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Extended fetal echocardiographic examination for detecting cardiac malformations in low risk pregnancies

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Abstract

Objective—To improve the rate of prenatal detection of cardiac malformations in a low risk population.

Design—Comparison of extended fetal echocardiography with the standard four chamber view in detecting abnormalities. Extended echocardiography comprised the four chamber view and visualisation of the left ventricular outflow tract, the right ventricular outflow tract, and the main pulmonary artery and its branches. In cases with abnormal results complete echocardiographic studies were performed by a paediatric cardiologist using M mode, Doppler, and colour flow mapping techniques.

Setting—Obstetric ultrasonographic unit at Shaare-Zedek Medical Centre, Jerusalem.

Subjects—5400 fetuses in low risk pregnancies between 18 and 24 weeks' gestation (mean 21 weeks); 53 were lost to follow up.

Main outcome measures—Detection of abnormality before and after birth.

Results—During the study 23 infants (0.4%) were born with cardiac abnormalities, 21 of whom had major structural and functional heart disease. 18 fetuses had heart disease diagnosed prenatally, 11 by the four chamber view alone (sensitivity 48%) and a further seven by extended echocardiography (sensitivity 78%). Five fetal cardiac defects were

missed prenatally (false negative rate 22%). These included coarctation of aorta, persistent truncus arteriosus, tetralogy of Fallot, ventricular septal defect, and pulmonic stenosis. Only one false positive diagnosis (coarctation of aorta) was made (specificity 99.9%, false positive rate 0.1%). The abnormality was correctly identified in 17 out of 18 cases.

Conclusions—The extended fetal heart examination detected 86% (18/21) of major abnormalities in a low risk population. The examination should be incorporated into routine prenatal ultrasonographic investigations.

Introduction

The incidence of congenital heart disease is 8/1000 live births. Half of the cases are considered minor and are easily corrected by surgery. The remainder are more serious and account for about 50% of deaths from lethal malformations in childhood.^{1,2} Congenital heart diseases are 6.5 times more common than chromosomal abnormalities and four times more common than neural tube defects.¹ Unlike chromosomal and neural tube defects, for which there has been extensive prenatal screening, congenital heart diseases are often not identified until the infant is born. The importance of early diagnosis of congenital heart disease is further

emphasised by the fact that 20% to 32% of perinatal deaths are due to congenital heart disease.⁴ Although recent technology has allowed fetal heart evaluation and detection of anomalies from the 17-18th week of gestation or even earlier with transvaginal ultrasonography, the prenatal diagnosis of congenital heart defects is still a challenge for the modern obstetric ultrasonographer.

The usefulness of fetal echocardiography as a clinical technique for the prenatal diagnosis of congenital heart disease was shown in the early 1980s.^{5,6} Allan *et al* detected 60% of severe cardiac anomalies using the four chamber view for screening congenital heart diseases.⁷ To increase the detection rate of fetal echocardiography, women at high risk of having children with congenital heart disease have been selected for detailed fetal echocardiographic examination in specialised referral centres.⁸ However, since most neonates with congenital heart disease are born to women without any previous known risk factors this

prenatal selection seems ineffective. We conducted a study to evaluate whether extended echocardiography in the low risk pregnant population can increase the detection rate of congenital heart disease.

Subjects and methods

Screening for congenital heart disease is offered to all pregnant women routinely attending the obstetric ultrasonographic unit at Shaare-Zedek Medical Centre, Jerusalem. Women with the following risk factors were excluded from our study: history of congenital heart disease, maternal diabetes or connective tissue diseases, exposure to alcohol or lithium, phenylketonuria, fetus small for gestational age, and viral infection during the first trimester. Only women below 35 years old, with well documented medical follow up and who had borne live infants were included in the study.

