Evaluation of the Fetal Heart at 14 to 18 Weeks' Gestation in Fetuses With a Screening Nuchal Translucency Greater Than or Equal to the 95th Percentile

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Objectives—The purpose of this study was to determine whether normal fetal cardiac anatomy could be successfully demonstrated and congenital heart disease detected transabdominally at 14 to 18 weeks' gestation in fetuses with a nuchal translucency greater than or equal to the 95th percentile.

Methods—In this retrospective chart review, grayscale images, *Z* scores, and Doppler evaluations, including pulsed, color, and spectral Doppler imaging, were reviewed to determine whether fetal heart evaluation findings at 14 to 18 weeks' gestation were normal or abnormal.

Results—Normal cardiac anatomy was successfully evaluated in 32 of 33 normal cases; only an aortic arch and a ductal arch were not successfully visualized in 1 case. Major congenital heart disease was detected prenatally in 4 abnormal cases.

Conclusions—The fetal heart can be successfully evaluated at an earlier gestational age but may be dependent on the skill of the sonographer and reading physician. Maternal decisions can be made earlier in gestation, before the pregnancy is obvious, and can allow planning for a pregnancy that will need to be delivered at a medical center that has a level 3 nursery.

Key Words—early second trimester; fetal echocardiography; nuchal translucency

Congenital heart disease is a national problem, with an occurrence rate of 6 per 1000, making it the most common of all birth defects.[1] The introduction of first-trimester screening combining a sonographic examination, which includes a measurement of the neck thickness (nuchal translucency), and maternal serum biochemical testing at gestational ages of 11 weeks to 13 weeks 6 days can identify at least 85% of fetuses with a major chromosomal abnormality.[2,3] An increased fetal nuchal translucency may be associated with chromosomal abnormalities, congenital heart disease, genetic syndromes, skeletal dysplasia, and fetal and postnatal death.[4–6]

Traditionally in the United States, fetal echocardiography is performed at 18 to 22 weeks' gestation to detect major congenital heart disease.[1,7] With first-trimester screening and the known association of fetal congenital heart disease with an increased nuchal translucency, researchers have begun to evaluate the fetal heart at 11 to 14 weeks' gestation.[8–11] Although researchers have evaluated the fetal heart transabdominally and transvaginally in the first trimester,

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Abbreviations
BMI, body mass index; CVS, chorionic villus sampling

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this technique has been beneficial primarily in determining normality of the fetal heart. It has been recommended to always perform follow-up fetal echocardiography after 18 weeks' gestation to confirm the diagnosis from the first-trimester fetal echocardiogram.[9,11]

The main objective of this study was to determine whether fetal cardiac anatomy could be reliably demonstrated transabdominally at 14 to 18 weeks' gestation using 2-dimensional, color flow Doppler, and pulsed Doppler imaging. Furthermore, the study sought to determine whether congenital heart disease could be successfully detected in fetuses with a nuchal translucency greater than or equal to the 95th percentile.

Materials and Methods

We identified a total of 48 early fetal echocardiograms obtained at 14 to 18 weeks' gestation, 37 of which were obtained when the nuchal translucency measurement was greater than or equal to the 95th percentile. Institutional Review Board approval was obtained for this retrospective study's review period between April 2006 and December 2011. The patients' mean age was 32.2 years and ranged from 23 to 41 years. Thirty-four of the women had singleton pregnancies, and 3 had multiple gestations: 2 with diamniotic dichorionic twin pregnancies and 1 with a quadruplet pregnancy. The 3 women with multiple gestations only had an early fetal echocardiogram, with a nuchal translucency measurement that was greater than or equal to the 95th percentile.

Equipment

This pre-experimental study used 3 commercially available diagnostic ultrasound machines. These machines were approved by the US Food and Drug Administration and manufactured by 2 different companies. The Sequoia, used for patient examinations in 2006 and 2007, was manufactured by Siemens Medical Solutions (Mountain View, CA). The other 2 machines, the Accuvix XQ and the V20, were manufactured by Samsung-Medison (Cypress, CA) and were used for all of the other patient examinations. Table 1 shows the number of fetuses evaluated with each machine and the frequency of the transducer used for each examination. At our facility, a fetal echo preset is always used when evaluating the fetal heart.

