Qualitative Real-time Cross-sectional Echocardiographic Imaging of the Human Fetus During the Second Half of Pregnancy

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SUMMARY In this study, we used high-resolution echocardiographic systems to investigate how early in pregnancy normal fetal cardiac anatomy could be noninvasively evaluated. Over a 2-year period, 84 of 88 fetuses were successfully imaged (27 were studied serially). Postnatal images of 73 were obtained during the newborn period. Estimated fetal age varied at initial examination from 19-41 weeks (mean 31 ± 0.5 weeks [± SEM]) of pregnancy. Estimated fetal weight using an ultrasound algorithm varied from 500-3100 g (mean 1580 ± 80 g [± SEM]). To evaluate fetal cardiac anatomy, we reproduced commonly used cross-sectional views of the heart. The four-chamber and the short-axis great artery views have been most successful for cardiac evaluation in the fetus. These views could be obtained in 96% and 95% of the patients, respectively. With these views, cardiac chamber and valve structures, as well as two great arteries, could be imaged in detail. The ascending and descending aorta, as well as the aortic arch and vessels to the arms and head, were visualized in 87% of examinations, and the inferior and superior venae cavae were visualized in 76%. In two of three RH fetuses, changes in cardiac chambers compatible with hydrops fetalis were demonstrated. We examined all fetuses after birth and verified clinically (or noninvasively) that no cardiac malformations were present. It appears, however, that the diagnosis of major congenital heart defects should be possible before birth.

ECHOCARDIOGRAPHY has had a major impact on the health care of infants and children born with congenital heart disease by providing accurate, noninvasive anatomic and functional information for diagnosis and serial follow-up. Ultrasound techniques for quantitative evaluation of fetal growth and maturity have also had a major impact on the practice of clinical obstetrics. Recent improvements in resolution have resulted in the prenatal diagnoses of various birth defects (i.e., hydrocephalus, anencephaly and hydronephrosis). Fetal cardiac imaging has been attempted in the past using M-mode and B-scanning. Use of static B-scanners for cardiac imaging is limited because the heart is a moving structure. M-mode echocardiography has limited value for fetal echocardiography because it lacks spatial orientation and is very difficult to interpret when the examiner has no information about changing fetal position within the uterus. With recent development of high-resolution, real-time, cross-sectional scanners, previously unrecognized capabilities in fetal cardiac imaging appear to warrant investigation. In the present study, we report studies that define the capabilities of cross-sectional imaging of the fetal heart and extend recent advances in cross-sectional echocardiography to the heart of the human fetus. We investigated how early in pregnancy it is possible to identify normal cardiac anatomy and assessed the possibilities for prenatal diagnosis of cardiac malformations.

Methods

Group I

We performed 94 satisfactory (of 106 attempted) real-time fetal examinations in 67 of 71 normal pregnancies. All mothers were referred for routine ultrasonic scanning for fetal dating at an estimated gestational age (EGA) of 19-41 weeks (mean EGA 31.4 ± 0.5 weeks [± SEM]). After they underwent the usual B-scan procedure for the determination of the fetal size and position, the patients underwent an additional real-time cross-sectional analysis of the fetal
heart. The real-time examination was performed after informed consent was obtained from the mother as part of a approved research protocol using human subjects. Twenty-seven of these fetuses were studied serially before birth.

Group 2

We also studied the 14 fetuses of another 13 healthy pregnant women (one with twins at 20 weeks) (all 20–28 weeks pregnant) with high-risk family or obstetrical histories for congenital heart disease in previous children (hypoplastic left heart, n = 5; tetralogy of Fallot, n = 4; single ventricle, n = 1; tricuspid atresia, n = 2; idiopathic hypertrophic subaortic stenosis, n = 1). As no cardiac malformation was found in any of those pregnancies, groups 1 and 2 are, in general, discussed as one group.

Group 3

Three pregnant women with RH incompatibility were also examined. Two of the hydropic fetuses required in utero transfusion.

Postnatal Studies

Seventy-three infants underwent physical examination after birth by one of the investigators; cross-sectional echocardiograms were performed in all 73 infants, 57 from group 1, 14 from group 2, and two from group 3.

