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Abstract

The optimal management of pregnancies involving fetal congenital anomalies is important because the events of perinatal period are strongly associated with perioperative mortality and long-term outcomes. Congenital heart disease (CHD) is one of the most prominent birth defects; however, few reports on obstetrical issues in pregnancy with fetal CHD have been published. In this chapter, we review antenatal and intrapartum management for fetuses with CHD focusing particularly on intrapartum electrical fetal heart rate (FHR) monitoring in CHD patients.

FHR monitoring has been widely used for antenatal and intrapartum management. Our previous study demonstrated that fetuses with structural heart anomalies tended to show variant heart rate patterns such as severe variable deceleration, recurrent late deceleration, prolonged deceleration, and loss of baseline variability. Single ventricle, isomerism, and tetralogy of Fallot frequently showed variant FHR patterns. Conversely, umbilical artery pH results showed that most CHD fetuses with variant FHR patterns did not have accompanying acidosis, even in cases of emergency Caesarean section (C-section). These data suggested that special consideration is needed when translating the findings of aberrant FHR patterns in fetuses with CHD. Although FHR monitoring is among the most validated tools to detect nonreassuring fetal status, additional strategies should be discussed in the future due to the difficulty of monitoring fetal well-being in CHD patients.

Keywords

Congenital heart disease · Fetal heart rate monitoring · Variant fetal heart rate pattern

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17.1 Introduction

Congenital heart disease (CHD) is one of the most frequently reported fetal anomalies, seen in 1 in 100 live newborns. One-third of CHD patients present severe forms associated with early infantile mortality. Despite the difficulty of accurate fetal diagnoses, remarkable advances of echocardiographic imaging in the last decade have contributed to increased early detection of structural heart defects. Intrauterine diagnosis and antenatal management are critical for determining the optimal interventions after birth, including catheter intervention (balloon atrial septostomy (BAS), etc.) or artificial respiratory or circulation support (extracorporeal membrane oxygenation (ECMO), etc.). Fetal and neonatal hemodynamics, as well as fetal well-being, are taken into consideration when making a birth plan. A team of fetal-maternal medicine specialists and cardiologists is required for understanding the whole picture of early-life treatment for patients diagnosed with CHD.

With these efforts in medical care, neonatal and infantile mortality due to CHD has dramatically decreased in recent years. However, it remains important to discuss the accompanying perinatal risks and their ideal management during pregnancy for CHD patients.

In this chapter, we discuss the optimal antenatal and intrapartum monitoring of fetal well-being using ultrasound evaluation or electronic fetal heart rate (FHR) monitoring.

17.2 Fetal Diagnosis: Screening and Detailed Diagnosis of Fetal Heart Disease

The primary goal of fetal management in CHD patients is to improve the perinatal outcome and long-term prognosis. To achieve this goal, the management of fetal cardiac disease should start from antenatal diagnoses. Pregnant women are highly recommended to join an antenatal screening program using fetal echocardiography. When abnormality is detected in fetal hearts by screening, fetal and pediatric cardiologists can perform more detailed assessments to propose ideal postnatal treatment plans according to the risk stratification.

The effectiveness of prenatal diagnosis of major CHD has been thoroughly discussed in previous published articles [1–9]. The postnatal courses of some patients become complicated if they are born without fetal diagnosis and outside the appropriate institutions, because some critical types of CHD develop into cardiac compromise shortly after birth. Several articles have suggested that fetal diagnosis and ideal postnatal care minimize the risk of death from cardiovascular deterioration prior to attempted neonatal cardiac surgery relative to cases diagnosed postnatally [1, 2]. For example, hypoplastic left heart syndrome (HLHS) is one of the most severe forms of patent ductus arteriosus (PDA)-dependent cardiac defects and requires both detailed examination of postnatal hemodynamics and specialized knowledge of perinatal management, which includes not only pediatric surgery but also pharmaceutical support to prevent cardiovascular compromise or respiratory

failure [2, 3]. A certain type of transposition of the great arteries (TGA) or intact ventricular septum with a restrictive foramen ovale (FO), ductus arteriosus (DA) constriction, or pulmonary hypertension may develop severe hypoxemia and become lethal immediately after birth. Careful preparation for BAS or neonatal cardiac surgery is essential for postnatal management [5, 6]. Prenatal diagnosis in fetuses with tetralogy of Fallot (TOF), coarctation of the aorta (COA), or truncus arteriosus similarly improves their neonatal outcomes [7–9].

