Who Should be Offered Fetal Echocardiography? One Center's Experience with 3965 Cases

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ABSTRACT: **Background:** Although the comprehensive evaluation of the fetal heart includes echocardiography by an experienced pediatric cardiologist, economic constraints sometimes dictate the need to select patients.

Objectives: To analyze the usefulness of fetal echocardiography in the detection of congenital heart disease according to the referral indication.

Methods: This retrospective survey relates to all 3965 FE studies performed in our center from January 2000 to December 2004. The diagnosed cardiac anomalies were classified as significant and non-significant malformations. All FE studies were done by a single operator (A.L.) at Meir Medical Center, a referral center for a population of about 400,000. The 3965 FE studies were performed for the following indications: abnormal obstetric ultrasound scans, maternal and family history of cardiac malformations, medication use during the pregnancy, and maternal request. The relative risk of detecting CHD was calculated according to the various referral indications.

Results: Overall, 228 (5.8%) cases of CHD were found. The most common indication for referral was suspicion of CHD during a four-chamber view scan in a basic system survey or during a level II ultrasound survey. No correlation was found between maternal age and gestational age at the time of scanning and the likelihood of finding CHD.

Conclusions: Our data suggest that a suspicious level II ultrasound or the presence of polyhydramnios is an important indication for FE in the detection of significant CHD.

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KEY WORDS: fetal echocardiography, congenital cardiac disease, four-chamber view, level II ultrasound, polyhydramnios

Congenital heart defect is the most common cause of infant mortality in the first year of life and has a prevalence of about 8 per 1000 live births [1-3]. It has been shown that prenatal detection of CHD may reduce perinatal mortality [4]. The four-chamber view of the fetal heart detects most CHDs that would lead to death within the first few years of life [4]. Prenatal detection of structural abnormalities of the cardiac outflow tract, such as transposition of the great arteries or coarctation, may also be life saving. With CHD, the risk of an aneuploidy is significant [5]. In addition, a prenatal diagnosis of CHD provides the opportunity to discuss the findings with the parents, describe the obstetric management plan, and raise the possibility of termination if appropriate. However, despite its importance, cardiac anomalies are the most frequently missed malformation when the sonographic scan is performed by obstetricians [6-8].

Fetal echocardiography plays a major role in the prenatal diagnosis of CHD. Following the technical improvements in ultrasonography in recent years, FE was shown to have a sensitivity of 78% and specificity of 99.9% when performed by an expert.

FE is commonly performed when CHD is suspected or anticipated. This suspicion may arise in the following circumstances: after a basic sonographic evaluation [10-15], a family history of CHD, maternal diabetes or systemic lupus erythematosus, fetal exposure to teratogens, fetal karyotype anomalies, and abnormal biochemical screening tests including the finding of increased fetal nuchal translucency [16]. The purpose of the present study was to analyze the contribution of each common indication for FE in the diagnosis of CHD.

PATIENTS AND METHODS

This retrospective survey includes the data of all 3965 FE studies that were performed at our medical center between January 2000 and December 2004. The studies were performed twice after gestational week 22 by an experienced FE technician followed by a single pediatric cardiologist (A.L.).

Fetal two-dimensional, M-mode and Doppler echocardiography was performed with an ATL 5000 ultrasound system (Bothell, Washington DC, USA) using a 5-3 MHz probe. The practice in our country at the time of the study was to

FE = fetal echocardiography
CHD = congenital heart disease

use the four-chamber view scan as a screening method in low risk patients, while a level II ultrasound survey was limited to high risk pregnancies.

The diagnosed cardiac anomalies were divided into two groups based on their long-term effects:

- *Major anomalies* were defined as those that affect the management of the pregnancy and the future quality of life and would probably require future multiple surgical interventions.
- *Minor malformations* were defined as those not likely to affect future quality of life, such as small septal defects [17].

Statistical analysis was done by SPSS using the *t*-test, chi-square test, and relative risk calculations.

RESULTS

From January 2000 until December 2004 a total of 3965 fetal echocardiographic studies were performed by a single operator (A.L.). The average maternal age was 30.0 ± 5.7 (mean ± standard deviation) and the mean gestational age at examination was 25.7 ± 3.0 weeks. No differences were found between the maternal age and gestational age in women with and without significant CHD. Overall, 3737 of the studies were normal (94.2%) while CHD were found in 228 studies (5.8%). However, a significant CHD was found only in 47 fetuses (1.2%).

