Echocardiographic Study of the Morphology and Growth of the Aortic Arch in the Human Fetus

Observations Related to the Prenatal Diagnosis of Coarctation

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**Background.** In a study of normal and abnormal growth of the aorta before birth, high-resolution echocardiographic imaging of the aortic arch in 92 normal fetuses aged 16–38 weeks was used to establish normal values for aortic arch dimensions at varying gestational ages.

**Methods and Results.** From long-axis views of the aortic arch, the internal diameter of the aortic root, ascending aorta, transverse aortic arch, aortic isthmus, proximal descending thoracic aorta, and left common carotid artery were measured. Correlation coefficients for the diameter of each aortic arch segment when related to gestational age varied from \( r=0.87 \) to \( r=0.94 \) (\( p<0.001 \) for each), and growth curves were derived from the third and 97th percentiles around each linear regression analysis. In most of the fetuses, there was progressive tapering of the aortic arch, with the smallest diameter being at the isthmus. The ratio of the transverse aorta, isthmus, descending aorta, and aortic root to the ascending aorta remained relatively constant with gestational age, with mean values of 0.94, 0.81, 0.96, and 1.13, respectively. In five fetuses in whom a prenatal diagnosis of aortic coarctation was confirmed postnatally, transverse aortic and isthmus measurements fell on or below the third percentile for gestational age from the above data. In each case, the ratio of left common carotid artery to transverse aorta was \( \geq 0.73 \) compared with \( \leq 0.62 \) for the 92 normal fetuses (mean ratios, 0.77\( \pm \)0.05 [SD] for coarctation versus 0.48\( \pm \)0.08 for normal fetuses; \( p\leq0.001 \)).

**Conclusions.** Use of normal growth curves for the developing aortic arch should facilitate the prenatal diagnosis of left heart and aortic arch abnormalities, particularly aortic coarctation, which until recently has been a difficult prenatal diagnosis to make with certainty. (Circulation 1992;86:741–747)

**Key Words** • echocardiography • fetus • aortic arch • coarctation

The delineation of cardiac anatomy and physiology in the human fetus has been substantially assisted by the advent of high-resolution echocardiography. As a result, a diverse range of intracardiac abnormalities have been diagnosed prenatally, and normal values now exist for ventricular size and wall thickness, atrioventricular and semilunar valve excursions,\(^1\)-\(^4\) and cardiac flow patterns\(^5\)-\(^7\) in the developing human fetus.

To date, most of the present knowledge of aortic arch growth has been derived from animal studies and postmortem morphometric descriptions in human fetuses and newborns. Rudolph et al\(^6\) described aortic arch growth in the fetal lamb in relation to the proportion of total cardiac output traversing each segment and hypothesized that similar growth occurs in the human fetus. Other investigators\(^8\),\(^9\) have provided measurements and growth curves for the aortic arch obtained at autopsy in human fetuses without cardiac malformations. Echocardiographic measurements of the aortic arch, however, have only recently been attempted in a relatively small population of human fetuses with a limited gestational age range of 23–27 weeks.\(^9\)

The purpose of the present study was to establish normal values for aortic arch growth and morphology in the human fetus throughout the second and third trimesters using high-resolution imaging techniques that might assist in the early recognition of aortic arch abnormalities.

**Methods**

**Study Population**

A retrospective review was performed of cross-sectional echocardiograms obtained from 124 normal fetuses and from five fetuses in whom a prenatal diagnosis of aortic coarctation was confirmed by postnatal echocardiography, angiography, and subsequent surgery.
Referral for detailed echocardiographic study was because of a family history of congenital heart disease in 82 cases (including four with coarctation), an incidental abnormality noted on obstetric sonography in 19, evaluation of a possible fetal arrhythmia in 14, and maternal diabetes in 14. Fetal gestational ages were determined from measurements of biparietal diameter using an algorithm for the 50th percentile, previously established by Hadlock et al.\(^1\) Studies in which there was poor resolution of the aortic arch and those performed before 16 weeks of gestation were excluded from consideration. With the exception of the five cases with documented coarctation of the aorta, the remaining 92 fetuses had structurally normal hearts both on fetal echocardiography and postnatal clinical examination.

