Isolated Fetal Cardiac Abnormalities: Are They Really Isolated?

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Am J Perinatol Rep 2018;8:e355–e358.

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Abstract

Objective To determine the rate of unsuspected noncardiac abnormalities in newborns suspected to have isolated cardiac abnormalities in the second trimester.

Study Design A review of the ultrasound database from the Weill Cornell Medical Center identified fetuses with a suspected cardiac abnormality from January 2006 to November 2016. Cases with prenatally suspected noncardiac structural abnormalities, abnormal fetal or neonatal karyotype or microarray, and those who delivered at an outside institution or underwent abortion were excluded. Neonatal records were reviewed to confirm prenatal findings and to identify anomalies not suspected in the second trimester.

Results Sixty-eight live births met the inclusion criteria. Five newborns (7.4%) had major abnormalities not identified in the second trimester. Three newborns had an imperforate anus. One newborn had left hydronephrosis and absent right lung, and one had hemifacial microsomia and fused ribs. All five newborns with unsuspected anomalies were in the group with suspected conotruncal anomalies, with a 11.9% rate of unsuspected anomalies versus 0% in those with nonconotruncal cardiac anomalies ($p = 0.15$).

Conclusion Patients with a suspected isolated fetal cardiac anomaly on ultrasound should be aware of the possibility of other major structural abnormalities, especially in cases of conotruncal cardiac anomalies.

Keywords

- cardiac abnormality
- cardiac anomaly
- conotruncal
- noncardiac abnormalities
- noncardiac anomalies

Cardiac abnormalities are among the most common congenital malformations and are present in an estimated 0.8% of live births.[1,2] In the United States, routine ultrasound has led to the prenatal detection of fetal cardiac malformations, though recent publications describe only a 36 to 39% detection rate for all congenital cardiac malformations.[3,4]

The etiology of congenital cardiac abnormalities is multifactorial, and risk factors include family history, teratogen exposure, and pregestational diabetes.[5] There is also an association with chromosomal abnormalities[6,7] and single-gene disorders. Previous studies have reported on the rate and type of extracardiac anomalies and aneuploidy identified in fetuses with cardiac anomalies,[8] and the prognosis with associated structural or genetic abnormalities is worse. Cardiac anomalies are associated with structural anomalies such as gastrointestinal or skeletal abnormalities that may be difficult to identify at the time of the anatomy ultrasound.[9] The likelihood of extracardiac anomalies that are not sonographically apparent in the setting of normal genetic testing is unclear.

Accurate prenatal diagnosis can improve perinatal and long-term outcome by optimizing the timing of delivery and ensuring that delivery occurs at a tertiary care center with advanced expertise in the management of these neonates.[6] Prenatal diagnosis of cardiac defects can also give the patient an opportunity to consider terminating the pregnancy.

received
April 27, 2017
accepted after revision
September 8, 2018

DOI https://doi.org/10.1055/s-0038-1675349.
ISSN 2157-6998.

Information about the likelihood of associated anomalies that are not apparent in the second trimester could inform these important medical decisions. Our objective was to determine the rate of unsuspected noncardiac abnormalities in newborns suspected to have isolated cardiac abnormalities in the second trimester.

Materials and Methods

We reviewed the obstetric ultrasound database from the Weill Cornell Medical Center and identified fetuses with a suspected cardiac abnormality (other than isolated atrial or ventricular septal defect) from January 2006 to November 2016. Isolated atrial and ventricular septal defects were excluded because the majority do not have clinical sequelae and most resolve spontaneously.[10,11] A detailed anatomical evaluation was performed in all patients in the second trimester, and cases in which noncardiac structural abnormalities were identified were excluded. Cardiac anomalies were categorized as either conotruncal or noncontruncal. Conotruncal anomalies included truncus arteriosus, malposition of the great arteries, tetralogy of Fallot, double-outlet right ventricle, and a ventricular septal defect with an overriding aorta. Structural abnormalities were defined as those that required medical or surgical intervention or had a substantial cosmetic or functional impact. All patients underwent fetal echocardiography to confirm the cardiac abnormality. Genetic counseling was offered to all patients, and cases with abnormal fetal or postnatal genetic testing were excluded. Patients without postnatal confirmation of fetal echocardiography findings, those who delivered at an outside institution, and those who underwent abortion were also excluded.

Neonatal records were reviewed to confirm prenatal findings and postnatal genetic testing and to identify anomalies not suspected in the second trimester. Postnatal imaging studies were also reviewed to correlate with prenatal findings. Categorical data were compared using Fisher's exact test and χ^2 analysis. Institutional Review Board approval was obtained.

