturation. Position of the UVC should be verified by x-ray prior to transfer to avoid complications associated with administration of caustic medications. In addition, if PGE is infused via UVC, it is important to avoid having the catheter tip in portal venous system as the medication may not be effective.

The patient should be transferred immediately to a center with interventional cardiology available to perform a BAS and can be taken directly to the catheterization lab if preferred. An abbreviated transthoracic echocardiogram can be quickly performed to confirm the cardiac anatomy and to assess the patency of the foramen ovale and the ductus arteriosus. Emergent BAS can be performed either in the catheterization lab under fluoroscopy or at the bedside in the ICU via echo guidance.

2.4. Obstructed total anomalous pulmonary venous return

TAPVR accounts for only 0.5–2% of CHD, but continues to have one of the lowest rates of prenatal diagnosis and highest risks for mortality [17–19]. In TAPVR, pulmonary veins fail to return normally to the left atrium, but rather return to the right atrium via anomalous venous channels. There are four anatomical subtypes of TAPVR: 1) supracardiac (connects to the innominate vein or superior vena cava) 2) intracardiac (connects to the coronary sinus or right atrium) 3) infracardiac (connects to portal vein, hepatic vein, ductus venosus, or IVC) and 4) mixed type (connects at two or more of the above locations). Drainage is usually via a vertical vein, which is an embryologic venous remnant. Obstruction to pulmonary venous return can occur at multiple locations including at the vertical vein due to its length, at insertion sites of the draining vertical vein to the systemic venous system such as the portal or hepatic veins, and at areas of extrinsic compression such as between the left pulmonary artery and bronchus in the case of the supracardiac type. Obstructed TAPVR has important clinical consequences including acute postnatal severe congestion and pulmonary hypertension as well as the chronic pathological effects on lung development in utero [20]. Prenatal studies of predictors of TAPVR suggest the presence of a venous confluence, termed the twig sign, in the space between the atria and descending aorta (Fig. 2), abnormal spectral pulmonary venous waveforms, a smooth appearance of the posterior left atrial wall, and findings of an additional vessel representing a vertical vein can help increase the chances for a TAPVR diagnosis [21,22]. Vertical vein Doppler peak velocity > 0.74 m/s has been used to predict postnatal pulmonary venous obstruction [19].

Due to the nature of fetal circulation and the relatively small amount of pulmonary blood flow, TAPVR is well tolerated in utero. However, after birth, there is complete mixing of pulmonary and systemic blood in the right heart resulting in cyanosis as well as a lack of egress for pulmonary venous return resulting in severe pulmonary

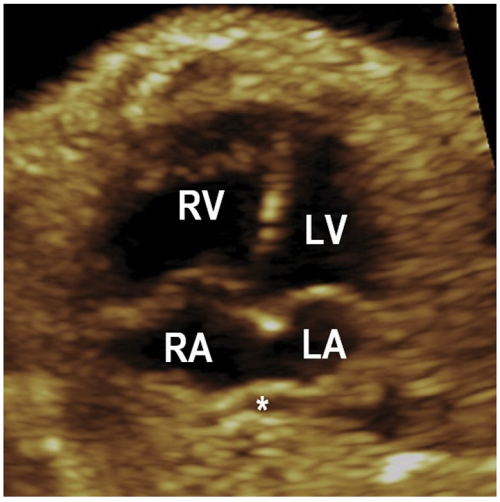

Fig. 2. Fetal echocardiogram of Total Anomalous Pulmonary Venous Return (TAPVR) case at 28 2/7 weeks' gestation demonstrating the “twig sign” with pulmonary veins seen draining into a confluence (*) behind the left atrium (LA) without a direct connection to the LA.

congestion and pulmonary hypertension presenting as severe respiratory distress.

2.5. Delivery room preparation

Due to the possibility of significant postnatal hemodynamic instability, a highly coordinated delivery plan should be in place to facilitate immediate stabilization and transfer for emergent TAPVR repair. In the case of TAPVR with concern for obstruction, scheduled C-section is recommended at most centers. The transport team should be on standby. The cardiothoracic surgery team should be prepared and operating room ready to receive the patient directly via transport as this remains one of the CHD lesions that can only be stabilized by emergent cardiac repair.