**Echocardiographic Measurements**

Echocardiographic studies were performed using an Acuson 128 dynamically focused scanner with a 3.5- or 5.0-MHz linear or sector transducer. From long-axis echocardiographic images of the aortic arch (Figure 1), the internal diameter of the aorta was measured at five different positions, independent of the cardiac cycle. Measurements included the largest diameter of the aortic root, the ascending aorta just proximal to the right brachiocephalic origin, the transverse aortic arch distal to the left common carotid origin, the isthmus (proximal descending aorta) immediately distal to the left subclavian origin, and the descending aorta below the entry of the ductus arteriosus (Figure 2). In addition, measurements of the internal diameter of the proximal left common carotid artery\(^6\) were also obtained. Measurements were made from still frames printed onto x-ray film at the time of the study, using calipers and a reference grid superimposed on each frame. Each measurement was made independently by two observers, and the mean of each pair of measurements was then used. In approximately 12% of cases, a measurement was excluded because one or both observers were unable to delineate the aortic arch diameter at a given site.

**Statistical Analysis**

Linear regression analysis was used to derive the line of best fit for the plot for each aortic arch segment against gestational age. The 97th and third percentiles for each arch segment at different gestational ages were defined by the upper and lower borders, respectively, of the 95% confidence limits around each regression analysis. These were obtained by calculating the standard deviation (SD) of each distribution at a point corresponding to the mean gestational age and drawing lines parallel to the line of best fit at a distance of $\pm 1.96$ SD.\(^2\) Individual ratios of the aortic root, transverse aorta, isthmus, and descending aorta to the ascending aorta were calculated for each fetus and compared using a paired Student’s $t$ test, assuming normal distribution of each data set. The ratio of left common carotid artery to transverse aortic diameter was also calculated for comparison with the five abnormal fetuses. Trends for each of these ratios throughout gestation were determined by linear regression analysis. In view of the small number of abnormal fetuses, comparison of median ratios between these and the normal fetuses was performed using the Mann-Whitney test.

**Results**

**Normal Fetuses**

Ninety-two of the 124 initially reviewed normal fetal echocardiograms provided adequate resolution of the aortic arch from which two or more of the measurements could be made. For a number of fetuses, one or more of the six measurements could not be made, as the inner diameter of the vessel was difficult to define and, therefore, these measurements were excluded from the growth curves. The relation between aortic diameter and gestational age for each arch segment is displayed.

**Figure 1.** Image of long-axis view of the aortic (AO) arch in a normal fetus showing origin of the brachiocephalic vessels.

**Figure 2.** Diagram of fetal aortic arch showing sites of measurement of internal diameter: 1, aortic root; 2, ascending aorta; 3, transverse aorta; 4, isthmus; 5, descending aorta; 6, left common carotid artery. In this diagram, the ductus arteriosus is shown connecting toward the main pulmonary artery, although these structures were usually not well profiled in the aortic arch long-axis view.
Abnormal Fetuses

In five fetuses, a prenatal diagnosis of coarctation of the aorta made between 22 and 34 weeks' gestation was subsequently confirmed. Associated intracardiac abnormalities in these five fetuses included a bicuspid aortic valve (n=2), a large perimembranous ventricular septal defect (n=1), single ventricle with malposed great vessels (n=1), and double-outlet right ventricle with a small, posteriorly located aortic root (n=1).

Superimposed on Figures 3-7 are the measurements for these five abnormal fetuses. Aortic root, ascending and descending aortic root and left common carotid artery measurements were frequently within the "normal" percentile range for each regression analysis and in several cases were in close proximity to the predicted mean for gestational age. In one fetus with a bicuspid aortic valve, images of the aortic root and ascending aorta were of poor quality, and measurements were

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**FIGURE 3.** Plot of aortic (AO) root diameter vs. estimated gestational age (E.G.A.) together with line of best fit and the third and 97th percentiles (r=0.94, y=0.22x−0.38, p<0.001 for each). *Abnormal fetus with coarctation.*

**FIGURE 4.** Plot of ascending aortic (ASC. AO) diameter vs. estimated gestational age (E.G.A.) together with line of best fit and the third and 97th percentiles (r=0.93, y=0.20x−0.46, p<0.001 for each). *Abnormal fetus with coarctation.*

