Anatomical and echocardiographic correlates of normal cardiac morphology in the late first trimester fetus

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Abstract

Objectives—To describe the normal cardiac morphology as seen by transvaginal ultrasound imaging in the first trimester fetus and to compare it with the morphology of the heart as seen by microdissection at the same gestational age.

Design—In 53 mothers undergoing early sonography, the fetal heart was examined and the images recorded. The gestational age range was 5–12 weeks of gestation, which represents 21 to 70 days after conception. Images were analysed frame by frame and compared with the anatomy of embryos and fetuses at the same gestational ages.

Results—After the 9th week of gestation, four cardiac chambers, the aortic origin, and the pulmonary artery could be identified on cross sectional echocardiography in conjunction with colour flow Doppler. At 9 weeks, the apex pointed anteriorly and the right ventricle and pulmonary artery lay to the right of the midline. By the 11th week of gestation, the apex pointed to the left and the pulmonary artery lay to the left of the midline as in the older fetus. Between 9 and 12 weeks' gestation the aorta was larger than the pulmonary artery. These findings were confirmed in the microdissected hearts.

Conclusions—The current quality of ultrasound images obtained using transvaginal transducers in the first trimester fetus allows the study of fetal cardiac anatomy. Some of the later developmental changes can be demonstrated. As technology improves further the details of earlier cardiac morphogenesis may also become visible.

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Advances in prenatal ultrasound imaging, especially the advent of cross sectional scanning, allowed the echocardiographic features of the normal mid-trimester fetus to be correlated with anatomical sections in 1980.¹ The study reported in 1980 showed that most of the features that characterise the normal heart in post-natal life can also be seen in the fetus. However, it also highlighted some of the differences between prenatal and postnatal cardiac findings, particularly the more horizontal position of the heart produced by the size of the fetal

liver and the equality of the right and left ventricular dimensions when imaged in a four chamber projection. In addition, as was expected from our knowledge of fetal physiology, the patent foramen ovale and the patent arterial ductal connection were visible in every normal fetus.

Since 1980 improvements in the resolution of vaginal transducers have led to the study of the conceptus at increasingly early stages of gestation. The evaluation of embryological features such as the appearance of the yolk sac and the physiological herniation of the midgut can be studied and even used to date the pregnancy accurately.² Many of the standard echocardiographic views can be obtained as early as 11 to 12 weeks of gestation³ and the atrioventricular and arterial Doppler flow velocity profiles can be analysed.⁴

The heart is one of the first organs to develop in the embryo, with cardiac motion seen between 26 and 32 days after conception⁵ (5–6 weeks post-menstrual age), when the crown-rump length is between 5 and 10 mm. The atrioventricular endocardial cushions and atrioventricular valves develop in post-menstrual weeks 6–7, the outflow tract septum is completed between post-menstrual weeks 7–8, and the interventricular foramen closes between post-menstrual weeks 8 and 9.⁶ The tricuspid valve is the last cardiac structure to complete its formation at post-menstrual weeks 9–10. We attempted to evaluate the fetal heart during the first trimester of pregnancy to see if any part of cardiac development was currently identifiable by the most modern high resolution transducers.

Patients and methods

ECHOCARDIOGRAPHIC IMAGES

In 53 patients the fetal heart was imaged using an Advanced Technical Laboratories HDI system with a 5 or a 9 MHz vaginal transducer. These patients were referred for ultrasound examination to confirm the presence of an intrauterine pregnancy or to establish viability after an episode of vaginal bleeding. The crown-rump length was used to estimate the gestational age, which ranged from 5 to 12 weeks. The gestational ages studied are shown in the table. The long axis view of the fetus was first obtained as in fig 1. The beam was then located at right angles to this section at the level of the heart. A horizontal sweep from the diaphragm to the neck was then recorded as cross sectional images with a colour flow mapping, in a similar fashion to the scanning method in the older fetus.⁷