2.6. Respiratory and cardiovascular support at birth

Initial DR management consists of assessment of respiratory effort, heart rate, circulation and color by the neonatology team. The neonate may develop respiratory distress as a result of obstruction of the egress of pulmonary venous return and the development of pulmonary edema. The patient can also manifest with poor cardiac output and circulation, particularly if there is associated pulmonary hypertension. Hypoxemia and cyanosis is a common presentation due to mixing of the oxygenated pulmonary venous return and deoxygenated systemic venous return. Target preductal oxygen saturation is in the range of 75%–85%, however, in severe cases may be even lower due to a variety of factors including pulmonary edema and pulmonary hypertension. Supplemental oxygen should be adjusted to achieve this goal. Endotracheal intubation is recommended if there are signs of respiratory distress or significant hypoxemia.

After the initial stabilization in the DR, venous access is obtained either by peripheral or umbilical venous line. While PGE was previously thought to be unhelpful in TAPVR, recent literature suggests potential benefit in selected cases for two reasons: 1) to maintain patency of the ductus venosus in the case of infracardiac TAPVR as this is often the location of obstruction and 2) to maintain patency of the ductus arteriosus in the setting of pulmonary hypertension to allow adequate right to left flow across the PDA to maintain systemic blood flow [23,24].

The patient should be immediately transferred to a center with cardiothoracic surgery available. If the patient can be stabilized, a transthoracic echocardiogram can be performed in the ICU to confirm the prenatal diagnosis and characterize the degree of pulmonary venous obstruction. However, if the patient remains unstable, he or she should be taken directly to the operating room for surgical repair with intraoperative transesophageal echocardiography. If surgical repair is unable to be performed immediately, ECMO can be considered for stabilization prior to surgery.

2.7. Ebstein anomaly with severe tricuspid regurgitation

Ebstein anomaly is a rare congenital malformation characterized by apical displacement of the tricuspid valve that leads to tricuspid regurgitation (TR, Fig. 3). It occurs in 1–5 in 20,000 live births but when diagnosed in utero carries a high perinatal mortality rate as high as 45% [25]. In cases with severe TR, there is a large volume load on the right heart with associated right ventricular dysfunction. In the setting of decreased antegrade blood flow from the right ventricle (RV), pulmonary stenosis or atresia can develop, resulting in retrograde (left to right) ductus arteriosus flow. In severe cases, pulmonary regurgitation (PR) develops resulting in a circular shunt physiology. In this scenario, blood in the aorta flows retrograde through the ductus arteriosus into the pulmonary artery then back into the RV and into right atrium due to PR and TR. The blood in the right atrium then shunts across the foramen ovale from right to left atrium and flows again through the left heart and into the aorta thus completing the circle; this results in a steal of systemic cardiac output. As a result of elevated right atrial and systemic venous pressures due to TR, hydrops fetalis may develop. The combination of hydrops and low cardiac output leads to poor end organ perfusion and acidosis and ultimately leading to fetal demise. A large multicenter cohort study found the following to be predictive of perinatal mortality: gestational age < 32 weeks at diagnosis, larger tricuspid valve annulus z-score, presence of PR and pericardial effusion [25]. Outside of cardiac involvement, cardiomegaly can have a negative impact on lung development and patients are at risk for pulmonary hypoplasia.

Because this disease is progressive throughout gestation [26], routine surveillance should be performed to monitor for signs of hemodynamic compromise that would warrant earlier delivery. Premature delivery of neonates with heart disease has been associated with worse outcomes [27], so timing of delivery should be determined based on thoughtful discussion in the scenario of evolving fetal compromise. Fetuses with severe Ebstein anomaly often have difficulty transitioning to neonatal circulation due to inadequate pulmonary blood flow and lung hypoplasia leading to cyanosis and low systemic blood flow.

2.8. Delivery room preparation

With the potential for significant respiratory and hemodynamic compromise, a highly coordinated delivery plan should be in place with the neonatologist present in the DR for immediate postnatal assessment and medical management. Transport team should be on standby for rapid transfer to a center with cardiology and cardiothoracic surgery services. The cardiothoracic surgery team should be made aware of the patient's delivery, as significant postnatal instability may necessitate ECMO support [28].

In addition to poor cardiac output as highlighted above, patients with Ebstein anomaly have a higher incidence of supraventricular tachyarrhythmias (at least 15%) and ventricular pre-excitation (10–29%) due to the abnormal development of the tricuspid valve [29]. Thus, antiarrhythmic medications such as adenosine should be prepared prior to delivery, especially if there is a known fetal arrhythmia.

