Prenatal echocardiographic diagnosis of congenital heart disease: comparison of past and current results

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The increased experience in interpretation of fetal echocardiographic images may change the accuracy of fetal echocardiography in diagnosing fetal heart defects. We thus decided to evaluate the specificity and the sensitivity of our fetal echocardiographic examinations in diagnosing congenital heart disease, focusing especially on the outcome of complex cardiac pathologies.

Between October 1999 and July 2003, 642 fetuses were followed until birth and underwent a postnatal reassessment of the cardiovascular system in our institution. These cases constitute our cohort. The postnatal reassessment was mainly done by echocardiography; some cases also had angiography. In case of intrauterine or postnatal death, an autopsy was performed. The prenatal and postnatal diagnoses were compared, and specificity and sensitivity of fetal echocardiography for congenital heart pathologies were determined.

Among 45 affected pregnancies, 31 cases had complex and 14 had significant cardiac defects. The sensitivity of fetal echocardiography for cardiac anomalies was 93.3%; the specificity was 100%. Compared to our previous study, the sensitivity was remarkably improved (in our previous study sensitivity was 78% and specificity 100%).

Echocardiography is a very useful and reliable tool in the evaluation of the fetal cardiovascular system, and has high sensitivity and specificity for congenital heart diseases.

Key words: fetal echocardiography, complex congenital heart defect.

The feasibility of studying fetal cardiovascular structures and function by means of ultrasound has been well established for over 20 years. Since the advent of fetal echocardiography, the fetal heart diseases can be correctly diagnosed[1,2]. Although small fetal structures, fetal malposition, abnormal amount of amniotic fluid, and obesity of the mother impose limitations on the optimal imaging of the fetal heart, the progress in ultrasound imaging technology and the experience in fetal heart disease have increased the sensitivity and the specificity of this tool. For this reason we decided to evaluate the specificity and the sensitivity of our fetal echocardiographic examinations in diagnosing congenital heart disease, focusing especially on the outcome of complex cardiac pathologies. We also compared these results with our previous study[3].

Material and Methods

The cohort was composed of 642 fetuses followed between October 1999 and July 2003 in our institution until their birth and underwent a postnatal reassessment of the cardiovascular system (Table I). These cases were mainly siblings of our patients with congenital heart defects from the Departments of Obstetrics and Gynecology of our institution. Some were referred from other centers by pediatric cardiologists or by obstetricians. A General Electric Vingmed System Five

Table I. Fetal Echocardiography Indications

Indication	Number of cases	Frequency
Family history of congenital heart disease	276	42.99%
Suspected fetal heart defect on routine fetal USG	139	21.65%
Maternal systemic disease affecting the fetus	141	21.95%
Maternal age over 35 years	18	2.80%
Fetal dysrhythmia	29	4.52%
Dysmaturity or suspected fetal anomaly on routine fetal USG	12	1.86%
Chromosomal anomaly	7	1.10%
Multiple gestation (microinjection)	7	1.10%
Oligo/polyhydramnios	4	0.62%
Medicine/teratogenic intake during pregnancy	2	0.31%
Hydrops fetalis	7	1.10%
Total	642	100%

USG: ultrasonography.

Performance echocardiographic scanner and 2.5-5 MHz transducers were used in the prenatal and postnatal echocardiographic examinations of the patients. The fetal examination included the standard positions used in fetal heart scanning technique[4]. Color flow mapping, Doppler and M-mode investigations were also done when necessary and appropriate[2]. The cardiac position and axis were determined according to the simple technique described by Cordes et al.[5]. Since only a few cases had intrauterine chromosomal analysis, this issue was not addressed in the current study.

Physical and echocardiographic examinations were done during the postnatal evaluation. If a cardiac anomaly was anticipated or detected, the cases were also evaluated with a telecardiogram, electrocardiogram (ECG) or cardiac catheterization as indicated. Twenty-one cases with congenital heart disease also underwent autopsy. The prenatal and postnatal diagnoses were compared, and the specificity, sensitivity, and positive and negative pred ictive values of fetal echocardiography in diagnosing congenital heart pathologies were determined. A modified classification system similar to that of Hunter et al.[6] and Wren et al.[7] was used to categorize the congenital heart defects (Table II). The results of the current study were compared to those obtained in our previous study conducted on 128 fetuses between October 1996 and October 1998[3].