Gestational age of fetuses studied

Weeks	n
5–6	4
6–7	8
7–8	6
8–9	14
9–10	8
10–11	6
11–12	7

Figure 1 This image was obtained in a fetus with a crown-rump length equivalent to 9 weeks 5 days gestational age (54 days post-conception). The fetus is imaged in a longitudinal plane from head to rump. The umbilical vein (UV) is prominent, passing from the cord through the liver to below the heart. The descending aorta is seen passing down the back in front of the spine and connecting to the umbilical artery (UA) in the cord. A large head vessel is seen. The heart (H) is seen in the thorax just above the diaphragm. The ultrasound beam is then positioned at right angles to this plane of section to cut through the heart in a transverse plane. The beam is then swept up and down the thorax to produce the type of images seen in fig 2.

Figure 2 (A-F) Sequential transverse planes of the fetal thorax. These images were obtained in a fetus with a crown-rump length equivalent to 9 weeks 2 days gestational age (51 days post-conception). Note the scale bar at the right indicating that the whole thorax at this stage measures about 1 cm and the pulmonary artery less than half a millimetre.

(A) The heart lies opposite the spine with the apex pointing directly anteroposteriorly. The right heart is located entirely in the right half of the chest. (B) The colour flow map confirmed this when the ventricles were filled. The arrow indicates the interventricular septum at the apex. (C) This is a horizontal section of the fetal thorax above the four chamber view. The walls of the pulmonary trunk could be clearly defined when it lay in this orientation to the ultrasound beam. It arose from the right ventricle and crossed the midline to connect to the descending aorta. (D) The colour flow map confirmed the flow in the pulmonary artery (seen in blue) crossing the midline. (E) In a horizontal section just above the four chamber view and just below the image of the pulmonary artery seen in fig C and D, the ascending aorta could be identified by colour flow mapping arising from the left ventricle (coloured red) and coursing rightwards initially. Note that this vessel appears considerably larger on colour flow mapping than the pulmonary artery seen in figs C and D. (F) The aorta then curves in front of the spine to form the arch, seen here in a transverse section. RV, right ventricle; LV, left ventricle; Ao, aorta; PA, pulmonary artery; Aao, ascending aorta.

Figure 3 (A–C) These images were obtained in a fetus with a crown-rump length equivalent to 11 weeks 4 days gestational age (67 days post-conception). (A) By this gestational age, the stomach can be usually be identified and used to identify the left side of the fetus. (B) As the image moves cranially from the stomach, the heart can be seen in the left half of the chest with the interventricular septum at an angle of about 40 degrees to the midline, which is characteristic of later pregnancy. (C) The pulmonary trunk and aorta can be seen in the horizontal projection, showing that the pulmonary artery is now in the left half of the chest. In this horizontal section of the thorax above the base of the heart, the connection between the pulmonary artery and ductus and the transverse aortic arch are seen to be running parallel to each other in the normal fetus. Although the pulmonary trunk is still smaller than the aorta, there is less difference in size than before. ST, stomach; SP, spine; RV, right ventricle; LV, left ventricle; AO, aorta; RVOT, right ventricular outflow track.

MICRODISSECTION IMAGES

Frontal and left profile photomicrographs of microdissected human embryonic and fetal hearts were selected from the collection described in detail by Pexieder and Janacek.⁸ Briefly, the embryos and fetuses were fixed by high flow/low pressure intraventricular perfusion⁹ with 2% glutaraldehyde and 1% formaldehyde. After postfixation in 1% osmium tetroxide, the embryos and fetuses were microdissected. Each step of the microdissection of the heart was documented by taking macrophotographs using the Wild M400 Photomakroskop.