2.9. Respiratory and cardiovascular support at birth

In severe Ebstein anomaly, initial assessment of respiratory status may reveal significant respiratory distress and cyanosis due to lung hypoplasia and thus these patients often require intubation in the DR. Regarding ventilator strategy, the minimum needed mean airway pressure to avoid atelectasis should be used to avoid hyperinflation [30]. If there is pulmonary atresia or regurgitation, the goal of

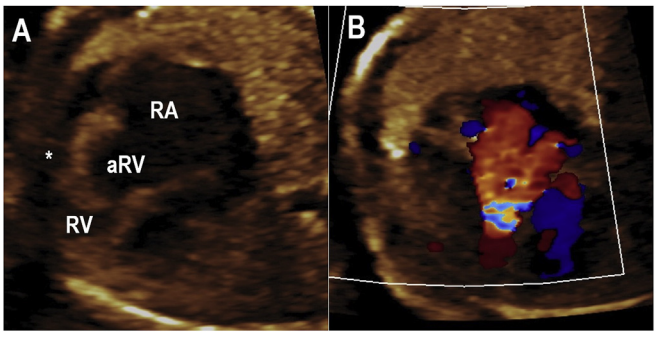

Fig. 3. Panel A: Fetal echocardiogram of Ebstein anomaly at 22 4/7 weeks gestational age with severe inferior displacement of the tricuspid valve into the right ventricle (RV) resulting in a large portion of atrialized right ventricle (aRV) and dilated right atrium (RA). A small pericardial effusion (*) is also noted. Panel B: the severe displacement of the tricuspid valve is associated with severe tricuspid regurgitation that has resulted in RA dilation.

management will be to lower the pulmonary vascular resistance to decrease the afterload that the struggling RV is facing. This can be accomplished with oxygen, inhaled nitric oxide, and correction of acidosis. When pulmonary artery pressure is lower than RV pressure, the pulmonary valve may open to allow antegrade pulmonary blood flow.

Intravenous access, preferably UVC, should be placed immediately given the potential need for medications for arrhythmias or inotropes in the case of low cardiac output. Target arterial oxygen saturations are 75–85% but profound hypoxemia may occur. PGE should be started to ensure pulmonary blood flow via PDA in cases of severe RV dysfunction. Initial management is mostly medical but cardiothoracic surgical team should be on standby in case ECMO is required.

2.10. Complete heart block

Immune-mediated CHB is seen in fetuses of mothers who are positive for SSA/SSB antibodies. Fetuses usually have structurally normal hearts and the mechanism of CHB is immune-mediated inflammation and fibrosis of the atrioventricular node (Fig. 4). Approximately 2–4% of pregnant mothers with positive antibodies develop fetal CHB, and if a prior sibling had CHB, the risk increases to 16% [31]. Many prophylactic treatments have been trialed including intravenous immunoglobulin, plasmapheresis and dexamethasone without noted decreases in the rate of fetal CHB; hydroxychloroquine is currently being studied [32,33]. While CHB is irreversible once it develops, treatment of second-degree heart block has been reported to be successful in preventing progression to CHB [34]. Unfortunately, the evolution of normal sinus rhythm into CHB is so rapid (usually < 24 h) that these fetuses are usually not identified in time to receive appropriate therapies [35]. Once CHB has developed, fetal management has relied on a weak evidence base for treatment with dexamethasone or intravenous immunoglobulin to prevent progression of immune-mediated effects on the heart such as atrioventricular valve insufficiency, ventricular dysfunction, endocardial fibroelastosis, and hydrops [36,37]. Sympathomimetics such as terbutaline or salbutamol have been used by some to increase the heart rate when average fetal heart rates fall below 55 bpm which predicts a poor prognosis [38]. After birth, the patient's heart rates, clinical status, ECG and ECHO findings need to be evaluated to determine need for neonatal support and timing of permanent pacemaker implantation.

2.11. Delivery room preparation

Due to inability to use heart rate as a measure of fetal well-being, an elective C-section is recommended at 39 weeks if the fetus is otherwise stable. If there is progression of cardiac disease involving the development of worsening heart failure or hydrops, an earlier delivery should be considered. A delivery plan should be made to include neonatology and cardiology teams. Isoproterenol, epinephrine and dopamine should be prepared and ready if needed for extremely low heart rates with evidence of low cardiac output. The transport team should be on standby and the cardiothoracic surgery team and cardiology notified in the cases that may require emergency temporary pacing followed by early pacemaker implantation.