Image Quality

Image quality is essential for assessing the fetal heart. For this study, the physician that interpreted the clips/images assessed the quality at 3 levels: poor, satisfactory, and good (Table 2). All of the clips/images in this study were assessed by a single physician, and these qualifiers were included in the final report, which was sent to the referring physician. The body mass index (BMI) was used to quantify the maternal body habitus. A BMI less than 25 kg/m^2 represented a low BMI, and a BMI greater than 25 kg/m^2 represented a high BMI.

Imaging

Grayscale imaging was recorded and evaluated on all of the early fetal echocardiograms. The following structures were evaluated on each fetus: 4 chambers, 4 cardiac valves, crossing outflow tracts, proximal great arteries, aortic arch, ductal arch, inferior and superior venae cavae, and pulmonary veins. The cardiac situs, rhythm, and function were evaluated, in addition to an evaluation for pericardial and pleural effusions and abdominal ascites.

Doppler Sonography

Doppler sonography was attempted on all early fetal echocardiograms and included spectral and color Doppler imaging to evaluate the following structures for potential flow disturbances. Color Doppler imaging was used to evaluate the aortic and pulmonary valves, aortic and ductal arches, intraventricular septum, and pulmonary veins. Spectral Doppler imaging was used to evaluate flow distal to the aortic and pulmonary valves, umbilical artery and vein, and ductus venosus.

Table 1. Patient Population by Ultrasound Machine

Patients, n	Ultrasound Machine	Transducer, MHz (Broadband)
7	Sequoia	5
22	Accuvix XQ	5–6
8	Accuvix V20	4–5

Table 2. Image Analysis

Image Quality	Definition
Poor	Inadequate imaging requiring a repeated study
Satisfactory	All cardiac structures visualized and visceral atrial situs defined; could not absolutely exclude some septal defects
Good	All cardiac structures visualized and visceral atrial situs defined; all cardiac structures identified clearly

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Cardiac Measurement Z Scores

Fetal cardiac measurements were obtained on all early fetal echocardiograms from the real-time grayscale images, normal as well as abnormal, and were based on gestational age. Fetal cardiac measurements were obtained for the aortic and pulmonary artery diameters at the level of the valve annulus and mitral and tricuspid valve diameters at the level of the valve annulus. *Z* scores were then calculated on an Excel spreadsheet (Microsoft Corporation, Redmond, WA) that was created by DeVore[12] from an article published by Schneider et al.[13] *Z* scores do not vary with age.

Results

Image Quality

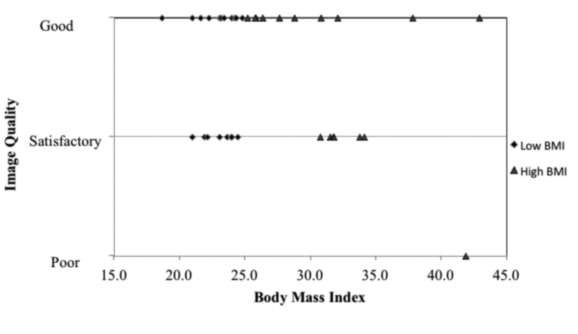
Figure 1 shows the image quality versus maternal BMI, where a BMI less than 25 kg/m^2 represents a low BMI, and a BMI greater than 25 kg/m^2 represents a high BMI. Table 3 compares the maternal BMI when 25 kg/m^2 or greater, ultrasound machine, image quality, and gestational age.

Imaging

Grayscale imaging was recorded and evaluated on all of the early fetal echocardiograms. Table 4 shows the visualization of cardiac structures for the cases that were read as a normal.

Eight patients received a follow-up fetal echocardiogram. Three repeated studies were performed because a cardiac anomaly was detected on the early fetal echocardiogram. The other repeated examinations were performed for various reasons. Two of the early fetal echocardiograms had good imaging, and all structures were visualized and believed to be normal, but both women had prior pregnancy losses: 1 with a late intrauterine fetal demise and 1 shortly after delivery of a neonate with lymphangiectasia. One fetal echocardiogram was repeated for technically challenging image quality due to an unfavorable fetal breech position. Two of the early fetal echocardiograms, 1 at 14 weeks' gestation and 1 at 15 weeks, were read as a normal but were repeated due to early gestational age. For the 1 patient in whom the aortic arch and ductal arch were not visualized well, the pediatric cardiologist requested follow-up echocardiography, but it was not performed.

