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Standardization of the first-trimester fetal cardiac examination using spatiotemporal image correlation with tomographic ultrasound and color Doppler imaging

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ABSTRACT

Objective *The challenges of the first-trimester examination of the fetal heart may in part be overcome by technical advances in three-dimensional (3D) ultrasound techniques. Our aim was to standardize the first-trimester 3D imaging approach to the cardiac examination to provide the most consistent and accurate display of anatomy.*

Methods *Low-risk women with normal findings on first-trimester screening at 11 to 13 + 6 weeks had cardiac ultrasound using the following sequence: (1) identification of the four-chamber view; (2) four-dimensional (4D) volume acquisition with spatiotemporal image correlation (STIC) and color Doppler imaging (angle = 20°, sweep 10 s); (3) offline, tomographic ultrasound imaging (TUI) analysis with standardized starting plane (four-chamber view), slice number and thickness; (4) assessment of fetal cardiac anatomy (four-chamber view, cardiac axis, size and symmetry, atrioventricular valves, great arteries and descending aorta) with and without color Doppler.*

Results *107 consecutive women (age, 16–42 years, body mass index 17.2–50.2 kg/m^2) were studied. A minimum of three 3D volumes were obtained for each patient, transabdominally in 91.6%. Fetal motion artifact required acquisition of more than three volumes in 20%. The median time for TUI offline analysis was 100 (range, 60–240) s. Individual anatomic landmarks were identified in 89.7–99.1%. Visualization of all structures in one panel was observed in 91 patients (85%).*

Conclusion *Starting from a simple two-dimensional cardiac landmark – the four-chamber view – the standardized STIC-TUI technique enables detailed segmental cardiac evaluation of the normal fetal heart in the first trimester. Copyright © 2009 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

Second-trimester fetal echocardiography is the gold standard for prenatal evaluation of fetal cardiac structure and function. The segmental approach (visualization of the four chambers, outflow tracts and transverse arches) provides a consistent and detailed evaluation of cardiac anatomy and situs, and theoretically allows demonstration of the majority of fetal cardiac defects[1,2]. Adding the upper thoracic transverse view allows prenatal detection of aortic arch abnormalities and associated syndromes[3,4]. Adaptation of these standardized examination techniques in a first-trimester application was described over a decade ago[5], but image resolution, definition of orthogonal planes and concerns about first-trimester fetal exposure to ultrasound energy have limited their clinical application. First-trimester fetal cardiac examination has largely been restricted to high-risk patients, typically identified by history[6], seen in specialized ultrasound units.

Several developments have prompted reconsideration of the role of first-trimester fetal cardiac examination. One of these developments is the ability to identify fetuses at risk for cardiac defects at the time of integrated first-trimester screening, combining nuchal translucency (NT), ductus venosus Doppler and evaluation of tricuspid regurgitation[7–11]. Improvement in the resolution of modern ultrasound equipment in two- (2D) and three-dimensional (3D) imaging modalities allows recognition of fetal anatomy in much greater detail[6]. Spatiotemporal image correlation (STIC) delivers a temporal resolution that corresponds to a B-mode frame rate of approximately

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80 frames/s, providing the examiner with a large number of images for review. This may not only shorten the time to evaluate cardiac structure but also enable reconstruction of a 3D rendered image that provides additional information not available from thin multiplanar slices[12]. A new technology, tomographic ultrasound imaging (TUI), allows the examiner to acquire volume datasets that simultaneously display multiple cross-sectional images at specific distances from the four-chamber view[13,14].

Real-time capture of 3D cardiac volume sets using STIC with TUI (STIC-TUI) enables the offline visualization of cardiac structures in 2D and 3D cine sequences. While standardized views of the fetal heart using STIC-TUI in the second trimester have been described, such an approach has not been validated in the first trimester[15]. Our aim was to validate a standardized first-trimester approach to the examination of the fetal heart using STIC-TUI with color Doppler through its ability to display recognized anatomic landmarks.