**FIGURE 5.** Plot of transverse aortic (TRANSV. AO) diameter vs. estimated gestational age (E.G.A.) together with line of best fit and the third and 97th percentiles (r=0.92, y=0.18x−0.37, p<0.001 for each). *Abnormal fetus with coarctation.*

**FIGURE 6.** Plot of isthmic diameter vs. estimated gestational age (E.G.A.) together with line of best fit and the third and 97th percentiles (r=0.92, y=0.17x−0.52, p<0.001 for each). *Abnormal fetus with coarctation.*
therefore not attempted. In all five cases, transverse aortic and isthmic measurements were below the third percentile for gestational age (Figure 8). In three of the five cases, a contrastopanel was visualized (Figure 8, lower panel), and in two cases, serial echocardiographic studies demonstrated the development of retrograde aortic flow from the descending aorta and ductus arteriosus back toward the aortic arch (Figure 8, lower panel). Among the abnormal fetuses, the mean right ventricular to left ventricular diameter was 1.3 (range, 1.1–1.5), and the pulmonary artery to the aortic diameter ratio was 1.5 (range, 1.1–2.1) compared with a mean value of 1.2 for both ratios, reported in other studies of normal fetuses.

In each of the five fetuses with coarctation, the ratio of the left common carotid artery diameter to that of the transverse aorta was larger than that of any of the remaining 92 normal fetuses (≥0.73 versus ≤0.62), and the difference in mean ratios between these two groups was highly statistically significant (0.77 versus 0.48, respectively, p<0.001). In each of four abnormal fetuses in whom these measurements were available, the transverse/ascending aortic and isthmic/ascending aortic ratios tended to be at the lower limit of normal and the descending to ascending aortic ratio approached the upper limit of normal, but despite a modest statistical difference in ratios between these and the remaining 92 fetuses, there was still some degree of overlap present.

### Discussion

In this study, high-resolution echocardiographic imaging was used to provide normal mean internal diameters together with third and 97th percentiles for different segments of the developing human aortic arch at gestational ages ranging from 16 weeks to term. From the present data, growth of all portions of the aortic arch appears to be linearly related to gestational age. This is consistent with the postmortem observations of Van Meurs-van Woezik et al, who related growth of aortic arch segments to body length in fetuses aged 21 weeks or more.

The present results suggest that there is progressive tapering of the aortic arch at all gestational ages that were studied, with the smallest diameter consistently represented by the isthmus. This gradation in growth is considered to reflect the proportion of fetal cardiac output traversing each aortic arch segment, with the smallest amount crossing the isthmus. In the fetal lamb, approximately 10–15% of cardiac output reaches the aortic isthmus, which has a diameter that is around 20% smaller than that of the descending aorta. The latter receives blood from both the aortic arch and the ductus arteriosus, amounting to as much as 67% of the combined cardiac output, thereby accounting for the increase in mean diameter distal to the point of ductal insertion. Similar observations have been made in premature and term infants at both postmortem study and cineangiography.

In previous necropsy studies, the size of the normal human aortic isthmus was found to be variable. Van Meurs-van Woezik et al noted significant isthmic narrowing in 10 of 21 perinatal cases, with a ratio of isthmic to descending aortic diameter that varied from 0.24 to 0.56, whereas in the remaining 10 cases, the same ratio exceeded 0.60. Angelini et al also demonstrated a significant difference in isthmic size relative to other arch segments from postmortem measurements, with the isthmus being 25% smaller than the descending aorta, which was in turn 20% smaller than the ascending aorta. In the same study, the echocardiographic measurements obtained from 20 living human fetuses with normal cardiac anatomy were consistently larger and more closely resembled our own findings with mean isthmic and descending to ascending aortic ratios of 0.73 and 0.90, respectively. The discrepancy between echocardiographic and autopsy measurements may in part have been the result of alterations in vessel structure at the site of ductal insertion due to the fixation technique. Based on the original fetal lamb studies in which the descending aorta received nearly 70% of the combined ventricular output, with the main pulmonary artery and the ascending aorta each receiving 50%, a relatively large ventricular output, resulting in a smaller proportion traversing the proximal descending aorta. In addition, Angelini et al demonstrated a smaller diameter for the ductus arteriosus in the human fetus than previously thought, based on fetal lamb studies suggesting that there might be less flow traversing the ductus,
and, therefore, the descending aorta in the human fetus, either because there is a greater amount of pulmonary blood flow or the output of the right ventricle is less than previously thought from fetal lamb models and previous human fetal Doppler echocardiographic studies.