Examination Technique and Equipment

B-scan

The patients underwent a typical ultrasound B-scan procedure with multiple scans of the uterus in the longitudinal and transverse axes. Either a single-transducer type scanner with gray scale (Unirad Sono II with GZD) or a large, multiple-crystal, computerized, waterbed-based B-scanner (Octoson) was used to determine the placentaion, fetal lie and fetal maturation (fig. 1). The fetal weight was calculated by using biparietal diameter and abdominal circumference as described by Warsof et al. Gestational age was determined from biparietal diameter and maternal dates. Fetal measurements were done from scan converted images stored on x-ray film with a computerized digitizing system (Numonics).

Real-time, Cross-sectional Examination of the Fetal Heart

The real-time examinations were performed with a 3.5-MHz, electronically focused, linear-array ultrasonic scanner or a 3.5-MHz, dynamically focused, experimental phased-array ultrasonic scanner. The linear-array system (Toshiba SAL 10A) was electronically focused (5-cm transmit focus) and had a 64-element transducer with a total length of 8.5 cm. The ultrasound beam was also focused in the y-axis (perpendicular to the scan plane). In this system, element groups also provide additional small-sector angling of ± 3°, resulting in an image with high line density (110 lines/frame) at 30 frames/sec, as well as excellent resolution. Beam profiles of both systems performed in our laboratory suggest that lateral resolution at 6 db down was about 1.5–2 mm and axial resolution was 0.2 mm at a depth of 6–10 cm from the transducer.

We preferred to use the linear-array format prenatally, as it has constant line density over the whole depth of view. Moreover, the large transducer was easy to manipulate on the abdominal wall of the mother, and more of the fetus could be imaged with the rectangular format. Although the phased array has the capability to derive spatially oriented simultaneous M-mode echocardiograms, the fetal ECG was not available and the M-mode capability was not used.

During the examination, the mother lay in a comfortable supine position, and was occasionally turned to either side to influence the fetal lie. The fetal lie was determined using images of the fetal head, spine and liver (fig. 1).

We then attempted to reproduce equivalents of commonly used cross-sectional views: long-axis, short-axis, apex four-chamber, and subxiphoid four-chamber. The examination lasted an average of 15–20 minutes. In six instances, the fetal lie was unsatisfactory (e.g., spine upward) and certain views could not be obtained to document great vessel and chamber anatomy. In those instances, the mother was asked to return at a later time or on a subsequent day, at which time the examination was successfully completed. Postnatal examinations were performed with the same equipment and an attempt was made to reproduce the same standard views.

Display and Recording

All studies were recorded in real time on video tape using a video camera. Video tapes could be reviewed in real-time or slow motion, or by frame-by-frame analysis. Still frames were stored either on Polaroid prints during the examination or photographed afterward from video tapes. As is often the case, problems arise in illustrating real-time cross-sectional observations with selected still frames. The actual examinations observed in real time on video tapes are more informative than still-frame illustrations.

Results

Group 1

Of a total of 106 exams of the 71 pregnant women in group 1, satisfactory images (confirmation of cardiac detail such as walls and valves) were obtained in 94 serial examinations in 67 patients. Four fetuses were never imaged satisfactorily for undetermined reasons. The EGA in the successfully imaged fetuses was 19–41 weeks of pregnancy, with a mean of 31.4 ± 0.5 weeks. The estimated fetal weight varied from 500–3100 g, with a mean of 1580 ± 80 g (± SEM). All fetal examinations documented normal
cardiac anatomy, and the follow-up physical and ultrasound examinations after birth confirmed normal cardiac anatomy in 57 cases. Ten infants were unavailable for follow-up echocardiographic examinations after birth but had normal physical examinations, according to their pediatricians.

To document fetal cardiac anatomy, we attempted to reproduce commonly used cross-sectional views of the heart. As there are no air-filled portions of the uterus, and the fetal lungs are fluid-filled, the window into the heart is unlimited, and only partially occluded by shadowing from the fetal ribs and spine. The heart was most easily imaged when the fetus was lying supine facing the anterior abdominal wall (fig. 1). As these cross-sectional views could be obtained from many angles on the fetal body, the cardiac image appears in orientations not usually obtained after birth. These variations often influence, for instance, the amount of right ventricle imaged in the fetus. The so-called apical four-chamber views could be obtained from the lateral side or the back of the thorax. Therefore, prenatal examination technique was different from postnatal technique. Often, especially in fetuses older than 32 weeks, it was necessary to find views to image under the fetal ribs or around the spine to avoid shadowing and dropout. Four of the 71 mothers in group 1 never had a satisfactory examination (two had two examinations attempted); all were more than 35 weeks EGA and two mothers weighed over 200 pounds.