A detailed biometric and structural evaluation of all fetuses was performed with sector scanners of 5 and

Fetal echocardiography showing (a) four chamber view; (b) long axis view through inlet and outlet of right atrium showing inferior and superior vena cava and (c) pulmonary vein entering left atrium—arrow indicates opening of foramen ovale; (d) long axis view showing left ventricular outflow tract obtained by slight cranial angulation of transducer from four chamber view and slight clockwise rotation of transducer on maternal abdomen in case of posterior fetal spine; (e) short axis view showing right ventricular outflow tract; (f) main pulmonary artery and its bifurcation obtained by further cranial angulation and counter clockwise rotation of transducer. LA = left atrium, RA = right atrium, LV = left ventricle, RV = right ventricle, IVC = inferior vena cava, SVC = superior vena cava, PV = pulmonary vein, FO = foramen ovale, RPA = right pulmonary artery, AAO = root of ascending aorta, MV = mitral valve, TV = tricuspid valve, AO = aorta in transverse section, LPA = left pulmonary artery, MPA = main pulmonary artery, and SPA = left pulmonary artery

TABLE I—Rate (per 1000 live births) of the types of congenital heart disease compared with rate derived from three large studies¹¹⁻¹³

Abnormality	No of cases	Observed rate	Mean (range) calculated rate	p Value
Tetralogy of Fallot	5	0.9	0.6 (0.4-0.8)	0.31
Hypoplastic right heart	3	0.5	0.2 (0.17-0.24)	0.06
Hypoplastic left heart	2	0.3	0.45 (0.3-0.6)	0.79
Coarctation	2	0.3	0.62 (0.45-0.8)	0.41
Persistent truncus arteriosus	2	0.3	0.12 (0.08-0.16)	0.08
Atrio ventricular septal defect	2	0.3	0.36 (0.32-0.4)	0.86
Double outlet in right ventricle	1	0.18	0.12 (0.016-0.24)	0.82
Ventricular septal defect	1	0.18	1.8 (1.2-2.4)	0.005
Pulmonic stenosis	1	0.18	0.4 (0.2-0.6)	0.43
Miscellaneous	4	0.7	1.13 (0.9-1.36)	0.42

TABLE II—Congenital heart diseases detected by four chamber view and by extended echocardiography examination

Anomaly	No of cases	Ultrasonographic findings
Abnormal on four chamber view (n=11):		
Hypoplastic heart syndrome	5	Single ventricle and atria
Atrioventricular septal defect	2	Abnormal crux
Heart failure	2	Pericardial effusion, cardiomegaly
Epstein anomaly	1	Giant right atrium, abnormal tricuspid
Ectopic Cordis	1	Extrathoracic heart
Normal on four chamber view, abnormal on extended examination (n=7):		
Tetralogy of Fallot	4	Septal defect in ventricular outlet, overriding aorta
Double outlet in right ventricle	1	Septal defect in ventricular outlet, two outlets, from right ventricle
Coarctation	1	Narrow aortic root, relatively small left ventricle
Persistent truncus arteriosus	1	Ventricular septal defect, single outlet vessel

TABLE III—Diagnostic accuracy of abnormal results on four chamber view and extended echocardiography

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Abnormal four chamber view (n=11)	11/23 (48%)	5323/5324 (99.9%)	11/12 (92%)	5323/5335 (99.8%)
95% Confidence interval	(38% to 58%)		(88% to 96%)	
Abnormal extended examination (n=18)	18/23 (78%)*	5323/5324 (99.9%)	18/19 (95%)	5323/5328 (99.9%)
95% Confidence interval	(71% to 85%)		(93% to 97%)	

*p=0.0078 Compared with four chamber view by correlated χ^2 test.

3.5 MHz mounted with pulsed wave Doppler (ESI 2000, Elscint, Haifa, Israel) and 3 MHz (ATL Mark IV, Squibb Medical Systems). Colour flow mapping was performed with a Hewlett-Packard (Ultra-system 77020A). During cardiac evaluation the standard four chamber view was visualised (figure (a)); once it was obtained simple rotation of the transducer along its axis by about 90° brought the major great veins (b and c) and major great arteries into view, allowing proper visualisation of the left ventricle outlet (d), the short axis of the right ventricle outlet with the main pulmonary artery (e and f), and sometimes the aortic arch and ductus.⁹ The average duration of routine echocardiographic examination was 15 minutes, giving a total time for fetal imaging of about 30 minutes. When a cardiac abnormality was detected further evaluation was performed in the paediatric cardiology unit by using Doppler colour flow and M mode techniques and the scans were recorded on videotape for later review. Personal data on each woman entering the study were recorded on a computerised medical file. The progress and the outcome of each pregnancy was followed up. Postmortem examinations and neonatal echocardiography were performed on affected infants to confirm the prenatal findings. The detection rate of the procedure (sensitivity) was the proportion of the fetuses with congenital heart disease who had a positive result on screening. This criterion could be ascertained only within the limitation of the study design—that is, diagnosis was based on neonatal physical examinations, and infants with asymptomatic heart disease that might develop later were not ascertained. Neonatal registration and personal communications with the only three paediatric cardiologist centres in our community were used to determine the true negative, false negative, and false positive cases. Three fifths of the fetuses studied were delivered

at Shaare-Zedek Medical Center; the remainder were delivered in three other university hospitals.