If the neonate is unable to undergo pacemaker placement immediately after birth, temporary pacing strategies can be initially utilized to stabilize prior to surgery. Transcutaneous and transvenous pacing are two common strategies, both of which have advantages and disadvantages. Transcutaneous pacing involves application of pacing pads, which can be difficult in a newborn due to the presence of vernix and may result in thermal injury. Furthermore, sedation of the newborn is often required and elective intubation is recommended due to complications with apnea from transcutaneous pacing. Transvenous pacing is performed by placing a pacing catheter directly into the right ventricular apex through a femoral, internal jugular, or umbilical venous approach [39]. While more often utilized in older children, transvenous pacing in the newborn can be challenging due to difficulty obtaining venous access in situations with low cardiac output as well as the additional complication risks of venous thrombosis and infection [40]. In one case of anticipated severe fetal bradycardia, an ex utero intrapartum treatment (EXIT) procedure was reported in which a uterine incision was performed and a temporary epicardial pacing wire was sutured directly onto the right ventricle through a subxiphoid approach, before the umbilical cord was clamped and the patient was delivered [37]. This allowed for immediate ventricular pacing at birth and resulted in a more stable completion of delivery and postnatal course before undergoing permanent pacemaker placement. While the above strategies are options in an emergent scenario, ultimately, surgical placement of an epicardial pacemaker lead is the definitive treatment.

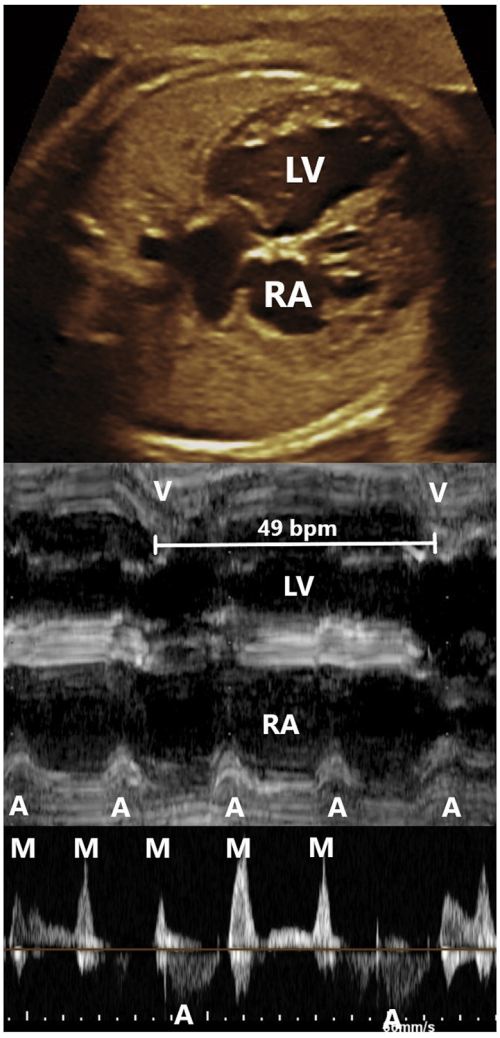

Fig. 4. Fetal echocardiogram of a fetus at 24 2/7 weeks' gestation with complete heart block secondary to maternal SS-A antibodies shows a severe cardiomegaly with a CTA ratio of 0.52 and a small pericardial effusion without evidence of hydrops (upper panel). There was also moderate mitral and tricuspid regurgitation (not shown). In the middle panel, a fetal M-mode through the left ventricle (LV) and right atrium (RA) shows complete dissociation of atrial (A) and ventricular (V) contraction with a ventricular rate of 49 bpm. In the lower panel, a pulse wave Doppler interrogation shows dissociation of the mitral valve (M) inflow and aortic (A) outflow.