**Figure 1.** (A) A B-scan of a fetus lying on its back, showing long- and short-axis approaches to the precordium. The transducer drawings relate to the orientations shown in figures 2-5, 8 and 9. (B) Transducer position over the spine of a fetus with its spine against the anterior placenta. The transducer position relates more closely to the images shown in figures 6 and 7.
Table 1. Structures Imaged

<table>
<thead>
<tr>
<th>Structure</th>
<th>View equivalent</th>
<th>Success rate (%)</th>
</tr>
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<tbody>
<tr>
<td>A) Ventricular structures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV + RV + septum</td>
<td>Long-axis</td>
<td>96%</td>
</tr>
<tr>
<td>MV</td>
<td>Short-axis</td>
<td></td>
</tr>
<tr>
<td>TV</td>
<td>4-chamber</td>
<td></td>
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<tr>
<td>B) Atrial structures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RA</td>
<td>4-chamber</td>
<td>92%</td>
</tr>
<tr>
<td>LA</td>
<td></td>
<td></td>
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<tr>
<td>Atrial septum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C) Great arteries</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AO + PUL valve</td>
<td>Short-axis and long-axis</td>
<td>95%</td>
</tr>
<tr>
<td>MPA spiral + AO + MPA bifurcation</td>
<td></td>
<td>91%</td>
</tr>
<tr>
<td>D) Aortic arch + carotids</td>
<td>Long-axis</td>
<td>57% (40 attempted cases)</td>
</tr>
<tr>
<td>E) Descending aorta (thoracic)</td>
<td>Long-axis</td>
<td>87% (40 attempted cases)</td>
</tr>
<tr>
<td>F) Vena cava INF and SUP</td>
<td>Long-axis</td>
<td>76% (25 attempted cases)</td>
</tr>
</tbody>
</table>

Data are for 84 fetuses successfully imaged of 88 attempts.

Abbreviations: RV = right ventricle; LV = left ventricle; MV = mitral valve; TV = tricuspid valve; RA = right atrium; LA = left atrium; AO = aorta; PUL = pulmonary; MPA = main pulmonary artery; INF = inferior; SUP = superior.

Cardiac Imaging

Table 1 shows how often normal cardiac structures were imaged and evaluated in different views or their equivalents in all 84 successfully imaged fetuses (groups 1, 2 and 3).

Four-chamber View

In all 84 successfully imaged fetuses, we could identify the right and left ventricles, mitral and tricuspid valves and the ventricular septum and ventricular walls, usually in a four-chamber view (96% success). Figure 2 shows a typical example of a four-chamber view equivalent, as seen from the apex in a fetus of 30 weeks EGA. The endocardial and pericardial surface of the ventricles could be outlined and quantitative ventricular measurements could be obtained. Atrial chamber size could also be compared. The size and mobility of both atrioventricular valves could be evaluated easily in real time. Atrioventricular valve and ring movement are the predominant features noted, and contribute most of what is commonly seen.
as "the heart" in a smaller fetus, or a low-quality heart image. Slight angling toward the outflow of the aorta was used to confirm which was the left ventricle. The left side was often additionally verified by imaging pulmonary veins entering the left atrium or identifying the superior and inferior cavae entering the atrium on the other side. As the foramen ovale flap exhibited considerable movement, it could be seen in most cases as a middle portion of the atrial septum oscillating between the atria (figs. 2 and 3). The atrial septum, a very thin structure, was not imaged satisfactorily in two patients because of marginal image quality (table 1). The four-chamber view equivalent appeared to be the most important view that was commonly obtainable, and gave the most reliable information about ventricular anatomy and size.

Short-axis View

The second most useful view was the short-axis image of great artery orientation (fig. 4). As this is a very precise cross section, it sometimes took considerable time to obtain it exactly. The central aorta appears as a circle with an opening and closing aortic valve. The pulmonary artery spirals around it and can be followed to the bifurcation, thus verifying normal great artery anatomy. Though we could almost always visualize two great vessels (table 1), the typical view equivalents for normal (spiral) great vessel orientation could be demonstrated in only 91% of studies.

Long-axis View

In the long axis of the left ventricle (fig. 5), we attempted to follow the course of the aorta and the aortic arch. Figure 6 is an example of the visualization of the ascending and descending aorta and aortic arch, as well as the vessels to the head and arms. To image all these structures in one plane at the same time was relatively difficult. In most cases, the aortic course was visualized in several parts. Our success rate of imaging was considerably better for the thoracic aorta (87%) than for the aortic arch and carotid arteries (57%). (These percentages refer to our most recent 40 examinations, when we looked for the structures systematically.)