Table II. Classification System Used for Fetal Heart Diseases

Category	Included cardiac defects
Complex: Absent or hypoplastic chamber or absent or hypoplastic valve or common valve Heart disease including all cases of heterotaxia or atrial isomerism Complex form of DORV	Complete AVSD HLHS Pulmonary atresia Tricuspid atresia Aortic atresia Mitral atresia Double inlet ventricle Truncus arteriosus
Significant: Congenital heart disease with four valves and four chambers requiring operation or intervention but not included in the complex group (excludes PDA, ASD)	Aortopulmonary window Critical aortic and pulmonary stenosis Partial AVSD Coarctation of aorta VSD Simple TGA Simple form of DORV TOF TAPVC cTGA
Minor: Congenital heart disease requiring no intervention (4 chambers, 4 valves)	VSD (small) Aortic stenosis Pulmonary stenosis

ASD: atrial septal defect, AVSD: atrioventricular septal defect, cTGA: congenitally corrected transposition of the great arteries, DORV: double outlet right ventricle, HLHS: hypoplastic left heart syndrome, PDA: persistent arterial duct, TAPVC: total anomalous pulmonary venous connection, TGA: transposition of the great arteries, TOF: tetralogy of Fallot, VSD: ventricular septal defect.

Results

The mean gestational age and maternal age at the time of examination were 27.6±5.8 weeks (range: 18-39 weeks) and 27.7±5.2 years (range: 18-42 years), respectively. Indications for the fetal echocardiographic examination of 642 fetuses are listed in Table I. Among 642 cases, 45 had cardiac anomalies in the postnatal evaluation. According to the classification given in Table II, 31 cases had complex cardiac pathologies and 14 cases had significant cardiac pathologies.

Among 31 cases with complex cardiac pathologies, four patients had hypoplastic left heart syndrome, 11 atrioventricular septal defect, 11 hypoplastic ventricle (right ventricle in 7, left ventricle in 4 patients), four patients anomalies of the origin of the great arteries with or without isomerism, and one patient absent pulmonary valve syndrome (Table III)[8,9]. Two patients had isolated levocardia - one had totally inverted situs and the other left atrial isomerism. One patient had isolated dextrocardia (Table III).

Table III. Complex Cardiac Anomalies

Complex anomalies (n=31)		Prenatal diagnosis: Echo./angio.	Prenatal diagnosis: Autopsy	Prognosis
HLHS	4	The same (n=1)	The same (n=3)	TOP (n=3), ND (n=1)
AVSD				
4 isolated[a]		The same (n=1)	The same (n=3)	TOP[a] (n=3)+ND (n=1)
1 with PA and MAPCA		The same	.....	ND
1 (SDD) TGA and imperforated PV		The same	.....	Unknown
1 (ADD) DORV, PS, LAI		The same	.....	Alive, no intervention
1 (ADD) LAI		The same	.....	Unknown
1 common inlet ventricle, MGA, hypoplastic pulmonary artery[b], RAI		.....	All+ hemitruncus*	IUD
1 common inlet vent., MGA, isolated dextrocardia		.....	The same	TOP
1 hypoplastic Ao, coarctation	11	.....	All+TAPVC*	IUD
Hypoplastic LV				
1 (SDD) DORV, VSD (inlet), hypoplastic Ao		.....	The same	TOP
1 (SDD) DIRV, VSD		.....	The same	TOP
1 DIRV, high venosum ASD, left AV valve atresia, PA and MAPCA, isolated levocardia		.....	The same	Alive, no intervention
1 (SDD) VSD[c]	4	The same	The same	ND
Hypoplastic RV				
1 (SLA) DORV, VSD (noncommitted), superoinferior ventricles (8)		All+PDA+PH	The same	ND
1 (SDD) DILV, TGA, VSD (sub Ao), hypoplastic Ao		.....	The same	TOP
1 (SDD) DILV, VSD (sub Ao), right AV valve atresia		.....	The same	TOP
1 single inlet LV, PA		.....	The same	ND
1 (SDD) single inlet LV, VSD, PS		The same	.....	Alive, no intervention
1 (SDD) VSD[c]		The same	.....	Alive, no intervention
1 (SDD) VSD, PS, tricuspid regurgitation[d]	7	The same	.....	Alive, no intervention
Absent pulmonary valve syndrome				
1 Absent pulm. valve, VSD	1	.....	The same	TOP
Abnormalities of the origin of the great arteries ± atrial isomerism				
1 (ADD) DORV, VSD (sub pulm. restrictive), PS, LAI, isolated levocardia	4	.....	.....	Alive, no intervention
1 (ADL) TGA, VSD (sub pulm. + trabecular), PS, LAI (9)		All + superoinferior ventricles*	.....	Alive, Glenn operation
2 (SDD) DORV, PS, VSD (Sub pulm. restrictive)[e].		.....	The same (n=2)	TOP