2.12. Respiratory and cardiovascular support at birth

Initial assessment includes evaluation of respiratory effort, heart rate, circulation and color. Due to normal cardiac anatomy, target saturations are within normal range. If heart rate is above 55bpm without other signs of respiratory or cardiovascular compromise, elective intubation is not recommended. If, however, the heart rates are below 50 bpm with history of decreased cardiac function or fetal hydrops, elective intubation and placement of umbilical catheters is recommended. The patient should be transferred immediately to a facility with cardiology and cardiothoracic surgery available. Isoproterenol can be initiated if heart rates remain < 55 bpm; additionally, epinephrine may be considered for both chronotropic and inotropic support. PGE is not recommended unless there is another associated congenital defect that is ductal dependent. If not responsive to medications, temporary pacing can be performed at bedside, but the cardiothoracic surgery team should be notified for impending need for surgical pacemaker placement. Once stabilized, electrocardiogram and echocardiogram should be performed. The patient should remain on telemetry for close observation of heart rate and rhythm.

3. Other considerations

3.1. Fetal intervention improving DR management

Fetal intervention has the potential to alter the CHD disease state prenatally and result in a lessening of the acuity at neonatal presentation of CHD and improving the pre-operative clinical condition. Although appropriately designed, controlled trials have not been performed yet and might not even be feasible, findings of large case series suggest that balloon valvuloplasty of the aortic valve in cases of critical aortic stenosis may prevent progression to HLHS resulting in a more stable biventricular circulation at birth [41,42]. These patients may go from being ductal dependent at birth to not requiring a PGE infusion and possibly avoiding neonatal surgery. HLHS with RAS can also be stabilized with prenatal/fetal intervention by the creation of an atrial communication using either balloon septostomy or inter-atrial stent placement in the fetus [43]. This has the potential to improve the physiology, stabilize the newborn, and avoid the need for emergent surgical or catheter based septostomy in the first hours after delivery. Medical fetal therapy with digoxin for fetal congestive heart failure, anti-arrhythmia drugs for fetal supraventricular tachycardia and fetal transfusion all have the potential to mitigate fetal congestive heart failure and reverse fetal hydrops. Therefore, these treatments can improve fetal status prior to delivery and result in better neonatal outcomes [44]. Emerging therapies such as implantable fetal pacemakers for congenital CHB may help carry a pregnancy to term or near term and reverse fetal hydrops, resulting in a better clinical status at birth prior to permanent pacemaker implantation [45,46]. While many of these fetal cardiac interventions are novel with results reported in relatively small numbers, this remains an active area of research with both US and international collaborations coming together to study their potential [42].

3.2. Delayed cord clamping

A 30–60 s delay in umbilical cord clamping in a vigorous term and preterm infants is currently recommended by the American College of Obstetricians and Gynecologists (ACOG) and endorsed by the American Academy of Pediatrics [47]. On the other hand, ACOG recommends immediate cord clamping, or individualized approach when there is a need for immediate neonatal resuscitation. There are significant benefits to delayed cord clamping (DCC) including increased hematocrit and iron stores as a result of placental transfusion. In the term neonate, about 16 and 23 ml/kg of blood is transfused from the placenta to the neonate with a 1- and 3-min DCC, respectively [48]. While not a consistent finding, the benefits of DCC may be greater among preterm infants including more stable hemodynamic status during the transitional period [49–52]. The onset of breathing before cord clamping promotes earlier establishment of pulmonary blood flow and increases left ventricular preload for a more gradual separation from the low resistance placental circulation which may facilitate better adaptation of the left ventricle to the postnatal increase in afterload [53]. While the above mechanisms may play a role in the observed improvement in transition, the findings of similar benefits with cord milking suggests that placental transfusion is the key factor [54–56].

There is a theoretical benefit to DCC among infants with CHD, especially those with cyanotic lesions. The increased oxygen carrying capacity and higher blood volume would improve tissue oxygenation when oxygen saturation and blood flow are low. On the other hand, increased viscosity associated with higher hematocrit and volume overload could be problematic in cases of depressed heart function. In addition, the need for prompt resuscitation in critical CHD makes DCC in such circumstances more controversial. An Italian task force recently recommended DCC for newborns with CHD taking an individualized approach to guide cord clamping in severe CHD cases (i.e. critical CHD) based on expert opinion and a small pilot RCT trial [57,58]. This trial compared delayed versus early cord clamping in newborns > 37 weeks' gestation with CHD (defined as heart lesions other than single ventricle physiology and likely to require surgery or cardiac catheterization within the first 30 days) [58]. They found DCC to be safe and feasible in this high-risk population. In addition, the DCC group had higher initial hematocrit and overall required less blood transfusion. Further studies are needed to confirm the safety and investigate short- and long-term implications of DDC in newborns with CHD.