Figure 1. Image quality versus BMI.



Doppler Sonography

Color Doppler imaging was used on all of the early fetal echocardiograms to evaluate flow across and distal to the aortic and pulmonary valves and the intraventricular septum. Beginning in December 2009, color flow Doppler imaging was also used to evaluate the pulmonary veins and ductus venosus and was used in 12 of the last 13 patient examinations. Spectral Doppler imaging was used to evaluate flow distal to the aortic and pulmonary valves, within the umbilical artery and vein, and within the ductus venosus. Spectral Doppler imaging was not consistently performed on the aortic and pulmonary valves. Spectral Doppler information was collected in 16 examinations for the aortic valve and 30 patient examinations for the pulmonary valve. The umbilical artery systolic to diastolic ratio and continuous flow in the umbilical vein were evaluated in 31 examinations.

Cardiac Measurement Z Scores

Fetal cardiac measurements were obtained on all early fetal echocardiograms as described in "Materials and Methods." Early in the study, cardiac measurements were not obtained, but for this retrospective chart review, cardiac measurements

Table 3. Body Mass Index, Ultrasound Machine, Image Quality, and Gestational Age

BMI, kg/m^2	Ultrasound Machine	Image Quality	Gestational Age, wk
25.2	Accuvix XQ	Good	16.0
25.8	Accuvix XQ	Good	14.0
25.8	Accuvix XQ	Good	16.5
26.4	Accuvix XQ	Good	16.3
27.6	Accuvix XQ	Good	17.1
28.8	Sequoia	Good	17.3
30.8	Sequoia	Satisfactory	18.4
30.8	Accuvix XQ	Good	17.4
31.6	Accuvix XQ	Satisfactory	15.6
31.7	Accuvix XQ	Satisfactory	18.5
31.8	Accuvix XQ	Satisfactory	17.1
32.1	Accuvix V20	Good	16.4
33.8	Sequoia	Satisfactory	16.6
34.2	Accuvix XQ	Satisfactory	17.5
37.9	Accuvix V20	Good	17.1
41.9	Accuvix XQ	Poor	16.5
42.9	Accuvix V20	Good	17.1

Table 4. Visualization of Cardiac Structures

Structure	Visualized Yes	Visualized No
Normal 4 chambers	33	0
Normal situs	33	0
Normal rhythm	33	0
Normal function	33	0
Normal valves	33	0
Crossing outflow tracts	33	0
Normal proximal great arteries	33	0
Normal aortic arch	32	1
Normal ductal arch	32	1
Inferior/superior venae cavae	33	0
Pericardial/pleural effusion or ascites	0	33
Pulmonary veins	26	7

for the first 7 cases were obtained at the time of chart review, as all images and clips were stored on a hospital picture archiving and communication system, and it was possible to go back and obtain the measurements.

Figures 2 and 3 show the *Z* scores for the aortic and pulmonary valves, respectively. For the aortic valve, the values were centered on a value of 0.0; 21 of the 33 normal cases (64%) had a score within 1 SD of this value, and 91% had a score within 2 SDs. For the pulmonary valve, the values were centered on a value of –0.3; 16 of the 33 normal cases (48%) had a score within 1 SD of this value, and 82% had a score within 2 SDs.

Figures 4 and 5 show the *Z* scores for the mitral and tricuspid valves, respectively, with most of the values below the mean. For the mitral valve, the values were centered on a value of –1.5; 20 of the 33 normal cases (61%) had a score within 1 SD of this value, and 88% had a score within 2 SDs. For the tricuspid valve, the values were centered on a value of –1.0; 23 of the 33 normal cases (70%) had a score within 1 SD of this value, and 88% had a score within 2 SDs.

Abnormal Cases

Four of the 37 patients examined in this study had abnormal fetal echocardiographic findings. The details are shown in Table 5. This table includes the results of the nuchal translucency examinations, information on whether sonography detected other anomalies, information on whether invasive testing such as amniocentesis or chorionic villus sampling (CVS) was performed (results if yes), and fetal and neonatal echocardiographic results and delivery outcomes.

Neonatal Assessment

All neonates born at The Ohio State University Wexner Medical Center have a thorough evaluation within 24 hours of birth to identify anomalies or a medical condition. This assessment is extensive, and the chest examination includes an evaluation of the lungs and cardiovascular system. Auscultation is performed with a stethoscope to evaluate the rate and rhythm, listening for the first and second heart sounds and the presence of a murmur.