**Prenatal Diagnosis of Aortic Coarctation**

Initial reports of antenatal detection of coarctation of the aorta consisted of isolated cases within several large series directed toward the in utero diagnosis of congenital heart disease. In most of these studies, the
diagnosis of coarctation was based primarily on the cross-sectional echocardiographic appearance of the aortic arch at the site of the contralud shelf and the accompanying area of tubular isthmic hypoplasia. However, imaging of the fine contralud shelflike structure can be difficult, and in the absence of normal aortic arch dimensions for comparison, the diagnosis may be missed. It was our hope that the presence of an abnormal growth pattern of aortic arch segments would provide a stimulus to careful examination during serial imaging in suspicious cases.

Because of these difficulties, recent reports have emphasized associated findings that might provide a clue to the in utero diagnosis of aortic coarctation. A greater than usual discrepancy in ventricular size favoring the right ventricle and an increase in pulmonary artery size relative to the aorta have been suggested by some investigators.18–20 In a recent collaborative review of a larger series of fetuses diagnosed with coarctation in utero,21 we found five of 12 fetuses with two-ventricle anatomy to have a right ventricular to left ventricular diameter ratio >2 SD above the mean for normal fetuses.1 Twelve of sixteen had a pulmonary artery to aortic root ratio that was >2 SD above the mean. Increased velocities of flow across the tricuspid valve and/or decreased aortic flow velocities by Doppler ultrasound have been additional observations made in fetuses with coarctation.20 However, all of these are indirect observations which, although consistent with present theories of the pathogenesis of aortic coarctation, are not specific for this condition, nor are they constant findings.

We hope that the normal values for human aortic arch growth provided in this study will permit the identification of even minimal changes in aortic arch dimensions at different gestational ages. In particular, the transverse aortic and isthmic measurements should facilitate the prenatal diagnosis of coarctation of the aorta, particularly when accompanied by some degree of isthmic hypoplasia, as is often the case with coarctation presenting in infancy.14 The calculation of left common carotid artery to transverse aortic ratio may well provide another clue to the in utero recognition of this entity. Previous studies22,23 have shown that in normal infants, the ratio of left common carotid artery diameter to that of the transverse aorta is approximately 0.50, whereas in cases of infantile coarctation, the same ratio is 0.80–0.96. Similar left common carotid artery to transverse aortic ratios were observed in normal fetuses in the present study compared with ratios of ≥0.73 among the fetuses with coarctation. As with absolute measurements of aortic arch segments, this ratio is likely to be of greatest help in those instances in which some degree of hypoplasia exists proximal to the site of obstruction.

Cases in which a discrete contralud shelf constitutes the only pathology, if such a form of coarctation exists in utero, may still remain difficult to detect, particularly if imaging of this site provides inadequate visualization of the relevant anatomic abnormality. In such instances, the indirect parameters of right heart size and Doppler flow patterns previously mentioned,18–20 perhaps in combination with color Doppler flow mapping,24 are presently the best indicators of in utero aortic arch obstruction.

Conclusions

This study provides a range of measurements for normal human fetal aortic arch development at different gestational ages. All aortic arch segments appear to grow in a linear fashion throughout the second and third trimesters and are relatively constant in proportion to each other. In five fetuses with documented coarctation of the aorta, measurements of transverse aortic and isthmic internal diameter fell below the third percentile for gestational age. The ratio of left common carotid to transverse arch diameter was also helpful in distinguishing the five cases with coarctation. In some patients, the prenatal diagnosis of aortic coarctation is likely to remain a challenge, requiring direct visualization of a contralud shelf as well as assessment of right heart size and flow patterns on Doppler ultrasound.

References


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