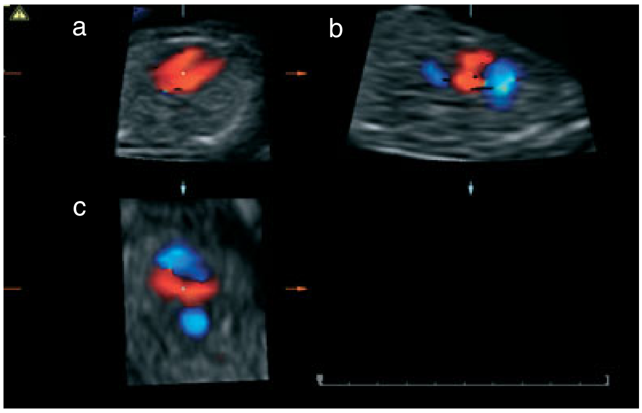

Figure 1 Multiplanar ultrasound image showing: the four-chamber view with the spine posterior (a), a sagittal view of the fetus with the head positioned at the right of the screen (b) and parallel and synchronous filling of the cardiac chambers using color Doppler (red) (c).

PATIENTS AND METHODS

This was a prospective observational study of women presenting for first-trimester screening at 11 + 0 to 13 + 6 weeks' gestation that was approved by the Institutional Review Board of the University of Maryland School of Medicine. Inclusion criteria were: normal findings on first-trimester integrated screening including normal NT; nasal bone present; normal ductus venosus Doppler; normal fetal anatomic survey; and exclusion of tricuspid regurgitation. This was planned as a validation study in a low-risk population; patients with risk factors for congenital heart disease (pregestational diabetes, epilepsy, family history of congenital heart defect, pregnancy after assisted-reproductive technology) were excluded. Patients were to be excluded if fetal anomalies were found at a later sonogram or at delivery.

Following informed written consent, the 3D ultrasound volume acquisition was performed by a standardized approach. A single operator (S. T.) performed all ultrasound examinations. NT thickness was measured following the guidelines of The Fetal Medicine Foundation (www.fetalmedicine.com). All sonograms were performed using the Voluson E8 (GE Healthcare, Wauwatosa, WI, USA) with a 4–8-MHz transabdominal probe and a 5–9-MHz transvaginal transducer. The four-chamber view was identified with color Doppler (Figure 1a). Low-frequency color Doppler was used with the following settings: color flow map 1, low flow resolution, artifact off, line filter 2, line density 7 and balance > 200. The STIC volume was acquired at the level of the four-chamber view. Acquisition time was 10 s at an angle set at 20°. Volume datasets with the following characteristics were considered to be of high quality: (1) fetal spine clearly seen minimizing shadowing from ribs or spine; and (2) minimal or no motion artifact observed in the sagittal plane (Figure 1b). Volume dataset acquisition was repeated as necessary to achieve three high-quality images. The ultrasound examination was performed using the ALARA (as low as reasonably achievable) principle, with ultrasound output settings set to yield thermal and mechanical index values below 0.8 in the region of interest[16]. Acquisition time was recorded.

Following acquisition of these volumes, offline tomographic ultrasound imaging was applied using Voluson 4DView software™. Visualization was selected in the multiplanar view (Figure 1). First, the sagittal image (Figure 1b) was rotated in the y-axis to place the fetal head to the right side of the image. The transverse plane (Figure 1a) was then rotated in the x-axis to place the spine at the '6 o'clock' position. These two steps standardized the position of the fetus for subsequent evaluation, simulating breech lie and spine posterior position. The reference dot was placed at the level of the crux. The TUI option was then selected. The index plane was advanced to the right (cephalad) until the four-chamber view appeared as the first image in the panel. The number of slices was set at 15. This setting was chosen because all the study slices from 0 to + 7 can be displayed on a single screen. The slice thickness was then adjusted to place the roof of the aortic arch at slice + 7 (Figure 2, bottom right image). These steps standardized the number of images to be evaluated and included all the images from the four-chamber view up to the top of the aortic arch. With these settings, the fetal stomach can be found in slice −7.