Discussion

In a systematic review by Randall et al,[14] 5 studies with 60,901 patients assessed the accuracy of fetal echocardiography among 1 unselected population and 4 low-risk populations. This systematic review for all of the populations revealed that "fetal echocardiography had close to 100% specificity for correctly diagnosing babies without congenital heart disease." Our small cohort of patients whose fetal echogradiograms were interpreted as being normal seems to be consistent with the systematic review by Randall et al.[14]

Fetal cardiac measurements were obtained and measured at specific places as determined by the technique of Schneider et al[13] so that a *Z* score could be calculated. Since the *Z* score values do not vary with age, they are useful

Figure 2. Aortic valve *Z* scores.

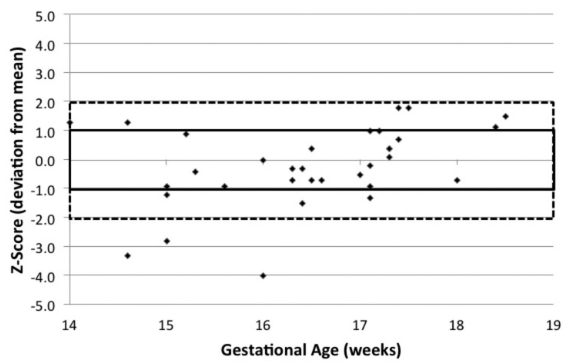
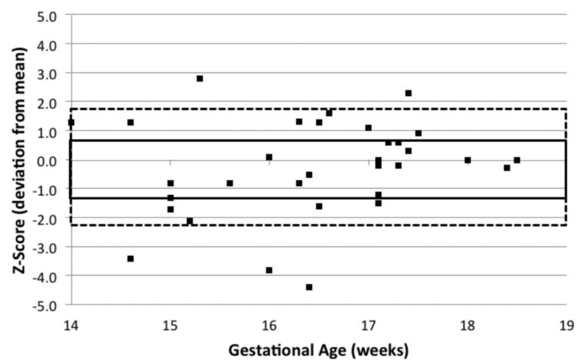


Figure 3. Pulmonary valve *Z* scores.



measurements for quantifying the size and growth of cardiac dimensions, especially in fetuses with cardiac anomalies that need multiple examinations throughout gestation to evaluate changes in fetal cardiac size. Our *Z* score results were very similar to those of Schneider et al[13] for the measurements of the aortic valve and had just a slightly larger deviation for the pulmonary valve. Our results do show a variation from the data of Schneider et al[13] for measurements of the mitral and tricuspid valve annuli, as our measurements were consistently smaller. This difference may have been technical since when evaluating the mitral and tricuspid valves, images are frequently acquired from an apical 4-chamber view of the heart, and if the frozen image is slightly off axis, the diameter measurement could be smaller than expected. Also, at this early gestational age, the cardiac valves are tiny, and fractions of a millimeter can make a huge difference in the calculated *Z* scores.

DeVore et al[15] found that maternal adipose tissue thickness and gestational age influenced successful imaging of the fetal heart during the second trimester. Surprisingly, we did not find an association between image quality and BMI, which can be affected by maternal adipose tissue. Image quality may also be related to other factors that were not evaluated in this study, such as flank scanning and scanning under a panniculus. Rolling patients to perform flank scanning frequently positions amniotic fluid between the transducer and the fetal thorax, which can improve image quality even though the structure of interest is still deep within the image. Scanning under a panniculus reduces soft tissue along the anterior abdominal wall and improves image quality. Both of these techniques are routinely used for patients with a high BMI at our institution and would not have been documented in the written report. These results may have been biased by the limited number of cases used in this study, and additional data might reveal an association.