Results

We identified 94 cases of isolated fetal cardiac abnormalities suspected on prenatal ultrasound. There were 68 live births meeting the inclusion criteria, and all fetal echo findings were confirmed postnatally. Conotruncal abnormalities were suspected in 42 (61.8%) cases (►**Table 1**). The most common conotruncal abnormalities were tetralogy of Fallot (20 cases; 47.6%) and transposition of the great arteries (11 cases; 29%). Of the nonconotruncal abnormalities, the most common were aortic coarctation in isolation or with other cardiac abnormalities (12 cases; 55%), and hypoplastic left or right heart (5 cases; 23%). Twenty-five patients had prenatal genetic testing through amniocentesis. All 25 had a karyotype, 15 (60%) had a microarray, and 4 (16%) had fluorescent in situ hybridization specific for 22q11.2 deletion performed. Neonatal genetic testing was performed on 20 of the 43 patients who did not have an amniocentesis. Neonatal genetic testing included a karyotype in all cases and microarray in eight cases, all of which were normal. Of the newborns who did not undergo genetic testing, none had any noncardiac clinical features of DiGeorge's syndrome.

There were five (7.4%) newborns with one or more major abnormalities not identified in the second trimester (►**Table 2**). There were no associated findings, such as a single umbilical artery, in any of these cases. Three newborns had an imperforate anus. One newborn had left hydronephrosis and an absent right lung. Another newborn had hemifacial microsomia and fused ribs. All five newborns

Table 1 Factors associated with unsuspected postnatal findings

	No noncardiac findings identified postnatally ($n = 63$)	Noncardiac findings identified postnatally ($n = 5$)	*p*-Value
Maternal age[a]	32 [26–35]	30 [27–32]	0.81
Race[b]			
White	23	1	0.27
Black or African-American	6	2	
Hispanic	8	–	
Asian	6	–	
Declined/other combinations, not described	20	2	
BMI[a]	24 [22–29]	25 [22–26]	0.63
Single umbilical artery[b]	8	0	0.40
Category of cardiac anomaly[b]			
Conotruncal	37	5	0.07
Nonconotruncal	26	0	

Abbreviation: BMI, body mass index.
[a]Data are presented as median [interquartile range]. [b]Data are presented as number of cases.

Table 2 Suspected isolated cardiac anomalies and postnatal findings

Case	Suspected cardiac anomaly	Neonatal sex	Was prenatal genetic testing performed?	Was postnatal genetic testing performed?	Postnatal findings
1	Tetralogy of Fallot, large ventricular septal defect, hypoplastic pulmonary arteries	Male	No	No	Imperforate anus VATER
2	Dextroversion, transposition of the great arteries, ventricular septal defect	Male	No	Yes, karyotype, microarray (all normal)	Left hydronephrosis, right hemivertebrae, absent right lung
3	Tetralogy of Fallot	Male	No	Yes, karyotype, microarray (all normal)	Imperforate anus
4	Tetralogy of Fallot	Female	Yes, karyotype (normal)	Yes, karyotype, microarray (all normal)	Imperforate anus, rectovaginal fistula
5	Double-outlet right ventricle, ventricular septal defect, overriding aorta	Male	No	Yes, karyotype microarray (all normal)	Torticollis, hemifacial microsomia, right fused ribs, left hemivertebrae at T9

Abbreviation: VATER, vertebral anomalies, anal atresia, tracheoesophageal fistula, esophageal atresia, and renal and radial anomalies.

with unsuspected anomalies were in the group with suspected conotruncal anomalies, with an 11.9% rate of unsuspected anomalies versus 0% in those with nonconotruncal cardiac anomalies ($p = 0.15$). There was no association of maternal age, body mass index, ethnicity, or single umbilical artery with unsuspected postnatal findings (►**Table 1**).

Four of the five cases with unsuspected major anomalies underwent postnatal genetic testing including karyotype and microarray, which were normal. One case did not undergo postnatal genetic testing, and this case was the only one associated with a defined syndrome. In this case (case 1), the findings were consistent with VATER (vertebral anomalies, anal atresia, tracheoesophageal fistula, esophageal atresia, and renal and radial anomalies).

Comment

Major noncardiac findings not suspected in the second trimester were not uncommon, particularly among newborns with conotruncal anomalies. The difference in rates of unsuspected findings in conotruncal versus other cardiac anomalies (11.9% vs 0%) was not statistically significant, though posthoc power analysis indicates that we only had 41.8% power to discern such a difference. Our study is unlike other studies characterizing the frequency of associated anomalies in fetuses with cardiac anomalies, as we included only cases with no sonographic evidence of associated anomalies at the time of prenatal diagnosis.

Conotruncal anomalies are a category of cardiac abnormalities characterized by a defect in the conotruncal septum and include truncus arteriosus, malposition of the great arteries, tetralogy of Fallot, double-outlet right ventricle, and a ventricular septal defect with an overriding aorta.[12] Published studies describe high rates of associated noncardiac anomalies, with a considerably worse prognosis in these cases.[7,12] Unlike our study, however, these studies included cases with anomalies detected in utero as well as those fetuses with chromosomal abnormalities. As our study excluded such cases, the rate of associated anomalies in our study population was considerably lower.