However, several issues are debated regarding the ethical aspects of early diagnoses. A high rate of artificial abortion has been reported after antenatal diagnoses of critical CHD [10]. Fetuses with CHD are often identified with coexisting deformities or genetic syndromes associated with undesirable prognoses. A multidisciplinary approach is required for the treatment of CHD infants. Experts from all fields of fetal-maternal medicine should work together with other specialists in genetics or ethics depending on the problem [11]. Families should be carefully informed about the current conditions of their babies and long-term prognoses to provide consent for birth plans and postnatal treatment. Because of the logistical and economic challenges for parents of such babies, social or public aid may play a pivotal role in their decisions. Moreover, the patients-caregiver relationship or family support could influence neonatal and infantile treatment decisions and the future growth and development of patients affected by CHD.

17.3 Antenatal Management: Obstetrical Management and Cardiologist Perspectives

Intrapartum management for pregnancies with fetal congenital heart anomalies is not clearly described in the obstetrical textbooks or literature. Thus, it is often unclear how to evaluate the well-being of patients with CHD or what are the best methods and timing of care delivery.

An accurate understanding of both cardiovascular morphology and hemodynamics is critical to determine the best strategy for perinatal management. Fetal cardiac function is usually evaluated by ultrasound methods such as ejection fraction, cardiac output, strain or strain ratio, E/A ratio, and isovolumic reaction time (IRT) [12]. Recent technological advances in echocardiography, including spatio-temporal image correlation (STIC) and tissue Doppler imaging (TDI), may contribute to the understanding of both detailed structural defects and cardiac function. Other biomarkers for the early detection of fetal heart failure have recently been investigated [13]. The combination of these parameters enable detection of the early signs of deterioration in fetal cardiac function, and once fetal heart failure progresses, hydrops or arrhythmia can sometimes easily be seen by ultrasound examination.

When deciding the timing of delivery, dynamic changes of hemodynamics from fetal to postnatal circulation should be discussed regarding the balance of benefit between intrauterine life and postnatal treatment. In the extreme example of Ebstein's anomaly, a circular shunt is often observed based on functional pulmonary atresia with absent forward flow. Circular blood flow occurs left to right across the

patent ductus arteriosus, retrograde through the pulmonary artery and Ebstein valve, across the patent foramen ovale, and out the aorta. Although the quantitative estimation of postnatal hemodynamics is difficult, a detailed examination of fetal circulation provides some insight of CHD severity.

Some general obstetrical and gynecological issues for pregnancies with CHD fetuses have been reported in relatively few papers [14, 15]. Pregnancies affected by CHD fetuses are associated with several adverse obstetric and neonatal outcomes. One population-based cohort in Sweden displayed increased risks for preeclampsia, preterm delivery, small size for gestational ages, and meconium aspiration [15]. Another study showed that fetuses with CHD have a threefold greater risk of developing intrauterine growth restriction [14]. The presence of other abnormalities hugely impacts prognoses and could be important for perinatal management. All of these fetal conditions are important when assessing pregnancy variables, as are obstetrical assessments such as uterine contractions and cervical length. Essential examinations for pregnant women should be performed, including fetal ultrasounds (biophysical profile score (BPS), amniotic fluid index (AFI), and fetal growth) or electronic FHR monitoring, but special additional knowledge of pregnancies with fetal CHD is required when discussing their management. All information should be integrated and discussed comprehensively when determining the optional timing and mode of delivery.

In the next section, we explore the obstetrical aspects of fetal heart disease, particularly FHR monitoring patterns in fetuses with congenital heart disease.

17.4 Intrapartum Management

17.4.1 Fetal Heart Rate Monitoring in Fetuses with CHD

Electronic FHR monitoring is one of the most recognized fetal management tools. It is often conducted at each hospital visit during pregnancy and repeatedly applied because of its easiness and convenience. FHR is continuously monitored and recorded until babies are born by spontaneous delivery or Caesarian section. The interpretation of fetal heart rate pattern is well established. Nonreassuring FHR patterns represent fetal distress and have huge clinical importance as a measurement of fetal oxygenation and acid-base status. This measurement may inform the next step of fetal-maternal management, whether action or waiting for spontaneous recovery.