4. Conclusions

Neonates with critical CHD are at increased risk of mortality and morbidity due to their underlying heart condition and the hemodynamic changes that occur immediately postnatal in the DR. Improvements in ultrasound scanning technology and enhanced screening guidelines continue to increase prenatal detection of CHD, identify reliable fetal echocardiographic markers for predicting emergent neonatal intervention and improve perinatal strategies for those newborns at greatest risk. Critical CHD requires a highly coordinated perinatal plan and DR management strategy for appropriate stabilization and immediate transition of care to the cardiac team. Once a diagnosis of critical CHD is made there should be a comprehensive care plan developed based on the anticipated postnatal acuity level and need for emergent intervention. Active perinatal strategies and DR protocols as well as close multidisciplinary collaboration hold the promise of improving the approach to complex CHD, but are still being refined. In the future, innovative fetal therapies may alter outcomes for some forms of critical CHD and allow for a less critical transition from fetal to postnatal life. However, until that is fully realized, the best opportunity to improve outcomes for our most critical CHD neonates is a well-developed and executed perinatal plan.

4.1. Learning points

1. While the altered fetal circulation associated with critical CHD is often well-tolerated in utero, the transition to neonatal circulation is complicated and these patients often require cardiorespiratory support in the delivery room.
2. Risk stratification and level of care management plans for prenatally diagnosed CHD are useful for predicting the postnatal care required and need for emergent intervention at birth.
3. Careful review of the prenatal findings including fetal echocardiogram and clear communication among the neonatologist, fetal cardiologist and the delivering obstetrician are crucial for successful resuscitation.

5. Research directions

1. Further refinement of prenatal prediction of need for delivery room intervention in critical CHD, especially for D-TGA.
2. Fetal intervention aiming at reducing the severity of CHD and mitigating the need for emergent intervention in the delivery room.

Declaration of competing interest

None of the authors had any conflict of interest.