Results

ECHOCARDIOGRAPHIC IMAGES

The videotape recorded was examined frame by frame. Images obtained with the 5 MHz proved noticeably coarser than those obtained with the 9 MHz transducer. The spine and umbilical cord were used as landmarks for posterior and anterior orientation respectively. The ultrasound images of cardiac morphology were difficult to understand in embryological terms between post-menstrual weeks five and nine and will be the subject of further analysis. After nine post-menstrual weeks, however, careful analysis of videotaped material allowed the recognition of characteristic features in the 21 fetuses in this group. At nine weeks the heart lay centrally in the thorax with the apex almost directly opposite the spine. The right heart was found in the right half of chest and the left heart in the left half of the chest (fig 2). The colour flow map enabled

us to confirm the suspected cross sectional findings. The pulmonary trunk was readily seen when it was located in perpendicular orientation to the ultrasound beam, as it was in the fetus illustrated. This vessel originated in the right chest and crossed the midline diagonally to join the descending aorta slightly to the left and in front of the spine. The ascending aorta could not be seen well on cross sectional scanning in this embryo-fetal position but the colour flow map showed it clearly. Flow within the aorta arose in the left ventricle and was directed rightwards initially before turning to form the aortic arch in the same manner as is seen in the older fetus.¹⁰ There was in addition a clear discrepancy between the aortic and pulmonary size at this gestational age, with the pulmonary trunk smaller than the aorta—the reverse of the findings at 18 weeks' gestation.¹¹

By the 10th week of gestation, the heart orientation was changing to a position more typical of later pregnancy.¹² The apex had moved to the left and the pulmonary trunk had become a more left sided structure, running towards the spine and the ductal junction with the descending aorta. The pulmonary trunk was still smaller than the aorta.

By the 11th week of gestation, the positional change was complete. In addition, the stomach was by now identifiable¹³ and could be used to confirm the interpretation of the left and right sides of the thorax. In addition the four chambers and great arteries were more readily identified (fig 3). By this stage the great arteries were becoming more equal in size.

These findings were consistent in the 21

Figure 4 (A–F)
 Macrophotographs of partially microdissected embryonic and fetal hearts. In all views of this figure the atria have been removed. Scale bars = 1 mm. (A) Frontal view at 9 weeks' gestation of the middle portion the aorta which shows that it is running almost parallel to the pulmonary trunk. Ramifications of the left anterior coronary artery are visible in the interventricular sulcus. The apex points directly anteriorly, with the right ventricle lying in the right chest. (B) Left lateral view of the same heart showing the branching of the pulmonary trunk into the arterial duct and the pulmonary arteries. The duct joins the descending aorta at an acute angle. Its diameter is less than that of the pulmonary trunk. (C) Frontal view at 10 weeks' gestation showing that the ascending aorta is now running more in parallel with the pulmonary trunk. The apex of the heart is pointing more caudally towards the diaphragm. (D) The left lateral view of the same heart shows the widening of the arterial duct, which is now almost as large as the pulmonary trunk. This duct is entering the descending aorta at almost a right angle. (E) Frontal view at 12 weeks' gestation showing that a real aortic arch has been formed and that the pulmonary trunk seems to be similar in size or larger than the ascending aorta. (F) In the same heart seen from the left the arterial duct has the same diameter as the pulmonary trunk, which is now aligned with the axis of the right ventricle. The blurred edges of the right ventricle in figs 4E and 4F are caused by the large size of the specimen, which is beyond the focal depth of the Photomakroskop. The Photomakroskop was focused on the roots of the great arteries. A, aorta; D, arterial duct; LV, left ventricle; PA, pulmonary artery; PT, pulmonary trunk; RV, right ventricle.

fetuses aged 9 to 12 weeks gestation. The four chamber view was identifiable in all these fetuses, though less easily during the 10th and 11th week than during the 9th week. Crossover of two great arteries was identified in three of six fetuses scanned during the 9th week and in 14 of the 15 remaining fetuses. In some cases, repeated frame by frame evaluation of the videotape was necessary especially if images had been recorded with the 5 MHz transducer (six studies). Of the fetuses scanned two were lost to follow up and two proceeded to therapeutic

abortion. The remaining 17 resulted in successful pregnancies with no cardiac abnormality found at birth by postnatal clinical examination.