FHR patterns are produced by the autonomic nervous system, composed of the sympathetic and parasympathetic nerves connecting the heart to the brain. This physiological understanding suggests that the structural abnormality of those cycles might influence the patterns of FHR. Several reports have addressed the unexpected aberrant patterns generated by congenital anomalies in FHR monitoring, especially the strong association between aberrant FHR patterns and anomalies of the central nervous system [16–18]. Conversely, relatively few articles examine the FHR patterns of congenital disease. Gertie et al., for example, analyzed several CHD patients

for FHR in association with congenital anomalies [16]. Here, we introduce the results of our research and discuss FHR monitoring for congenital cardiovascular defects.

17.4.1.1 Research Question 1: Is There Any Difference in the Prevalence of Caesarean Sections due to Variant FHR Patterns in CHD?

FHR patterns of fetuses with congenital heart disease (CHD) were analyzed [19]. We retrospectively examined the FHR records of 116 CHD cases delivered from 2000 to 2007 at the National Cardiovascular Center, Osaka, Japan. Corresponding to each study subject, four consecutive controls matched for gestational age and birth weight were selected. All CHD cases were diagnosed in utero using ultrasound and classified into 12 categories: heart isomerism, univentricular heart (UVH), TOF, transposition of the great arteries, double outlet of the right ventricle, HLHS, common arteriovenous canal, ventricular septal defect, coarctation or interruption of the arch (COA/IAA), aortic stenosis, pulmonary stenosis or atresia (PS/PA), and an “other” category consisting of fewer than 5 cases. Demographic and historical characteristics were compared between the groups.

Table 17.1 shows the background data of each group. When controlling for birth weight and gestational age, an Apgar score of less than 7 was significantly more prevalent in infants with CHD than in the controls at both 1 (17.2% vs. 6.0%, $p < 0.05$) and 5 (9.5% vs 1.5%, $p < 0.05$) min after birth. The summary of the mode of delivery for CHD patients and controls is also shown in Table 17.1. Patients affected by CHD were more likely to be delivered by emergency Caesarean section, but this difference was not statistically significant. The incidence of emergency

Table 17.1 Population characteristics

Characteristics	Study subjects ($n = 116$)	Control patients ($n = 464$)	<i>P</i> value
Birth weight (g)	2729 ± 553	2754 ± 531	NS
Gestational age (w)	38 + 2	38 + 2	NS
Apgar score			
<7 (1 min)	20 (17.2%)	28 (6.0%)	<0.05
<7 (5 min)	11 (9.5%)	5 (1.0%)	<0.05
Sex			
Male	63 (54.3%)	245 (52.8%)	NS
Female	53 (45.7%)	219 (47.2%)	NS
Delivery			
Induction	55 (47.4%)	204 (44.0%)	NS
Operative	18 (15.5%)	45 (9.7%)	NS
Emergency CS	29 (25.0%)	84 (18.1%)	NS
Due to variant FHR	15 (12.9%)	15(3.2%)	<0.05
Due to arrest of delivery	14 (12.1%)	69 (14.9%)	NS

Ueda K, et al., Am J Obstet Gynecol. 2009 Jul;201(1):64.e1-6

NS not significant, CS cesarean section

Table 17.2 Incidence of FHR deceleration and minimal baseline variability in patients with congenital heart disease

Characteristics	Study subjects (<i>n</i> = 116)	Control patients (<i>n</i> = 464)	<i>P</i> value
Severe variable	35 (30.2%)	40 (8.6%)	<0.05
Prolonged	11 (9.5%)	15 (3.2%)	<0.05
Recurrent late	4 (3.4%)	23 (5.0%)	NS
Loss/decreased variability	4 (3.4%)	4 (0.9%)	NS
None	62 (53.4%)	384 (82.3%)	<0.05

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NS not significant

Caesarean section due to variant FHR patterns was significantly higher in CHD patients (12.9% vs 3.2%, $p < 0.01$). However, the frequency of emergency Caesarean section due to other reasons, such as arrest of delivery or induction delivery, did not differ between groups.

Table 17.2 shows the incidence of each aberrant FHR pattern in patients with CHD. All signs of FHR were assessed according to the National Institutes of Child Health and Human Development guideline [20]. Aberrant patterns of FHR were observed in 46.6% of patients with CHD, which was significantly higher than the incidence of controls (17.7%, $p < 0.01$). Severe variable deceleration was found more frequently during the delivery of patients affected by CHD compared to the controls (30.2% vs 8.6%, $p < 0.01$), as was prolonged deceleration (9.5% vs 3.2%, $p < 0.01$). Fewer cases were observed with recurrent late deceleration and lost or decreased baseline variability, and no significant differences were found between the two groups.