[a]Down syndrome, [b]frequent supraventricular tachycardia attacks, [c]twin gestation in 24th week gestation, [d]twin gestation in 24th week; the other fetus is normal, [e]maternal homocystinuria in a patient, *false-negative.

ADD: situs ambiguus, D-loop ventricles, dextroposition of aorta, ADL: situs ambiguus, D-loop ventricles, levoposition of aorta, Angio: angiography, Ao: aorta, ASD: atrial septal defect, AV: atrioventricular, AVSD: atrioventricular septal defect, DI: double inlet, DORV: double outlet right ventricle, Echo: echocardiography, HLHS: hypoplastic left heart syndrome, IUD: intrauterine death, LAI: left atrial isomerism, LV: left ventricle, MAPCA: major aortopulmonary collateral, MGA: malposition of the great arteries, ND: neonatal death, Pulm: pulmonary, PA: pulmonary atresia, PDA: patent ductus arteriosus, PH: pulmonary hypertension, PS: pulmonary stenosis, PV: pulmonary valve, RAI: right atrial isomerism, RV: right ventricle, SDD: situs solitus, D-loop ventricles, dextroposition of aorta, SLA: situs solitus, L-loop ventricles, anterior position of aorta, TGA: transposition of great arteries, TOP: termination of pregnancy, TAPVC: total anomalous pulmonary venous connection, VSD: ventricular septal defect.

Various congenital heart defects were associated in all three of these patients. One patient had dextroposition of the heart due to left-sided diaphragmatic hernia and another patient had mesocardia with left pleural effusion. These two patients had normal cardiac anatomy. All the other cases had levocardia and left cardiac axis between 60° and 90°.

Accuracy of Fetal Echocardiography in Different Categories of Cardiac Anomalies

There were three false-negatives in the patients with complex cardiac pathologies, in terms of fetal echocardiographic diagnosis. Two of these patients had atrioventricular septal defects with associated cardiac anomalies. One patient had right atrial isomerism, common inlet right ventricle, malposition of the great arteries and hypoplastic pulmonary artery. Hemitruncus was missed prenatally in this patient. The other patient had hypoplastic aorta and coarctation of the aorta. Total anomalous pulmonary venous connection was detected at autopsy. The third patient with false-negative diagnosis had left atrial isomerism, ventricular septal defects, L-transposition of the great arteries and pulmonary stenosis. The superoinferior ventricles were additionally detected in postnatal echocardiography (Table III). A patent arterial duct and pulmonary hypertension were additionally diagnosed in the postnatal echocardiogram of another patient. Since these are physiological prenatally, they were not considered as false- negative diagnoses.

There were 14 significant cardiac pathologies, which were diagnosed correctly, in fetal echocardiography (Table IV). No minor cardiac defects were detected in this study.

Overall, there were three false-negative results, and no false-positive results. The sensitivity of the prenatal echocardiographic examination in diagnosing cardiac defects was calculated as 93.3%, and the specificity was 100%. The positive and negative predictive values were 100% and 99.5%, respectively. The figures for complex and significant cardiac defects are depicted separately in Table V.

Table IV. Significant Cardiac Anomalies

Significant anomalies (n=14)		Postnatal diagnosis		Prognosis
		Echo./angio.	Autopsy	
Abnormalities of the origin of the great arteries				
1 (SLL) TGA, VSD	3	The same	.....	Alive, no intervention
1 (SLL) TGA, VSD, PS, AV block		The same	.....	Alive, no intervention
1 (SLL) DORV, VSD (Sub Ao), PS		The same	.....	Alive, no intervention
TOF	3	The same (n=3)	.....	Alive, no intervention
VSD				
2 VSD (with anterior mal-alignment)	3	The same (n=2)	.....	Alive, no intervention
1 VSD (sub Ao)		The same	.....	Alive, no intervention
Critical AS				
2 mitral stenosis+regurgitation, EFE*	3	The same (n=1)	The same (n=1)	ND (n=1), Unknown
Severe PS				
1 PS		The same	.....	Alive, valvuloplasty
Single atrium	1	The same	.....	Alive, no intervention
Ebstein anomaly	1	The same	.....	Alive, no intervention

* Premature closure of the patent foramen ovale in a patient.