Statistical analysis was performed with the χ^2 or correlated χ^2 test.¹⁰ The level of significance was set at p<0.05.

Results

During August 1988 to April 1990, 5400 fetuses, including 50 pairs of twins, were screened at 18-24 weeks' gestation. Of the fetuses screened, 53 were lost to follow up and therefore omitted from the study, leaving 5347 fetuses. The average age of the women was 24.6 (range 18-45) years. The mean gestational age at the first routine screening was 21 (18-24) weeks; a four chamber view was obtained in 5240 (98%) of the fetuses; the extended fetal heart examination was completed in 4812 (90%). Twenty three fetuses were born (0.4%) with congenital cardiac anomalies. Table I lists the cardiac malformations in the 23 cases. The observed rate of each malformation has been compared with the mean of the rates obtained in three large studies.¹¹⁻¹³ There was broad agreement between the observed rate and the calculated rates for most of the anomalies. However, the rate of right hypoplastic heart syndrome was increased in our study, while the rate of ventricular septal defect was lower.

Prenatal echocardiography with the four chamber view detected 11 out of the 23 fetuses with cardiac malformations (table II). These included five fetuses with the hypoplastic heart syndrome (three right and two left); two with atrioventricular septal defect, two with congestive heart failure—due to paroxysmal atrial tachycardia in one fetus and twin to twin transfusion in the second; one with Epstein anomaly; and one with ectopic cardia. Extended echocardiographic evaluation of the ventriculoarterial connections detected cardiac anomalies in an additional seven fetuses. Outlet ventricular septal defect associated with large overriding aortic root was pathognomonic of tetralogy of Fallot in four of these seven cases; the other three fetuses had double outlet in the right ventricle, persistent truncus arteriosus, and coarctation of aorta. Five fetuses with cardiac abnormalities (22%) did not have the abnormalities detected by echocardiography. Of these five, two had minor abnormalities (ventricular septal defect and pulmonic stenosis) and three had major abnormalities (persistent truncus arteriosus, tetralogy of Fallot, and coarctation of aorta). Only in one normal fetus was a false positive diagnosis of coarctation of aorta made by screening (specificity of 99.9%).

The malformation was misdiagnosed in only one case, in which tetralogy of Fallot was erroneously identified as tricuspid atresia with ventral septal defect. In all other fetuses postnatal examination by a paediatric cardiologist or pathologist confirmed the prenatal diagnosis.

Table III summarises and compares the diagnostic accuracy of four chamber view echocardiography and extended examination in terms of sensitivity, specificity, and positive and negative predictive values. Sensitivity of screening increased from 48% to 78% with the extended examination, and the positive predictive value increased from 92% to 95%. The specificity and negative predictive value were not significantly different for the four chamber view and extended examination.

Chromosomal analysis was performed prenatally in four cases. Two (9%) abnormal karyotypes were detected: trisomy 21 and trisomy 18. Table IV gives the outcomes of the pregnancies. Five pregnancies were terminated and the mortality of fetuses in completed pregnancies was 28% (5/18). Overall, 10 of 23 fetuses (43%) with cardiac anomalies died. Two of the 13 surviving fetuses, had severe genetic syndromes.

TABLE IV—Outcome of pregnancies with fetuses with congenital heart defects

Abnormality	No of cases	Termination of pregnancy	Neonatal death	Survived
Tetralogy of Fallot	5	1		4*
Atrioventricular septal defect	2	1		1*
Right hypoplastic heart syndrome	3		3	
Left hypoplastic heart syndrome	2	1	1	
Persistent truncus arteriosus	2	1		1
Ectopic cordis	1		1	
Double outlet in right ventricle	1	1		
Miscellaneous	7			7
Total	23	5 (22%)	5 (22%)	13 (56%)

* One case had a severe genetic syndrome.