The common indications for performing the study and the results are presented in Table 1. The reason why the cardiac final diagnoses are sometimes only partial is related to the fact that some of the patients delivered elsewhere or did not consent to autopsy when the pregnancy was terminated.

The most common indication was suspected CHD during a four-chamber view scan or during level II ultrasound survey, which accounted for 1087 (27.4%) of the studies and for 117 (10.8%) of the abnormalities diagnosed, of which 32 (2.9%) were significant CHD.

The incidence of CHD was similar in women who underwent FE due to a familial history of CHD or due to maternal request alone (a group of patients who can serve as controls). However, five fetuses had significant CHD (1.3%) in the former group in comparison to only one case of tetralogy of Fallot (0.27%) in the latter group. We diagnosed two fetuses with large ventricular septal defect and one case of hypoplastic left heart (0.36%) in women referred for FE due to intracardiac echogenic focus. However, this difference did not reach statistical significance when compared to the elective controls.

High rates of any CHD were found when the indications

Table 1. Results of fetal echocardiography by the indications for the study

No.	Indication	Total	Normal (% of total)	Abnormal (% of total)	Major abnormal (% of abnormal/% of total)
1	Suspected congenital heart disease on level II ultrasound	1087	970 (89.2)	117 (10.8)	32 (27.3/2.9)
2	Echogenic intracardiac focus (tip of papillary muscle)	822	808 (98.3)	14 (1.7)	3 (21.4/0.4)
3	Familial cardiac malformations	384	368 (95.8)	17 (4.4)	5 (29.4/1.3)
4	Maternal request alone	368	352 (95.7)	16 (4.3)	1 (6.3/0.3)
5	Poor imaging on ultrasound	373	356 (95.4)	17 (4.6)	1 (5.9/0.3)
6	Maternal diabetes mellitus	222	210 (94.6)	12 (5.4)	2 (16.7/0.9)
7	Polyhydramnios	154	141 (91.6)	13 (8.4)	5 (38.5/3.2)
8	Elevated hCG	134	129 (96.3)	5 (3.7)	1 (20.0/0.8)
9	Fetal arrhythmias	127	124 (97.6)	3 (2.4)	0
10	Non-cardiac sonographic findings*	109	107 (98.2)	2 (1.8)	1 (50/0.9)
11	Single umbilical artery	82	79 (96.3)	3 (3.7)	1 (33.3/1.2)
12	Oligohydramnios	20	18 (90.0)	2 (10.0)	0
13	Maternal medications	20	20 (100)	0	–
14	Intrauterine growth retardation	13	10 (76.9)	3 (23.1)	0
15	Maternal collagen diseases	12	12 (100)	0	–
16	Intrauterine fetal death	6	5 (83.3)	1 (16.7)	0
17	Increased nuchal translucency	5	4 (80.0)	1 (20.0)	–
18	Other**	27	24 (88.9)	3 (11.1)	0

* Cystic hygroma, syndactyly, club foot, feta lateral neck cyst, hydronephrosis, polydactyly, choroid plexus cyst, pyelectasis, gastroschisis, dextrocardia.
** Familial syndromes, maternal Epstein-Barr virus infection, maternal cytomegalovirus infection, postfetal reduction.

were suspected CHD on level II ultrasound (10.8%) and the presence of polyhydramnios (8.4%). When analyzing only the significant CHD, the leading indications were polyhydramnios, which accounts for 3.2% of all the CHD, suspected CHD (2.9%), followed by family history (1.3%). This difference did not reach statistical significance. We know of three cases in which FE missed abnormal findings: all three were small VSD; however, none was significant.

DISCUSSION

Cardiac embryogenesis occurs in the first 6 to 7 weeks of development. A structural heart defect usually develops during this period. CHDs differ in their severity; they may progress "normally" throughout pregnancy or may become hemodynamically significant resulting in the appearance of other anomalies such as fetal hydrops. Consequently, CHD might have various intrauterine manifestations. Moreover, some CHDs develop and become apparent during the neonatal period or even later in life [3].

This study reviewed 3965 FE examinations and analyzed the indications and their yield in the detection of CHD. As far as we know this is one of the largest reported studies of FE performed by a single operator.

Despite the recent development of new devices and techniques that enable detection of CHD already early in the second trimester of pregnancy, most centers still perform fetal echocardiography around 20 weeks gestation by using transabdominal transducers [18]. In the current study most FE studies were performed between 23 and 26 gestational weeks. All examinations were done transabdominally by a single operator (who was both a pediatric cardiologist and fetal echosonologist), thus eliminating inter-observer variability concerns. However, at the same time, since there is no verification, a single operator might make a false diagnosis. This potential drawback was addressed by performing all FE studies after an initial study that was performed by an experienced FE technician.