Ao: aorta, Angio: angiography, AS: aortic stenosis, AV: atrioventricular, DORV: double outlet right ventricle, Echo: echocardiography, EFE: endocardial fibroelastosis, ND: neonatal death, PS: pulmonary stenosis, TGA: transposition of great arteries, TOF: tetralogy of Fallot, VSD: ventricular septal defect.

Outcome of Pregnancies with Congenital Cardiac Defects

All patients were followed until the end of the pregnancy. Thirteen pregnancies (41.9%) were terminated before 25 weeks of gestation because of complex cardiac defects (Table III). There were two intrauterine deaths (6.5%) and five neonatal deaths (16.1%) among patients with complex cardiac defects. Only seven patients (22.6%) outlived the neonatal period and one of those had a Glenn operation afterwards. The prognoses of two patients are unknown

Table V. Comparison of the Results with the Previous Study

	Previous study	Current study
Complex cardiac anomalies (n)	**4**	**31**
False-negative	2	3
False-positive	0	0
Sensitivity	50%	90.3%
Specificity	100%	100%
Positive predictive value	100%	100%
Negative predictive value	98.4%	99.5%
Number of terminations	0 (0%)	13 (41.9%)
Neonatal death	1 (25%)	5 (16.1%)
Intrauterine death	0 (0%)	2 (6.5%)
Neonatal interventions	0 (0%)	1 (3.2%)
Significant cardiac anomalies (n)	**5**	**14**
False-negative	0	0
False-positive	0	0
Sensitivity	100%	100%
Specificity	100%	100%
Positive predictive value	100%	100%
Negative predictive value	100%	100%
Number of terminations	0 (0%)	0 (0%)
Neonatal death	0 (0%)	1 (7.1%)
Intrauterine death	0 (0%)	0 (0%)
Neonatal interventions	0 (0%)	1 (7.1%)
Overall (including other categories) (n)	**128**	**642**
False-negative	2	3
False-positive	0	0
Sensitivity	78%	93.3%
Specificity	100%	100%
Positive predictive value	100%	100%
Negative predictive value	98.3%	99.5%

because the parents preferred to be followed in another institution, and no contact was available after delivery. None of the pregnancies were terminated because of a significant cardiac defect (Table IV). There was only one neonatal death in this group. This patient had critical aortic stenosis, mitral stenosis and endocardial fibroelastosis. Prognosis of another patient with a similar cardiac pathology is not known. The remaining patients survived the neonatal period (85.7%), and one of them underwent pulmonary valvuloplasty.

Comparison of the Results with the Previous Study

In our previous study[3] conducted on 128 fetuses, the sensitivity of the fetal echocardiography was 78% and the specificity 100%. The positive and negative predictive values were calculated as 100% and 98.3%, respectively. When these results are compared with the results of the current study, the sensitivity (93.3%) of fetal echocardiography has increased considerably in the current study (Table V). The number of annual fetal echocardiographic examinations has more than doubled, and the number of complex cases in the current study has increased (64 cases/year with 3.9% complex and 3.1% significant cardiac anomalies in the previous study versus 183 cases/year with 4.8% complex and 2.2% significant cardiac anomalies in the current study). No pregnancy was terminated in the previous study; however, 41.9% of the pregnancies were terminated in the current study (Table V). Conversely, there has been a slight increase in the frequencies of neonatal death and intrauterine death in the current study (previous study neonatal death: 11%, intrauterine death: 0%; current study neonatal death: 16.1%, intrauterine death: 6.5%). It is of note that the frequency of interventions during the neonatal period was very low in both studies (11% in the previous study, 10.3% in the current study).