Discussion

Although much has been published on the ability of ultrasonography to detect heart defects prenatally,¹³ routine screening of the general population and its feasibility has been scarcely reported. Our results are noteworthy because they emphasise the importance of routine ultrasonography in detecting congenital heart malformations and show that most congenital heart diseases may be detected by an obstetric ultrasonographer with an interest in fetal heart imaging. The 0.4% incidence of congenital heart defects observed in our study agrees with the reports of the Royal Brompton hospital¹¹ and the New England regional infant care programme,¹² which cited incidences of 0.3%.

Furthermore the observed rate of most of the various types of heart defects did not differ significantly from the rate calculated from three large studies (table I), suggesting that all infants with major congenital heart diseases were detected by our screening programme. The increased rate of right hypoplastic heart syndrome in our study may be explained by the fact that the three studies gave rates for surviving infants not for prenatal diagnosis. If we omit from the analysis the fetus that died in utero of right hypoplastic heart syndrome the observed rate becomes 0.3/1000 live births, which does not differ significantly from the calculated rate. The calculated rate of ventricular septal defect was significantly higher than the observed rate; this is because of the inability of ultrasonography to detect the smallest of these defects.

Regarding the reproducibility of fetal cardiac imaging at 21 weeks' gestation the four chamber view could be imagined in 98% of cases and the extended examinations could be completed in 90% of cases; only 10% of patients required repeat ultrasonography at 24 weeks. Recently DeVore and Platt concluded in an extensive review that the ability to obtain the four chamber view increased from 9% at 14 weeks to 20% at 20 weeks.¹³ The authors examined 400 low risk fetuses between 15 and 23 weeks of gestation. They were able to obtain the four chamber view in 90% of the cases. Allan *et al*, were the first to report a sensitivity of 66% for diagnosing fetal congenital heart disease with the four chamber view.⁷ Copel *et al* reported 92% sensitivity with the four chamber view.¹⁴ However, the data in their study were drawn from a biased group, based on patients with a high risk for congenital heart disease who had been referred for fetal echocardiography. Therefore the high sensitivity obtained by these authors reflects the prevalence of the diseases rather than the accuracy of the four chamber view. Benacerraf *et al* examined a mixed group of high and low risk women for fetal heart defects and found similar results to those in other studies on high risk pregnancies, in which severe forms of heart disease were reliably detected.¹⁵

In our study the four chamber view detected 48% of fetal cardiac anomalies; this rate is comparable with the findings of Allan *et al* in the general population.⁷ The

addition of two relatively simple echocardiographic investigations at the level of the left and right ventricular outflow resulted in a significant increase in the detection rate, particularly of abnormalities in the ventriculoarterial connection. This simple extended fetal heart evaluation achieved a sensitivity of 78%, with only 22% of congenital anomalies undetected during the prenatal life. Of the five fetuses with false negative results, two had severe malformations (tetralogy of Fallot and truncus arteriosus). Since these fetuses were among the first screened in our programme, these results probably reflect our lack of experience. The other three cases had minor defects (ventricular septal defect, pulmonic stenosis, and coarctation), and we believe this represents the true limitation of the method. The false positive rate of 0.1% encourages us to believe that only a few parents would be worried unnecessarily as a result of the screening programme.

As most of the undetected anomalies were minor—that is, small septal defects and valvular lesions—their contribution to perinatal mortality and morbidity was negligible. Detection of the major congenital heart diseases in utero has a considerable impact on the prenatal counselling and perinatal management. After counselling by a paediatric cardiologist and a perinatologist, four patients had genetic evaluation. In two cases, the finding of trisomic fetuses persuaded the parents to terminate the pregnancy. Termination of pregnancy was requested in five cases (22%), thus avoiding further neonatal mortality and morbidity. The high early neonatal death rate (28%) among the affected fetuses surviving to term confirms that some of the cardiac anomalies detected were associated with poor chances of survival. Early prenatal diagnosis of the type of the cardiac anomaly and cooperation with the paediatric cardiologist permit accurate informed decisions regarding obstetrical management—for example, avoidance of caesarean section for lethal anomaly or the continuation of pregnancy with delivery in a tertiary centre.

Widespread teaching of the technique will result in increased prenatal diagnosis of congenital heart disease and should reduce perinatal mortality and morbidity. We have shown prenatal screening of cardiac anomalies to be accurate, and it therefore should be incorporated into standard fetal surveillance.

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