Our findings are consistent with those of previous population cohort studies [15, 21] showing high rates of emergency Caesarean sections or fetal distress in CHD patients. Other articles have reported that a high prevalence of Caesarean sections is mainly seen in multiparous pregnancies [22]. The lack of information about null and multiparous pregnancies in our data could have limited our observations. Additionally, as is common in retrospective analysis, the indication of intervention was not perfectly manipulated. This limitation occurred due to the physicians' intolerance when looking at severe structural defects at risk of unfavorable prognoses or variant patterns of FHR in fetuses with CHD.

Although the generalizability of small studies is debatable, we believe an important clinical implication can be drawn from our results: fetuses diagnosed with CHD are more likely to show intrapartum aberrant FHR patterns, which often indicate an emergency Caesarean section.

17.4.1.2 Research Question 2: What Subtypes of CHD Most Likely Show Variant FHR Patterns?

Because congenital malformations constitute a heterogeneous group of structural lesions, our next research question considered what types of heart defect tend to be associated with aberrant FHR patterns.

Table 17.3 Incidence of variant FHR patterns in subjects of CHD

Subjects of CHD (<i>n</i>)	Variant FHR	Severe VD	Prolonged D	Recurrent LD	Minimum variability	Normal FHR
Isomerism (<i>n</i> = 13)	6 (46.2%) ^a	1	3	0	2	7
UVH (<i>n</i> = 8)	6 (75.0%) ^a	3	3	0	0	2
TOF (<i>n</i> = 12)	10 (83.3%) ^a	7	1	1	1	2
DORV (<i>n</i> = 7)	1 (14.3%)	1	0	0	0	6
VSD (<i>n</i> = 8)	3 (37.5%)	3	0	0	0	5
HLHS (<i>n</i> = 7)	2 (28.6%)	1	0	1	0	5
TGA (<i>n</i> = 7)	2 (28.6%)	2	0	0	0	5
AS (<i>n</i> = 7)	4 (57.1%) ^a	4	0	0	0	3
CAVC (<i>n</i> = 7)	2 (28.6%)	1	0	1	0	5
PS/PA (<i>n</i> = 5)	2 (40.0%)	1	1	0	0	3
CoA/IAA (<i>n</i> = 13)	6 (46.2%) ^a	4	0	1	1	7
Others (<i>n</i> = 22) ^b	10 (45.5%)	7	3	0	0	12
Total (<i>n</i> = 116)	54 (46.6%)	35	11	4	4	62

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^aIncidence of variant FHR patterns of this category was significantly higher than that of study subjects ($p < 0.05$)

^bOthers included Ebstein's anomaly ($n = 4$), truncus of the arteriosus ($n = 2$), heart tumor ($n = 4$), and patent ductus arteriosus ($n = 2$)

UVH: univentricular heart; TOF: tetralogy of Fallot; DORV: double-outlet right ventricle; VSD: ventricular septal defect; HLHS: hypoplastic left heart syndrome; TGA: transposition of the great arteries; AS: aortic stenosis; CAVC: common atrio-ventricular canal; PS/PA: pulmonary stenosis/pulmonary atresia; COA/IAA: coarctation of aorta/interrupted aortic arch

Table 17.3 presents the analysis of deceleration patterns of FHR fetuses according to the subtype of fetal diagnosis. Fetuses with TOF (83.3%), UVH (75%), aortic stenosis (57.1%), isomerism (46.2%), and COA/IAA (57.1%) showed statistically higher incidences of variant FHR patterns. Ebstein's anomalies corresponded to higher occurrence of variant FHR patterns, but few cases were included ($n = 4$). After excluding 44 fetuses associated with IUGR, chromosomal abnormalities, or other major structural anomalies that might have confounded the interpretation of FHR patterns, aberrant patterns were still frequently detected in the FHR of study subjects compared to the controls (38.8% vs. 17.7%, $p < 0.05$), in particular for cases with TOF or UVH. Severe variable deceleration and prolonged deceleration were the most visible patterns among fetuses with CHD.