References

[1] Rudolph AM. Distribution and regulation of blood flow in the fetal and neonatal lamb. Circ Res 1985;57:811–21.
[2] Kiserud T, Acharya G. The fetal circulation. Prenat Diagn 2004;24:1049–59.
[3] Prsa M, et al. Reference ranges of blood flow in the major vessels of the normal human fetal circulation at term by phase-contrast magnetic resonance imaging. Circ Cardiovasc Imaging 2014;7:663–70.
[4] Sanapo L, et al. Fetal echocardiography for planning perinatal and delivery room care of neonates with congenital heart disease. Echocardiography 2017;34:1804–21.
[5] Tworetzky W, et al. Improved surgical outcome after fetal diagnosis of hypoplastic left heart syndrome. Circulation 2001;103:1269–73.
[6] Pruetz JD, et al. Outcomes of critical congenital heart disease requiring emergent neonatal cardiac intervention. Prenat Diagn 2014;34:1127–32.
[7] Berkley EMF, Goens MB, Karr S, Rappaport V. Utility of fetal echocardiography in postnatal management of infants with prenatally diagnosed congenital heart disease. Prenat Diagn 2009;29:654–8.
[8] Donofrio MT, et al. Specialized delivery room planning for fetuses with critical congenital heart disease. Am J Cardiol 2013;111:737–47.
[9] Słodki M, Respondek-Liberska M, Pruetz JD, Donofrio MT. Fetal cardiology: changing the definition of critical heart disease in the newborn. J Perinatol 2016;36:575–80.
[10] Peterson AL, et al. Impact of mode of delivery on markers of perinatal hemodynamics in infants with hypoplastic left heart syndrome. J Pediatr 2011;159:64–9.
[11] Trento LU, Pruetz JD, Chang RK, Detterich J, Sklansky MS. Prenatal diagnosis of congenital heart disease: impact of mode of delivery on neonatal outcome. Prenat Diagn 2012;32:1250–5.
[12] Jouannic J-M, et al. Sensitivity and specificity of prenatal features of physiological shunts to predict neonatal clinical status in transposition of the great arteries. Circulation 2004;110:1743–6.
[13] Punn R, Silverman NH. Fetal predictors of urgent balloon atrial septostomy in neonates with complete transposition. J Am Soc Echocardiogr 2011;24:425–30.
[14] Vigneswaran TV, Zidere V, Miller OI, Simpson JM, Sharland GK. Usefulness of the prenatal echocardiogram in fetuses with isolated transposition of the great arteries to predict the need for balloon atrial septostomy. Am J Cardiol 2017;119:1463–7.
[15] Słodki M, et al. New method to predict need for Rashkind procedure in fetuses with dextro-transposition of the great arteries. Ultrasound Obstet Gynecol 2018;51:531–6.
[16] Talemal L, Donofrio MT. Hemodynamic consequences of a restrictive ductus arteriosus and foramen ovale in fetal transposition of the great arteries. J Neonatal Perinat Med 2016;9:317–20.
[17] Hoffman JI. Incidence of congenital heart disease: II. Prenatal incidence. Pediatr Cardiol 1995;16:155–65.
[18] Quartermain MD, et al. Variation in prenatal diagnosis of congenital heart disease in infants. Pediatrics 2015;136:e378–85.
[19] Domadia S, Kumar SR, Votava-Smith JK, Pruetz JD. Neonatal outcomes in total anomalous pulmonary venous return: the role of prenatal diagnosis and pulmonary venous obstruction. Pediatr Cardiol 2018;39:1346–54.
[20] Haworth SG. Total anomalous pulmonary venous return. Prenatal damage to pulmonary vascular bed and extrapulmonary veins. Br Heart J 1982;48:513–24.
[21] Ganesan S, Brook MM, Silverman NH, Moon-Grady AJ. Prenatal findings in total anomalous pulmonary venous return: a diagnostic road map starts with obstetric screening views. J Ultrasound Med 2014;33:1193–207.
[22] Tongsong T, Luewan S, Jatavan P, Tongprasert F, Sukpan K. A simple rule for prenatal diagnosis of total anomalous pulmonary venous return. J Ultrasound Med 2016;35:1601–7.
[23] Adeagbo ASO, Kelsey L, Coceani F. Endothelin-induced constriction of the ductus venosus in fetal sheep: developmental aspects and possible interaction with vasodilatory prostaglandin. Br J Pharmacol 2004;142:727–36.
[24] Cirstoveanu C, et al. Prostaglandin e1 on infradiaphragmatic type of total anomalous pulmonary venous connection - a case report. Maedica (Buchar) 2012;7:167–72.
[25] Freud LR, et al. Outcomes and predictors of perinatal mortality in fetuses with Ebstein anomaly or tricuspid valve dysplasia in the current era: a multicenter study. Circulation 2015;132:481–9.
[26] Selamet Tierney ES, et al. Assessment of progressive pathophysiology after early prenatal diagnosis of the Ebstein anomaly or tricuspid valve dysplasia. Am J Cardiol 2017;119:106–11.
[27] Costello JM, et al. Birth before 39 weeks' gestation is associated with worse outcomes in neonates with heart disease. Pediatrics 2010;126:277–84.
[28] Arunamata A, et al. Chronic antepartum maternal hyperoxygenation in a case of severe fetal Ebstein's anomaly with circular shunt physiology. Ann Pediatr Cardiol 2017;10:284–7.