Another important point when assessing the reliability of the present study is the percentage of missed diagnoses. In the period of the study, we knew of three cases whose diagnosis was missed: all of them had a small muscular ventricular septal defect and none was diagnosed as having a significant CHD.

Overall, our data show that CHD was detected in 5.8% of the studied cases. This rate is higher than the rate reported by Barsoom et al. [19], who found cardiac malformations in 3.4% of their patients studied.

The primary indications for performing FE according to the American College of Cardiology are suspected fetal heart abnormalities or fetal arrhythmia detected by routine prenatal sonography, familial history of CHD, maternal diabetes, maternal systemic lupus erythematosus, fetal exposure to teratogens, fetal karyotype abnormality, and other fetal system abnormalities [11]. Previous studies have pointed to fetal, maternal, and other grounds for performing FE. Among the fetal reasons are extracardiac anomalies (omphalocele, duodenal atresia, spina bifida, VACTERL association, trisomies, etc.), and abnormal four-chamber view. Maternal indications for FE include cardiac anomalies and diabetes mellitus. In addition, teratogenic exposure [10,13] and increased nuchal translucency have been suggested as markers for CHD [12].

According to our data the high rate of CHD was found among fetuses that were referred for FE following suspected CHD during a four-chamber view scan or a level II ultrasound survey (10.8%). This observation is in contrast to most other studies, which have shown a more than 60% confirmation of abnormality for this referral reason. The probable reasons for that controversy are a too high suspicion index, easy accessibility to FE study, and resolution of the CHD since many of them are suspected during early second-trimester ultrasound survey and the formal FE is done around 22 weeks gestation. Other indications included polyhydramnios, oligohydramnios and intrauterine growth retardation. However, it should be emphasized that the number of studies in those categories are relatively small. In face of that limitation, our data show similar detection rates of CHD following these common referral indications and in studies that were performed without any medical indication. Among our patients, only in cases with previous abnormal fetal heart during ultrasound scan and with polyhydramnios was FE found to be justified [Table 2].

Lynch et al. [20] reached similar conclusions: the highest rate of CHD in their population was seen in fetuses referred

VSD = ventricular septal defect

Table 2. The relative risk for CHD (total/significant) by the indication for FE compared to maternal request group

Indication	No.	Proportion of abnormality of total (%) (CHD/major CHD)	RR	CI 95%
Maternal request	368	4.3/0.3	1/1	
Suspected cardiac defect in level II ultrasound	1087	10.8/2.9	2.47/11.10	1.49–4.12/1.84–454.46
Familial cardiac malformation	384	4.2/1.3	0.95/4.84	0.49–1.89/0.54–229.61
"Golf ball"	822	1.7/0.4	0.39/1.34	0.19–0.79/0.11–70.76
Maternal diabetes	222	5.4/0.9	1.24/3.34	0.6–2.58/0.17–197.36
Arrhythmia	127	2.4/-	0.54/-	0.16–1.83/-
High hCG levels in II trimester screen	134	3.7/0.8	0.85/2.76	0.32–2.3/0.04–217.18
Polyhydramnios	154	8.4/3.2	1.94/12.32	0.96–3.94/1.35–584.02
Single umbilical artery	82	3.7/1.2	0.84/4.53	0.25–2.82/0.06–356.59
Non-cardiac sonographic findings	109	1.8/0.9	0.42/3.56	0.1–1.81/0.05–280.54

RR = relative risk, CI = confidence interval.

because of an abnormal cardiac exam on routine screening ultrasound (55.6%) or following the detection of other fetal anomalies (8.2%). These two indications were responsible for 77.8% of identified cases of CHD.

The present study is somewhat limited due to the fact that the information regarding the precise actual diagnosis is incomplete as many patients who opted for pregnancy termination refused autopsy mostly for religious reasons. Another limitation is the fact that the control group is not an ideal one and some cardiac diagnoses are very non-specific. In addition, the pediatric cardiologist was not blind to the referral indication.

In summary, the rate of cardiac malformations in this study was not different in women who underwent the scan because of acceptable indications to the rate in the group of patients who underwent FE owing to maternal request without any medical reason. Our data suggest that suspected CHD during a four-chamber view scan or during a level II ultrasound and polyhydramnios are valuable indications for FE based on the detection rate of significant CHD of such studies.

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