Although the samples were limited, the data may imply that structural features originating in the early stages of heart development and involving a larger lesion of deformities tend to present aberrant patterns. Right or left heart isomerism is a positioning disarrangement usually diagnosed with heterotaxy or spleen abnormality. The normal arrangement of the viscera is disrupted and commonly associated with

single anatomies of the ventricle. Single ventricle is a structural abnormality in which only one ventricle occurs in the heart, which significantly impairs normal blood flow. Compared to cases of CHD with a four-chamber structure in situs solitus, single ventricle contains more complexity in anatomy and embryology. The dynamic alterations of morphology and physiology may confuse autonomic nervous system control because the pathways of those nerves could be affected by the deformity.

Another explanation is required for the development of aberrant FHR patterns with TOF, PS/PA, and COA/IAA. All of these deformities present pressure overload on the ventricles. After eliminating IUGR or other major anomalies, COA/IAA did not have a high incidence of apparent FHR; therefore, CHD involving right ventricle pressure overload could impact FHR patterns. Although the number of cases was small, other heart conditions involving right ventricle pressure load, such as right heart tumor ($n = 2$, 100%, variant FHR) and hypertrophy of the right ventricle of unknown cause ($n = 1$, 100%, variant FHR), were also observed in this study.

Cases of CHD with normal four-chamber anatomy, including ventricular septal defect (VSD), common arteriovenous truncus (CAVD), double outlet of the right ventricle (DORV), and conotruncal abnormalities such as transpositions of great arteries (TGA) [22], seem to support an intact electrical conduction system. However, these cases display a variety of structural defects, and severity differs widely among them. Careful interpretation of the results and a larger sample size are required. Additionally, the ambiguity of fetal diagnosis should be considered when translating the study findings to the practical world, because TGA is among the most intricate types of CHD for fetal echocardiographic examination.

17.4.2 Umbilical Arterial pH

Umbilical blood testing has been used for the retrospective evaluation of intrauterine fetal oxygenation. Umbilical arterial pH can be easily obtained after delivery without any invasion of the mother or fetus. Low values of pH indicate fetal acidosis in utero, and a pH < 7.2 is usually considered abnormal. Variant FHR patterns are well correlated with fetal acidotic status during delivery as reflected by umbilical

Table 17.4 Comparison of umbilical arterial pH between the groups

pH	Study subjects ($n = 116$)	Control patients ($n = 464$)	<i>P</i> value
Average	7.290 ± 0.097	7.304 ± 0.076	NS
<7.0	2 (1.7%)	2 (0.9%)	NS
7.0–7.1	2 (3.4%)	7 (1.9%)	NS
7.1–7.2	8 (10.3%)	26 (7.5%)	NS
>7.2 ^a	104	429	NS

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NS not significant

^a7.2 > pH: tetralogy of Fallot 3, isomerism 3, ventricular septal defect 2, univentricular heart 2, common atrio-ventricular canal 1, hypoplastic aorta 1

Table 17.5 Comparison of umbilical arterial pH in emergency C-section cases between the groups

pH	Study subjects (<i>n</i> = 15)	Control patients (<i>n</i> = 15)	<i>P</i> value
Average	7.307 ± 0.041	7.249 ± 0.134	NS
<7.0	0	1 (6.7%)	NS
7.0–7.1	0	1 (13.3%)	NS
7.1–7.2	0	1 (20.0%)	NS
>7.2	15	12	NS

Ueda K, et al., Am J Obstet Gynecol. 2009 Jul;201(1):64.e1-6

NS not significant

arterial pH. Therefore, variant FHR patterns and acidotic findings from umbilical arterial pH should be associated.

Table 17.4 shows that umbilical arterial pH values were similar in both groups (study subjects vs controls, 7.290 ± 0.098 vs 7.304 ± 0.076). These data suggest that no significant differences occurred between the two groups in fetal acidotic status. Interestingly, this pattern was also observed in the subgroup delivered by emergency Caesarian section due to variant FHR (7.307 ± 0.041 vs 7.249 ± 0.134, respectively: *p* > 0.05). Two cases with umbilical arterial pH < 7.2 were observed among the controls, but no cases were observed among patients with CHD (Table 17.5).