We ultimately learned to identify the vena cava system (fig. 7). Our success rate for imaging improved,
and was 76% in our latest 25 cases. The inferior vena cava is nearly the same size as the thoracic aorta, and shows phasic pulsation, but at a lesser amplitude than the aorta. The differentiation of the inferior vena cava from the abdominal aorta was achieved by following both vessels from the abdomen superiorly to show the confluence of the more anterior inferior vena cava through the liver into the right atrium.

Group 2

Because of the special importance in demonstrating normal cardiac anatomy in detail in group 2 patients, four of the mothers underwent more than one 15-minute examination to obtain all views; great vessel orientation and aortic arch anatomy were verified completely in all 13 of these pregnancies.

Group 3

We verified normal cardiac anatomy in all three fetuses in group 3, and made qualitative observations consistent with hydrops fetalis in two (fig. 8). In one case, marked right ventricular enlargement was demonstrated in the long-axis and four-chamber views. A considerable amount of ascites was also present. Figure 9 shows the liver of this 1200-g hydropic fetus, which was surrounded by ascitic fluid.

Postnatal Examinations

Seventy-three postnatal echo examinations were performed on two group 3 hydropic infants, 14 group 2 infants, and 57 group 1 infants, all of whom were clinically examined. All standard views were successfully obtained on each of these normal newborn infants.

Discussion

Recent developments and improvement of resolution capabilities of ultrasonic scanners have made it possible to study fetal cardiac anatomy in detail during the second half of pregnancy. The recently developed cross-sectional cardiac view equivalents and an understanding of spatial (two-dimensional) cardiac anatomy can be applied to the problem of imaging of the fetal heart. In contrast to the limited window for echocardiographic examination in the newborn with air-filled lungs, there is a nearly unlimited window to the fetal heart and major vessels that is only inhibited by the fetal heart and major vessels.
Figure 7. The course of the fetal inferior vena cava (IVC) and superior vena cava (SVC) can be followed to the right atrium (RA). This view was obtained in a plane nearly parallel to the view in figure 6.

Figure 8. Long-axis view of a hydropic fetus. The right ventricular enlargement (13 mm right ventricular inner dimension compared with 8 mm left ventricle [LV] in a 26-week fetus) is obvious. RV = right ventricle; AO = aorta; LA = left atrium.

Figure 9. Ascites in the hydropic fetus seen in figure 8 was easily visualized as a clear space around the liver.
toward effects of ultrasound at diagnostic levels have been documented at follow-up of human fetuses exposed in utero.14

Although we have not made or missed the diagnosis of any cardiac malformation, the diagnosis of gross anomalies of the great arteries, hypoplasia of the right or left ventricles or their atrioventricular valves, atrioventricular canal, and single or common ventricle, should be detectable by this method. If these diagnoses were made before birth, the pediatric and obstetrical care for these infants could be coordinated and postnatal care improved.

Finally, the demonstration of normal anatomy in the fetus can be very helpful, too. In a mother who has previously given birth to an infant with a serious cardiac malformation, our technique has enabled us to reassure these mothers that there was no major cardiovascular malformation apparent in the examination, thus eliminating some of the tensions of the last half of pregnancy. We have not yet investigated a fetal heart at less than 16 weeks of pregnancy because the resolution of the systems does not provide enough detail in smaller fetuses. At 16 weeks in three recent studies, however, we could still determine the presence of two atrioventricular valves and two ventricular chambers.

Our studies show that quantitative evaluation of the fetal heart is possible, and quantitative studies of chamber or great artery size and growth compared in normal fetuses should be important adjuncts to prenatal assessment.15 As we defined our success rate for being able to verify normal cardiac anatomy of the unborn human fetus, we also began to discuss with our obstetrical colleagues and the pregnant mothers the important ethical questions raised by this technique. Our learning curve to master this technique (2 years) suggests that decisions based upon these capabilities should be approached with great caution. We still perform these studies with informed consent and, until further verification of their diagnostic capabilities is available, view the procedure as experimental.

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Qualitative real-time cross-sectional echocardiographic imaging of the human fetus during the second half of pregnancy.
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*Circulation.* 1980;62:799-806
doi: 10.1161/01.CIR.62.4.799

*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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