Ability to visualize the following 12 anatomic landmarks using gray-scale and color Doppler was noted: (1) four-chamber view; (2) descending aorta; (3) heart size; (4) cardiac axis at 45°; (5) two equal-sized atria; (6) two equal-sized ventricles; (7) two opening atrioventricular valves; (8) visualization of two great arteries; (9) two great arteries crossing; (10) two great arteries of equal diameter; (11) arch and duct similar in size in transverse view; and (12) forward flow in both arches.

Second-trimester fetal echocardiography was used to confirm normal cardiac anatomy. Descriptive statistics, chi-square and Fisher's exact test were used for statistical

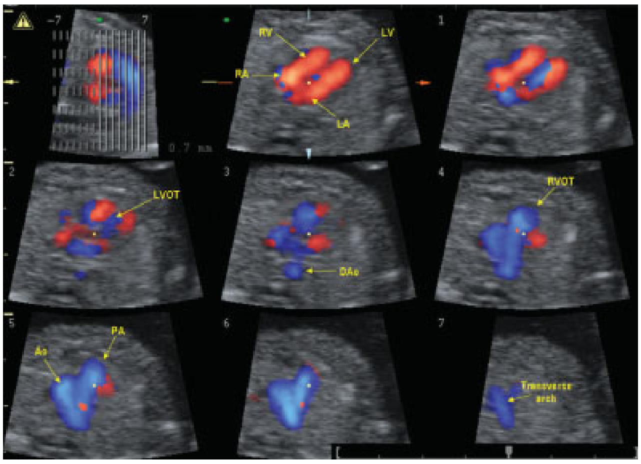

Figure 2 Tomographic ultrasound images. The four-chamber view image appears at the top center. The top of the transverse arch of the aorta is in the last image, bottom right. Ao, aorta; DAo, descending aorta; LA, left atrium; LV, left ventricle; LVOT, left ventricular outflow tract; PA, pulmonary artery; RA, right atrium; RV, right ventricle; RVOT, right ventricular outflow tract.

analysis (SPSS 13, SPSS Co, Chicago, IL, USA), and $P < 0.05$ was accepted as statistically significant.

RESULTS

During the period from January to June 2008, 107 consecutive singleton pregnancies at 11 + 0 to 13 + 6 weeks' gestation were evaluated. Median maternal age and body mass index were 28 (range, 16–42) years and 24.9 (range, 17.2–50.2) kg/m^2, respectively. Median gestational age was 12 + 3 (range, 11 + 1 to 13 + 6) weeks, mean crown–rump length was 62.9 (range, 45–82.9) mm, and mean NT was 1.6 (range, 1.0–2.5) mm. No patients were excluded for fetal anomalies diagnosed subsequently. Maternal and fetal characteristics of the study population are listed in Table 1. The integrated first-trimester scan was accomplished by transabdominal scan in 98 (91.6%) patients. In all these patients transabdominal STIC acquisition was successful, but nine (8.4%) required transvaginal ultrasound in order to complete the first-trimester screening; in these women the STIC volume was acquired transvaginally. No patient required a separate transvaginal exam simply to obtain STIC volumes. In 80% of patients, the first three volume datasets were of high quality. In the remaining 22/107 (20.6%) up to nine volumes were required, owing to fetal movement artifact. This subgroup included 15 (15.3%) of the 98 patients scanned transabdominally. Their median gestational age was 12 + 3 (range, 11 + 1 to 13 + 6) weeks. Of the nine scanned transvaginally, six required extra volumes. Their median gestational age was 12 + 4 (range, 11 + 6 to 13 + 3) weeks. Neither the abdominal nor the vaginal approach demonstrated a gestational age difference between those with adequate datasets in the first three attempt vs. those requiring extra volumes. The examination time was not prolonged significantly by four-dimensional (4D) acquisition so that all patients had a completed study within 20 min, even if transvaginal imaging was required.