Only 4 of the 37 early fetal echocardiograms were interpreted as abnormal because a major cardiac anomaly was detected on each. Two of the 4 early echocardiographic results were in complete agreement with the neonatal evaluation: a balanced atrioventricular septal defect and a form of hypoplastic left heart syndrome. The mother of the fetus with the atrioventricular septal defect did not have any invasive testing during the pregnancy, and the neonate did have trisomy 21. One fetus with multiple anomalies and a ventricular septal defect was delivered at 32 weeks' gestation as a stillbirth and did not have an autopsy, but pathologic examination of the placenta revealed a suspected body stalk anomaly. The fourth case, at 17 weeks' gestation, was interpreted as a ventricular septal defect of the membranous portion of the ventricular septum with an overriding aorta (Figure 6). A subsequent echocardiogram at 24 weeks 6 days revealed a balanced atrioventricular septal defect with relatively discrete right and left atrioventricular valves but a shared leaflet spanning a septal defect. Another echocardiogram at 34 weeks 6 days revealed a balanced atrioventricular septal defect with a large overriding aortic root, ascites, diffuse skin edema, and a slight pleural effusion. A neonatal examination revealed a balanced atrioventricular septal defect with tetralogy of Fallot and trisomy 21. Although confirmation is not available for the stillbirth, the other 3 abnormal early fetal echocardiograms did reveal major congenital heart diseases. These earlier scans led to the correct diagnosis so that repeated examinations were performed.

In 2005, Makrydimas et al[16] published data from major centers performing fetal echocardiography in London, England. All of the 637 cases also had a fetal nuchal translucency measurement evaluated during the first trimester. The median nuchal translucency measurement in fetuses with a normal karyotype was significantly lower than in fetuses with an abnormal karyotype: 1.8 versus 4.3 mm.

Figure 4. Mitral valve *Z* scores.

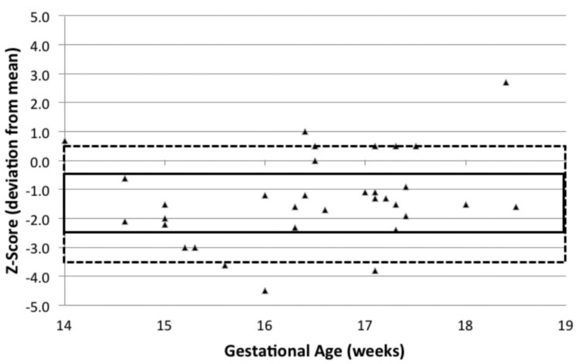
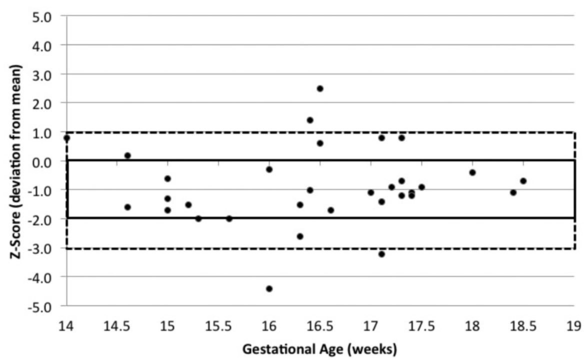


Figure 5. Tricuspid valve *Z* scores.



In our small cohort, the 2 patients who had CVS and a normal karyotype had nuchal translucency measurements of 4.5 and 7.5 mm, respectively. In the 2 fetuses with a diagnosis of trisomy 21 after delivery, the nuchal translucency measurements were 3.1 and 2.8 mm. Comparing our small cohort results to the data of Makrydimas et al,[16] we came to the opposite conclusion in that the nuchal translucency measurement in our chromosomally normal fetuses was significantly higher than in the chromosomally abnormal fetuses. Even though the data of Makrydimas et al[16] were from London, the technique used to acquire the nuchal translucency measurement is standardized, and all sonographers regardless of their place of employment need to be credentialed to perform this specific measurement. Our results may look different with a larger cohort.

In 2003, Wong et al[17] reported that the experience of the sonographer did influence the detection rate of structural heart diseases. This aspect was a major strength of our study in that most the early fetal echocardiographic examinations were performed by a single sonographer with more than 25 years of experience in performing fetal echocardiography. Likewise, the early fetal echocardiograms were interpreted by a pediatric cardiologist with more than 25 years of experience in reading fetal echocardiograms. Since both the sonographer acquiring the clips/images and the physician interpreting them had advanced skills with fetal echocardiography, these results may not necessarily be generalized to all sonographers and physicians involved with fetal echocardiography.