Discussion

While having some technical limitation[2], fetal echocardiography is an important tool directing or altering the obstetric follow-up of a pregnancy. The accuracy of this tool in correctly diagnosing congenital heart defects is of paramount importance when termination of pregnancy is being considered for the more severe cases. This study indicates that cardiac anomalies can be diagnosed in fetal life by echocardiography with a high degree of accuracy (sensitivity: 93.3%, specificity 100%). We obtained correct and complete diagnosis in 93.3% of the cases. In less than 7%, the diagnosis was incomplete, although a congenital heart defect was diagnosed, and the incomplete diagnoses were among the cases with complex cardiac pathologies. When compared with our previous study[3], the sensitivity of fetal echocardiography has improved considerably over the years (sensitivity: 78%, specificity: 100%).

More complex cardiac defects were detected in the current study both in quantity and quality. Considering the false-negative results in the previous study, they were mostly outflow lesions (transposition of the great arteries and pulmonary atresia) including a case with atrioventricular discordance, a four-chamber defect. There was no difficulty in diagnosing outflow lesions in the current study. This apparently is due to the increased experience of our institution in such cases. Despite this, cases with total anomalous pulmonary venous connection, hemitruncus and superoinferior ventricles were missed. The prenatal diagnoses of these structural abnormalities are still very difficult. Driggers et al.[10] also emphasized the difficulty of diagnosing total anomalous pulmonary venous connection prenatally. We are not aware of a case with superoinferior ventricles that had an intrauterine diagnosis with the exception of the one previously reported from our institution[8]. This case, which also had double outlet hypoplastic right ventricle and noncommitted ventricular septal defect, is included in our present study.

This study also indicates that the prognosis of complex and significant cardiac defects is poor. As a whole, 46.7% of the fetuses with complex and significant cardiac anomalies died, including the elective terminations (28.9%) in complex cardiac pathologies. The fetal spectrum of disease is different from that seen postnatally[11]. Furthermore, some studies have shown that the outcome of malformations diagnosed prenatally is poorer than expected when compared to postnatal diagnoses[12-15]. In this setting, other than providing added knowledge about congenital heart disease in fetal life, the principal function of fetal echocardiography seems to be the identification of malformations which are associated with a poor outcome, so that terminating the pregnancy may be an option[6].

The rate of termination was increased from none to 28.9% in our current series. In fact, many studies report a high rate of termination in severe cases[16,17]. The expansion in termination rate is difficult to explain, since the parents met with the same counsellors in both series. The increased rate in detection of complex cardiac pathologies may have played a role. All the terminated pregnancies were diagnosed before the 24th week of gestation, whereas only two cases with complex cardiac defects diagnosed before the 24th week of gestation continued with the pregnancy. The social psychology and the dynamics of the community with which we are involved may be different from that in other studies. We noticed that parents who had a family history of congenital heart defect were likely to decide on termination of the pregnancy, especially if they had a healthy child.

It is possible that more severe cases were enrolled in this study in part due to the special interest of our institution in fetal cardiology. Therefore our study may not reflect the true spectrum of fetal cardiac disease.

It is easier for the obstetrician to recognize complex cardiac defects, especially when associated with extracardiac anomalies[17]. Available studies confirm high diagnostic rates at secondary referral[18,19]. Detection of a minor cardiac anomaly is much more difficult during a general scan in an unselected population[17]. Therefore, we also agree that fetal cardiac examination should be a routine part of the prenatal ultrasonographic examination. In order to achieve this in our country, a nation-wide training program, similar to that carried out by Hunter et al.[6] in northern England, is needed for obstetric ultrasonographers. In conjunction with this, the gestational age at diagnosis is likely to decrease. As a result, interruption of pregnancy may become more frequent,

particularly in complex cases[11]. Furthermore, fetal echocardiography is mostly a postgraduate education and is not widely practiced to meet the demands of our country. We believe that if these issues are addressed properly in a population with high parental consanguinity and birth rate, as in Turkey, fetal echocardiography will have great impact on the handling of fetal and neonatal cardiac disease.

In conclusion, fetal echocardiography is highly sensitive and specific in detecting cardiac defects prenatally. It has a potential impact on the prognosis of postnatal cardiac disease, although there is concern that prenatally diagnosed cases still have poor prognosis. We are not, however, satisfied with the higher accuracy of our fetal echocardiographic examinations. We expect that establishing a fetal cardiac screening program as a part of routine obstetric ultrasonographic examination will increase the detection rate of congenital heart disease prenatally and provide new insights into our current knowledge.

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