While the absence of associated genetic or major structural abnormalities apparent in utero is reassuring, patients should be aware of the possibility that major structural abnormalities could be identified after birth. As such abnormalities could be associated with a poorer prognosis, this information could inform decisions regarding continuing versus terminating an affected pregnancy. Third-trimester ultrasound to look for evidence of associated anomalies could be considered; however, some anomalies such as an imperforate anus, the most common unsuspected anomaly in this series, is rarely identified in utero.[13]

A limitation of the study was the relatively small number of cases, as a large proportion of fetuses with cardiac anomalies have associated genetic or structural abnormalities identified in utero, and many patients in our population do not continue pregnancies after the diagnosis of major fetal cardiac anomalies. Another limitation is that genetic testing was not performed on all cases. While we acknowledge the possibility of undiagnosed genetic conditions in our study group, some patients with cardiac anomalies diagnosed by ultrasound decline genetic testing. As counseling these patients about the possibility of unsuspected structural anomalies is important, our data may be relevant to these patients. We also acknowledge that genetic testing has advanced considerably since the beginning of our study period and that many anomalies formerly considered isolated may now be recognized to have an associated genetic abnormality.

Among the strengths of this analysis was the single-institution design, which allowed us to compare prenatal and postnatal findings with precision. Detailed anatomical fetal evaluation was performed in all cases under a uniform

imaging protocol. Neonatal follow-up was available in all cases, and all patients had fetal and neonatal echocardiography performed in the same pediatric cardiology unit.

In summary, patients with a suspected isolated fetal cardiac anomaly on ultrasound should be aware of the possibility of other major structural abnormalities, especially in cases of conotruncal anomalies. Our results provide a different perspective on apparently isolated cardiac anomalies. While neonatal prognosis largely depends on the severity of the cardiac anomaly, the outcome may also depend on the presence and severity of associated noncardiac findings.

Note

Presented at the 37th Annual Pregnancy Meeting of the Society for Maternal-Fetal Medicine, January 23–27, 2017, Las Vegas, NV.

Conflict of Interest

The authors report no conflict of interest.

Funding

There is no source of financial support for the research.

References

1 Small M, Copel JA. Indications for fetal echocardiography. Pediatr Cardiol 2004;25(03):210–222
2 Rajiah P, Mak C, Dubinksy TJ, Dighe M. Ultrasound of fetal cardiac anomalies. AJR Am J Roentgenol 2011;197(04):W747–W760
3 Friedberg MK, Silverman NH, Moon-Grady AJ, et al. Prenatal detection of congenital heart disease. J Pediatr 2009;155(01): 26–31, 31.e1
4 Pinto NM, Keenan HT, Minich LL, Puchalski MD, Heywood M, Botto LD. Barriers to prenatal detection of congenital heart disease: a population-based study. Ultrasound Obstet Gynecol 2012;40(04):418–425
5 Ailes EC, Gilboa SM, Riehle-Colarusso T, et al; National Birth Defects Prevention Study. Prenatal diagnosis of nonsyndromic congenital heart defects. Prenat Diagn 2014;34(03):214–222
6 Todros T, Capuzzo E, Gaglioti P. Prenatal diagnosis of congenital anomalies. Images Paediatr Cardiol 2001;3(02):3–18
7 Paladini D, Rustico M, Todros T, et al. Conotruncal anomalies in prenatal life. Ultrasound Obstet Gynecol 1996;8(04):241–246
8 Fesslova' V, Nava S, Villa L; Fetal Cardiology Study Group of the Italian Society of Pediatric Cardiology. Evolution and long term outcome in cases with fetal diagnosis of congenital heart disease: Italian multicentre study. Heart 1999;82(05):594–599
9 Solomon BD. VACTERL/VATER Association. Orphanet J Rare Dis 2011;6:56
10 Chaoui R, Pilu G. Ventricular septal defects. Visual Encyclopedia of Ultrasound in Obstetrics and Gynecology. www.isuog.org. Accessed April 27, 2017
11 Radzik D, Davignon A, van Doesburg N, Fournier A, Marchand T, Ducharme G. Predictive factors for spontaneous closure of atrial septal defects diagnosed in the first 3 months of life. J Am Coll Cardiol 1993;22(03):851–853
12 Tometzki AJP, Suda K, Kohl T, Kovalchin JP, Silverman NH. Accuracy of prenatal echocardiographic diagnosis and prognosis of fetuses with conotruncal anomalies. J Am Coll Cardiol 1999;33 (06):1696–1701
13 Brantberg A, Blaas HG, Haugen SE, Isaksen CV, Eik-Nes SH. Imperforate anus: a relatively common anomaly rarely diagnosed prenatally. Ultrasound Obstet Gynecol 2006;28(07):904–910