Our data suggest a discrepancy in the clinical interpretation of findings from FHR monitoring and umbilical arterial pH in patients with CHD. It is puzzling that variant patterns of FHR in CHD patients cannot be translated in the same way as for patients without CHD. One possible interpretation may involve the mechanisms of formulating FHR patterns. Fetal autonomic activity has been established as a reliable marker of central nervous system function and could be reflected in the control of fetal heart rate. Therefore, an abnormality of the brain, heart, and nerves that connects two organs may be associated with variant FHR patterns. Some types of CHD are likely to accompany variant FHR, but the correlation between FHR patterns and real fetal acidosis could be confounded or even exaggerated by the unique features of the autonomic conduction system. This hypothesis is supported by the observations of Siddiqui et al., who found that autonomic development in fetuses with CHD began to detectably deviate from the normal trajectory of autonomic nervous system regulation within 19 weeks of gestation [23].

Further investigations are needed to determine the relationship between aberrant patterns in CHD patients and the mechanism of formulating FHR patterns.

17.4.3 Other Tools for Evaluating Fetal Well-Being for CHD

FHR monitoring is a well-validated tool for the evaluation of fetal well-being. However, this method is limited when examining fetuses with fetal acidosis and structural heart defects. Aside from FHR monitoring, fetal echocardiography, and umbilical arterial pH values, relatively few tools exist for the fetal diagnosis of fetal

distress. Before delivery onset, the risks of progressing acidosis can be evaluated by a low BPS score, blood flow, or resistance in fetal brain vessels or umbilical vessels. Fetal scalp blood sampling of pH or lactate can examine fetal acidosis directly, but this invasive procedure is seldom performed. The use of fetal scalp blood sampling data for intrapartum management in an emergency situation is unrealistic.

Several other studies have examined fetal well-being and CHD [22, 24]. A fetal oximeter can measure fetal oxygenation directly during the intrapartum period. This new device is expected to determine fetal distress with high sensitivity and specificity, thereby reducing Caesarian section rates. Considering the present evidence from the Cochrane review, which compiled negative data from several systematic studies (including six comparing fetal pulse oximetry and FHR vs DHR alone), it remains difficult to conclude that the fetal oximeter provides a strong alternative to FHR monitoring [24]. A better method or improved device for pulse oximetry is necessary to enhance the overall evaluation of fetal well-being during labor. Another possibility is the evaluation of the ST segment in fetal electrocardiography. Gay et al. compared the frequencies of different ST events between fetuses with and without CHD. Their results showed that CHD does not modify the frequencies of ST events [22]. Fetal electrocardiography (STAN) was developed to avoid unnecessary Caesarean sections due to suspected fetal acidosis. The mechanism of STAN is related to heart muscle oxygenation and the biphasic ST segment, and T/QRS ratios represent fetal hypoxic episodes. The clinical translation of this study data is challenging, as the authors did not provide the data of their FHR monitoring, but the results could be useful for further investigation of the relationship between aberrant HFR patterns and patients with CHD.

17.5 Conclusion and Further Research Questions

Some observations introduced in this chapter still require further examination. However, in conclusion, these findings generate relevant clinical implications and suggest new research questions for both obstetricians and fetal and pediatric cardiologists.

A better understanding of fetal physiology and innovative thinking could help solve several remaining problems in pregnancies involving CHD fetuses. Although several operational devices or technical innovations could be applied to improve the long-term mortality and morbidity of CHD infants, these technologies would still not fulfil physician and patient demands. Furthermore, fetal interventions have been widely discussed to support term pregnancies or improve fetal circulation status in several types of CHD. To generate new technological advancements, more detailed investigation of the basics of fetal life is important. A more sophisticated collaborative approach between a variety of experts in the field should be established to address this challenge [25].

True innovation will arise from a careful analysis of present technology, and physicians should identify its current limitations. Many opportunities remain in this field for both daily practice and research.