Table 1 First-trimester maternal and ultrasound characteristics

Characteristic	*Value*
Maternal age (years)	28 (16–42)
Parity	
0	49 (46)
1	35 (33)
2	16 (15)
≥ 3	7 (6)
Ethnicity	
Caucasian	48 (45)
African-American	49 (46)
Asian	10 (9)
Body mass index (kg/m^2)	24.9 (17.2–50.2)
Gestational age (weeks)	12 + 3 (11 + 1 to 13 + 6)
Crown–rump length (mm)	62.9 ± 7.93
Nuchal translucency thickness (mm)	1.6 (1.0–2.5)
Number of acquired volumes	4 (3–9)
Duration of offline analysis (s)	100 (60–240)

Data are given as median (range), *n* (%) or mean ± SD.

The four-chamber heart view was obtained in all patients, and all twelve parameters were demonstrated in 91 (85.0%). Demonstration of individual parameters was somewhat variable: descending aorta in 106 (99.1%), normal heart size in 105 (98.1%), and normal cardiac axis in 104 (97.2%) cases. Two equal-sized atria, two equal-sized ventricles, and two opening atrioventricular valves were shown in 104 (97.2%), 104 (97.2%) and 99 (92.5%), respectively. In the assessment of the great arteries, two were seen in 100 (93.5%) and their equal size and crossing was demonstrated in 100 (93.5%) and 96 (89.7%) patients, respectively. The arch and duct were shown to be similar in size in the transverse view in 96 (89.7%), and forward flow with color Doppler in both arches was seen in 96 (89.7%) fetuses. Median time for offline TUI analysis was 100 (range, 60–240) s.

DISCUSSION

Second-trimester examination of the fetal heart is based on the ability to identify key anatomic landmarks at image resolutions that allow for accurate discrimination between normal and abnormal cardiac anatomy. In the first trimester, expectations for fetal cardiac examination have been limited by the inability to image the smaller structures, lack of available expertise and uncertainty about defining risk groups. For several reasons, these limitations have become less significant. First, ultrasound image resolution has dramatically improved. Second, the integrated screening approach has shown high accuracy in identifying populations at high risk for congenital heart disease at the time of the first-trimester examination. Wider access to 3D ultrasonography, including 3D color Doppler, and particularly STIC technology, opens the door for high-resolution fetal cardiac imaging with the option for offline expert analysis. We studied the ability of a standardized examination approach to identify essential anatomic landmarks for the cardiac examination in a low-risk population.

Our study illustrates the ability to visualize essential cardiac landmarks in a high proportion of patients, starting with the universally recognized four-chamber view. The visualization rates for individual landmarks ranged from 89.7 to 99.1% and all structures were visualized in 85% of our population. In this unselected group of low-risk patients, as long as the first-trimester scan could be done, the cardiac volumes could be obtained. No patients required vaginal scans just for STIC acquisition, and while fetal movement required extra volumes to be collected in 20%, all scans were completed within the normal scan time. While fetuses earlier in this gestational age window move more, a change in examination scheduling is not required because the time added is minimal. Within the narrow gestational age window we studied, gestational age difference (e.g. 11 vs. 13 weeks) did not correlate with the need for additional volume acquisition. Our study shows that first-trimester STIC-TUI imaging is practicable, providing a high yield in the depiction of fetal cardiac anatomy and offering several advantages.

The first advantage is the context of first-trimester screening. One benefit of integrated first-trimester screening is to identify a population at high risk of anomaly that would benefit from early detailed cardiac assessment. Becker and Wegner[17] showed that 31.4% of major anomalies were present in the group with NT < 2.5 mm, and 45.3% of major anomalies and 44.7% of major congenital heart defects were discovered in patients younger than 35 years old. These figures indicate that screening for fetal cardiac anomalies can be productive even in low-risk populations[17].