The major limitation of this study was related to its design as a pre-experimental research study. Our patient group was a convenience sample, and the findings were specific to the sample of fetuses who had a nuchal translucency measurement that was greater than or equal to the 95th percentile from our institution. Not all fetuses evaluated during the studied time frame with a nuchal translucency greater than or equal to the 95th percentile had an early fetal echocardiogram. Early fetal echocardiography is not a routine examination at our facility but was offered by the maternal-fetal medicine physician to selected families that wanted information as early as possible. This approach is in line with the maternal-fetal medicine trend to provide families with as much information about the well-being of their fetuses earlier in the pregnancy. A sec-

Table 5. Abnormal Cases

Case	Test/Procedure	Gestational Age, wk d/7	Finding
1	Nuchal translucency	13 0/7	4.5 mm > 99th percentile
	Anomaly scan	16 0/7	Large anterior wall defect and omphalocele
	Invasive testing	16 0/7	CVS: 46,XX, normal female karyotype
	Echocardiogram	17 6/7	Ventricular septal defect
	Delivery	32 0/7	Stillbirth; pathologic examination of placenta revealed suspected body stalk anomaly
2	Nuchal translucency	12 3/7	2.8 mm; 95th percentile was 2.4 mm
	Invasive testing	No	
	Echocardiogram	15 3/7	Atrioventricular septal defect; high ventricular septal defect with large single atrioventricular valve; right ventricle larger than left ventricle
	Echocardiogram	24 2/7	Balanced atrioventricular septal defect
	Delivery	39 2/7	Balanced atrioventricular septal defect; trisomy 21
3	Nuchal translucency	13 5/7	3.1 mm; 95th percentile was 2.6 mm
	Invasive testing	No	
	Echocardiogram	17 6/7	Ventricular septal defect; membranous portion of ventricular septum with overriding aortic root
	Echocardiogram	24 6/7	Balanced atrioventricular septal defect; relatively discrete right and left atrioventricular valves but shared leaflet spanning a septal defect
	Echocardiogram	34 6/7	Atrioventricular septal defect with large overriding aortic root; ascites, diffuse skin edema, and slight pleural effusion
	Delivery	34 6/7	Balanced atrioventricular septal defect with tetralogy of Fallot; trisomy 21
4	Nuchal translucency	13 2/7	7.5 mm > 99th percentile
	Invasive testing	Yes	CVS: 46,XX, normal female karyotype
	Echocardiogram	16 2/7	Hypoplastic left heart syndrome; hypoplasia of mitral valve and left ventricle
	Echocardiogram	20 6/7	Hypoplastic left heart syndrome; small left atrium; very small left ventricle; left ventricular outflow tract quite small; mitral leaflets not seen; probable small muscular defect in lower muscular portion of ventricular septum as antegrade flow from left ventricle into small aorta
	Delivery	37 3/7	Form of hypoplastic left heart syndrome; infant died at 5 mo of age

ond limitation of this study was the small data set due to the availability of patients at our single site. In this pre-experimental study, the sensitivity and specificity were near 100%. It is likely that the sensitivity and specificity will be less than 100% when a large population is considered.

Another limitation of this study was that neonatal echocardiographic examinations were only performed on the fetuses who were suspected of having congenital heart disease. The fetuses who were delivered at The Ohio State University Wexner Medical Center and had normal early fetal echocardiographic findings had a normal neonatal assessment, which would exclude major congenital heart disease. The Nationwide Children's Hospital cardiac sonographers perform, and the pediatric cardiologist interprets, all neonatal echocardiographic examinations from all of the Columbus hospitals. If any of the neonates born at the other hospitals had a neonatal echocardiogram, the results would have been available for this study, as the pediatric cardiologist who interprets all of the early fetal echocardiograms is on the faculty at the Nationwide Children's Hospital and tracks all cardiac anomalies in the Columbus area.

Clearly, these preliminary results demonstrate that the fetal heart, normal or abnormal, can be well evaluated at 14 to 18 weeks' gestation, so women do not need to wait until 18 to 22 weeks for a fetal echocardiogram. An early second-trimester fetal echocardiogram that is interpreted as normal can effectively reassure most parents that there is no major cardiac defect, and a follow-up fetal echocardiogram is not necessary.

Figure 6. Ventricular septal defect of the membranous portion of the ventricular septum with an overriding aortic root. The left ventricle (L), right ventricle (R), and aortic root (AO) are labeled. The nuchal translucency obtained at 13 weeks 5 days was 3.1 mm. The patient declined invasive testing.

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