References

1. Holland BJ, Myers JA, Woods CR Jr (2015) Prenatal diagnosis of critical congenital heart disease reduces risk of death from cardiovascular compromise prior to planned neonatal cardiac surgery: a meta-analysis. *Ultrasound Obstet Gynecol* 45(6):631–638
2. Levey A, Glickstein JS, Kleinman CS et al (2010) The impact of prenatal diagnosis of complex congenital heart disease on neonatal outcomes. *Pediatr Cardiol* 31:587–597
3. Satomi G, Yasukouchi S, Shimizu T et al (1999) Has fetal echocardiography improved the prognosis of congenital heart disease? Comparison of patients with hypoplastic left heart syndrome with and without prenatal diagnosis. *Pediatr Int* 41:726–732
4. Tworetzky W, McElhinney DB, Reddy VM et al (2001) Improved surgical outcome after fetal diagnosis of hypoplastic left heart syndrome. *Circulation* 103:1269–1273
5. Coltri A, Burtera G et al (1999) Detection of transposition of the great arteries in fetuses reduces neonatal morbidity and mortality. *Circulation* 99:916–918
6. Maeno YV, Kamenir SA, Sinclair B et al (1999) Prenatal features of ductus arteriosus constriction and restrictive foramen ovale in d-transposition of the great arteries. *Circulation* 99:1209–1214
7. Duke C, Sharland GK, Jones AM et al (2001) Echocardiographic features and outcome of truncus arteriosus diagnosed during fetal life. *Am J Cardiol* 88:1379–1384
8. Franklin O, Burch M, Manning N et al (2002) Prenatal diagnosis of coarctation of the aorta improves survival and reduces morbidity. *Heart* 87:67–69
9. Pepas LP, Savis A, Jones A et al (2003) An echocardiographic study of tetralogy of Fallot in the fetus and infant. *Heart* 13:240–247
10. Smythe JF, Copel JA, Kleinman CS et al (1992) Outcome of prenatally detected cardiac malformation. *Am J Cardiol* 69:1471–1474
11. Sholler GF, Kasparian NA, Pye VE et al (2011) Fetal and post-natal diagnosis of major congenital heart disease: implications for medical and psychological care in the current era. *J Paediatr Child Health* 47(10):717–722
12. Crispi F, Gratacos E (2012) Fetal cardiac function: technical considerations and potential research and clinical applications. *Fetal Diagn Ther* 32:47–64
13. Luterek K1, Szymusik I, Bartkowiak R et al (2011) N-terminal pro-B-type natriuretic peptide: a potential marker of fetal heart failure in hemolytic disease. *Neuro Endocrinol Lett* 32(5):657–662
14. Wallenstein MB, Harper LM, Odibo AO et al (2012) Fetal congenital heart disease and intrauterine growth restriction: a retrospective cohort study. *J Matern Fetal Neonatal Med* 25(6):662–665
15. Cedergrena MI, Källénb BA (2006) Obstetric outcome of 6346 pregnancies with infants affected by congenital heart defects. *Eur J Obstet Gynecol Reprod Biol* 125(2):211–216
16. Gartie TJ, Linzey M, Freeman RK et al (1979) Fetal heart rate and fetal distress in fetuses with congenital anomalies. *Obstet Gynecol* 53:716–720
17. Biale Y, Brawer-Ostrovsky Y, Insler V (1985) Fetal heart rate tracing in fetuses with congenital malformation. *J Reprod Med* 30:43–47
18. Terao T, Kawasahima Y, Noto H et al (1984) Neurological control of fetal heart rate in 20 cases of anencephalic fetuses. *Am J Obstet Gynecol* 149:201–208
19. Ueda K, Ikeda T, Iwanaga N et al (2009) Intrapartum fetal heart rate monitoring in cases of congenital heart disease. *Am J Obstet Gynecol* 201(1):64.e1–64.e6
20. National Institutes of Child Health and Human Development Research Planning Workshop (1997) Electronic fetal heart rate monitoring: research guideline for interpretation. *Am J Obstet Gynecol* 177:1385–1390
21. Walsh CA et al (2014) Mode of delivery in pregnancies complicated by major fetal congenital heart disease: a retrospective cohort study. *J Perinatol* 34(12):901–905
22. Gay E, Bornallet G, Gaucherand P et al (2015) Intrapartum electrocardiogram alteration in fetuses with congenital heart disease: a case-control study. *Eur J Obstet Gynecol Reprod Biol* 194(8):111–114

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23. Siddiqui S, Wilpers A, Myers M et al (2015) Autonomic regulation in fetuses with congenital heart disease. *Early Hum Dev* 91(3):195–198
 24. East CE, Begg L, Colditz PB et al (2014) Fetal pulse oximetry for fetal assessment in labour. *Cochrane Database Syst Rev* 7(10)
 25. Pavlovic M, Acharya G, Huhta JC (2008) Controversies of fetal cardiac intervention. *Early Hum Dev* 84(3):149–153