A second advantage is the ease of application of the STIC technique. Standard fetal echocardiography requires meticulous scanning techniques such as appropriate angulation of the probe to visualize small cardiac structures, emphasized even more with small first-trimester structures. The STIC-TUI technique makes acquisition of fetal cardiac images less operator dependent. True orthogonal planes of the fetal heart can be obtained in a short time period without excessive manipulation. Selecting TUI slice thickness below one millimeter allows acquisition of very small fetal cardiac images with appropriate definition and precision. The systematic reorientation of the image volumes we describe further enhances pattern recognition.

Widespread application of first-trimester fetal cardiac examination has traditionally been limited by the availability of expertise in acquiring and interpreting cardiac imaging at such an early gestational age. Obtaining representative imaging planes using a standardized STIC-TUI approach might bypass the limitations of the practice setting if independence from sonographers' experience can be demonstrated. The performance of STIC if used in the general community requires further evaluation as there may be discrepancies in the acquisition and reviewing when compared to high-risk centers. Digital offline analysis allows re-slicing and optimal identification of cardiovascular landmarks by referencing the ideal orthogonal plane[12]. Viñals *et al.* showed that volume datasets of the first-trimester fetal heart can be analyzed offline with good interobserver variability. In their study, an operator not experienced in fetal cardiac imaging obtained the volume datasets using STIC and sent the images over the Internet to be reviewed by expert cardiologists[18]. In our study, by developing a standardized technique with STIC-TUI, first-trimester cardiac examinations may be performed with more ease and confidence by operators who are experienced in first-trimester screening but not necessarily experienced in performing first-trimester fetal cardiac examination.

Another advantage of STIC-TUI offline analysis is that it may reduce the need for prolonged ultrasound exposure of the fetus. Inability to obtain appropriate imaging may be due to an actual anomaly requiring further evaluation[19] or it may simply be a technical limitation. Real-time discrimination between these two possibilities – extending the scan, repeating the scan, adding modalities – results in ongoing exposure of the fetus to ultrasound energy. This is completely avoided by offline analysis of images that require less than 30 s acquisition time, but the potential benefits of early detection and referral for appropriate management are maintained[20].

Our study has some limitations. First, not all subjects had all landmarks demonstrated – acquisition was dictated by the scan technique required to complete first-trimester integrated assessment. Visualization of all 12 cardiac parameters might be improved by extending scanning time, transvaginal sonography, or further post-processing of the stored volumes. Second, optimal gestational timing of this examination was not assessed: patients were studied in a narrow gestational age window, so the influence of fetal movement, crown–rump length, and the precision of the 2D examination were not evaluated. Also, all initial acquisitions were obtained by an operator experienced in first- and second-trimester cardiac examination. It is possible that this introduces a study bias, as the quality of acquisition could be more readily assessed by an experienced examiner who obtained more volumes and therefore avoided submitting an inadequate study for offline analysis. While further studies are necessary to clarify the clinical significance of these factors, our anecdotal experience is that re-analysis of the original volumes by a separate operator may often identify 'missing' views. While the extended screening described here may result in referral of the 4D volumes for consultation, only a small fraction of these are likely to require referral of the patient *per se*. Further, our data show that the large majority of cases have only a single variable missing. In this circumstance, suspicion of an underlying defect can be low unless indirect markers for congenital heart defect are apparent. In the large majority, this issue may be resolved by revised rendering, or simple observations at the 18-week anomaly scan. Cumbersome central referral of large numbers of patients to pediatric cardiology will probably not be required unless the anomaly scan is abnormal and/or specific questions need to be addressed by specialized referral. Clearly, the principles must be tested prospectively in larger populations in order to determine which defects (if any) may be missed, and to evaluate the most appropriate pathways for diagnosis and referral of anomalies that are detected.

In conclusion, we have shown that starting with a universally recognized 2D cardiac landmark – the four-chamber view – a standardized STIC-TUI technique enables a detailed cardiac evaluation on multiple orthogonal planes in the first trimester to be carried out.

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