MICRODISSECTION IMAGES

At nine postmenstrual weeks, the embryonic heart was in a horizontal position (fig 4B). The origin of the pulmonary trunk lay to the right so that this vessel had to cross the midline (fig 4A), joining the descending aorta, via the arterial duct, at an acute angle (fig 4B). At this stage diameter of the arterial duct was smaller than

the diameter of the pulmonary trunk. Ramification of the anterior interventricular coronary artery was already visible.

At 10 postmenstrual weeks the root of the pulmonary trunk had moved closer to the midline (fig 4C) and seemed to be slightly smaller than the ascending aorta. The size of the arterial duct had increased (fig 4D) and the apex of the heart was starting to point caudally.

At 12 postmenstrual weeks the origin of the pulmonary trunk lay slightly on the left of the midline and almost perpendicular to the aortic arch (fig 4E). The diameter of the pulmonary trunk began to approximate to that of the ascending aorta. At the same time the size of the arterial duct had further increased (fig 4F). By comparing figs 4B, 4D, and 4F, we could follow the change in orientation of the pulmonary artery, from antero-posterior oblique (fig 4B) to cranio-caudal (fig 4F).

Discussion

The organogenesis of the heart has always fascinated cardiologists. This is partly because of its intriguing complexity and partly because of its importance in the formation of the abnormal heart, particularly those malformations which involve abnormal looping or abnormalities of conotruncal (outflow tract) septation. Anatomical studies of early abortus specimens⁷ have detailed the morphological features of the heart as it develops in the first weeks after conception. If the normal characteristics and sequence of cardiac development could be visualised and described, deviations from this normal pattern or delay in cardiac formation might indicate a nascent malformation. This may help to identify primary aetiological factors contributing to the malformation, because they would be acting when development was abnormal.

This study was not designed to identify all the usual normal cardiac connections in early pregnancy with a view to offering early prenatal diagnosis. Although this may be possible in time, in the first instance the normal features of the fetal heart must be understood and not misinterpreted. For example, if the heart in the mid-trimester fetus is in a central position it may indicate a cardiac malformation.¹⁴ In addition, in later pregnancy a pulmonary trunk smaller than the aorta indicates some degree of right ventricular outflow tract obstruction.¹⁵ In the late embryos and early fetuses we studied, these were normal features of early development. This was confirmed when we compared the echocardiographic findings with anatomical studies of the fetal heart at the same gestational age. In addition, despite experience of over 13 000 fetal heart examinations (LA), identification of cardiac structures was qualitatively difficult in the smallest fetuses or those in whom the lower resolution transducer was used and it required intensive study of recorded material. Therefore, with current ultrasound equipment at the present time, the technique is not likely to be useful for clinical diagnosis. Also the study was opportunistic in that images were recorded during evaluation of early pregnancy and not specifically for cardiac examina-

tion. There is no known risk to the early fetus associated with the use of ultrasound or colour flow mapping. Colour flow mapping is a normal part of this assessment and its use was kept to a minimum in the cardiac analysis.

The embryos and fetuses we studied were 5 mm to 55 mm long. The fetal heart is known to be very prominent anteriorly and to occupy most of the fetal chest in the smallest fetuses. This has been documented in both anatomical studies and by transvaginal scanning.^{16,17} The cardiac images which we were able to interpret with confidence, and have described here, were obtained in fetuses over 20 mm long. The developmental changes that involve the formation and fusion of the endocardial cushions, conotruncal septation, and closure of the interventricular foramen occur before this time, when the embryo is between 5 and 20 mm long. However, the cardiac anatomy of the smaller fetuses and embryos proved difficult to identify and will require further study and probably higher resolution transducers to interpret.

CONCLUSION

The most recently developed high resolution transvaginal transducers allow visualisation of the later developmental changes in cardiac morphology. The interpretation of these findings can be confirmed by study of microdissected embryos and early fetuses.

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