[29] Khositseth A, Danielson GK, Dearani JA, Munger TM, Porter CJ. Supraventricular tachyarrhythmias in Ebstein anomaly: management and outcome. J Thorac Cardiovasc Surg 2004;128:826–33.
[30] Jaquiss RDB, Imamura M. Management of Ebstein's anomaly and pure tricuspid insufficiency in the neonate. Semin Thorac Cardiovasc Surg 2007;19:258–63.
[31] Buyon JP, et al. Autoimmune-associated congenital heart block: demographics, mortality, morbidity and recurrence rates obtained from a national neonatal lupus registry. J Am Coll Cardiol 1998;31:1658–66.
[32] Izmirly PM, et al. Evaluation of the risk of anti-SSA/Ro-SSB/La antibody-associated cardiac manifestations of neonatal lupus in fetuses of mothers with systemic lupus erythematosus exposed to hydroxychloroquine. Ann Rheum Dis 2010;69:1827–30.
[33] Izmirly PM, et al. Maternal use of hydroxychloroquine is associated with a reduced risk of recurrent anti-SSA/ro associated cardiac manifestations of neonatal lupus. Circulation 2012;126:76–82.
[34] Cuneo BF, Ambrose SE, Tworetzky W. Detection and successful treatment of emergent anti-SSA mediated fetal atrioventricular block. Am J Obstet Gynecol 2016. https://doi.org/10.1016/j.ajog.2016.07.006.
[35] Cuneo BF, et al. Home monitoring for fetal heart rhythm during anti-ro pregnancies. J Am Coll Cardiol 2018;72:1940–51.
[36] Donofrio MT, Gullquist SD, Mehta ID, Moskowitz WB. Congenital complete heart block: fetal management protocol, review of the literature, and report of the smallest successful pacemaker implantation. J Perinatol 2004;24:112–7.
[37] Martin TA. Congenital heart block: current thoughts on management, morphologic spectrum, and role of intervention. Cardiol Young 2014;24(Suppl 2):41–6.
[38] Eliasson H, et al. Isolated atrioventricular block in the fetus: a retrospective, multinational, multicenter study of 175 patients. Circulation 2011;124:1919–26.
[39] Li X-M, et al. Emergency pacing via the umbilical vein and subsequent permanent pacemaker implantation in a neonate. Pediatr Cardiol 2017;38:199–201.
[40] Rein AJ, et al. Noninvasive external pacing in the newborn. Pediatr Cardiol 1999;20:290–2.
[41] Freud LR, et al. Fetal aortic valvuloplasty for evolving hypoplastic left heart syndrome: postnatal outcomes of the first 100 patients. Circulation 2014;130:638–45.
[42] Moon-Grady AJ, et al. International fetal cardiac intervention registry: a worldwide collaborative description and preliminary outcomes. J Am Coll Cardiol 2015;66:388–99.
[43] Marshall AC, et al. Creation of an atrial septal defect in utero for fetuses with hypoplastic left heart syndrome and intact or highly restrictive atrial septum. Circulation 2004;110:253–8.
[44] Donofrio MT, et al. Diagnosis and treatment of fetal cardiac disease: a scientific statement from the American Heart Association. Circulation 2014;129:2183–242.
[45] Zhou L, et al. A percutaneously implantable fetal pacemaker. Conf Proc IEEE Eng Med Biol Soc 2014;2014:4459–63.
[46] Bar-Cohen Y, et al. Preclinical testing and optimization of a novel fetal micropacemaker. Heart Rhythm 2015;12:1683–90.
[47] Committee Opinion No. 684. Delayed umbilical cord clamping after birth. Obstet Gynecol 2017;129:e5–10.
[48] Yao AC, Moinian M, Lind J. Distribution of blood between infant and placenta after birth. Lancet 1969;2:871–3.
[49] Baenziger O, et al. The influence of the timing of cord clamping on postnatal cerebral oxygenation in preterm neonates: a randomized, controlled trial. Pediatrics 2007;119:455–9.
[50] Sommers R, et al. Hemodynamic effects of delayed cord clamping in premature infants. Pediatrics 2012;129:e667–72.
[51] Popat H, et al. Effect of delayed cord clamping on systemic blood flow: a randomized controlled trial. J Pediatr 2016;178. 81–86.e2.
[52] Popat H, et al. Associations of measures of systemic blood flow used in a randomized trial of delayed cord clamping in preterm infants. Pediatr Res 2019;86:71–6.
[53] Bhatt S, et al. Delaying cord clamping until ventilation onset improves cardiovascular function at birth in preterm lambs. J Physiol (Lond) 2013;591:2113–26.
[54] Hosono S, et al. Blood pressure and urine output during the first 120 h of life in infants born at less than 29 weeks' gestation related to umbilical cord milking. Arch Dis Child Fetal Neonatal Ed 2009;94:F328–31.
[55] Takami T, et al. Umbilical cord milking stabilizes cerebral oxygenation and perfusion in infants born before 29 weeks of gestation. J Pediatr 2012;161:742–7.
[56] Katheria AC, Truong G, Cousins L, Oshiro B, Finer NN. Umbilical cord milking versus delayed cord clamping in preterm infants. Pediatrics 2015;136:61–9.
[57] Ghirardello S, et al. Italian recommendations for placental transfusion strategies. Front Pediatr 2018;6:372.
[58] Backes CH, et al. Early versus delayed umbilical cord clamping in infants with congenital heart disease: a pilot, randomized, controlled trial. J Perinatol 2015;35:826–31.