Cardiac axis in fetuses with abdominal wall defects

S. L. BOULTON, D. S. McKENNA, G. C. CLY, D. C. WEBB, J. BANTZ and J. SONEK

Department of Obstetrics and Gynecology, Wright State University School of Medicine, Dayton, OH, USA

KEYWORDS: abdominal wall defects; fetal cardiac axis; gastroschisis; omphalocele

ABSTRACT

Objectives To investigate whether fetal cardiac axis is affected by the presence of an abdominal wall defect (AWD) independent of congenital heart disease (CHD).

Methods Video ultrasound records from fetuses with AWDs identified from 1991–2004 were reviewed. Still images of the fetal cardiac four-chamber view were digitized and two independent examiners measured the cardiac axis. A cardiac axis of >65° or <25° was considered abnormal. Maternal charts were reviewed for fetal echocardiogram results and neonatal charts were reviewed for confirmation of CHD and type of AWD.

Results Of 17 fetuses with omphalocele and 42 fetuses with gastroschisis, 16 (27%) fetuses had an abnormal cardiac axis, while only seven (12%) had CHD. Fifty-nine percent of fetuses with omphalocele had an abnormal cardiac axis and 35% had CHD. Fourteen percent of fetuses with gastroschisis had an abnormal cardiac axis and 2% had CHD. Of 43 fetuses with a normal cardiac axis, only one had CHD.

Conclusions Fetal cardiac axis is often affected by the presence of an AWD independent of CHD. A normal cardiac axis in fetuses with AWDs is an accurate predictor of the absence of CHD, the negative predictive value being 97.7%. Copyright © 2006 ISUOG. Published by John Wiley & Sons, Ltd.

INTRODUCTION

Evaluation of the four-chamber view is part of the standard second or third-trimester obstetric ultrasound examination. Standard evaluation of the fetal four-chamber view includes assessment of the cardiac situs and axis. Fetal cardiac axis is defined as the angle between a line through the anterior spinous process and the sternum, which divides the thorax into two equal halves, and a line through the fetal atrioventricular septum. Comstock studied 183 fetuses and defined normal fetal cardiac axis to be 45° ± 20° (mean ± 2 SD). Smith et al. and Shipp et al. found that left-axis deviation is associated with congenital heart disease (CHD). Smith et al. found left-axis deviation in six cases of fetuses with omphalocele, but only three of the six had CHD. It was speculated that this may be due to simultaneous embryological disruptions of the developing heart and anterior abdominal wall. The purpose of this case series was to investigate whether the fetal cardiac axis is associated with the presence of an abdominal wall defect (AWD) independent of CHD.

METHODS

This was a retrospective case series. The institution’s human subjects committee approved the protocol. All cases of AWDs from 1991–2004 diagnosed at a single center were identified from a log of abnormal ultrasound examinations. When a woman had more than one ultrasound, the earliest second or third-trimester scan was used for the study. All ultrasounds were performed with an Acuson XP-128 or Sequoia with a 2.5–5-MHz transabdominal probe (Siemens, Mountain View, CA, USA). The images were stored on standard VHS format videotape. The videotape was reviewed for a transverse view of the fetal thorax at the level of the four-chamber cardiac view in the second or third trimester. If the videotape could not be obtained or did not contain a four-chamber view with the appropriate landmarks the patient was excluded from the study. The image was frozen and converted to high-quality digital still image and saved on digital media. The cardiac axes were calculated using CorelDraw™ version 9.0 (Corel Corporation, Ottawa, Ontario, Canada). The digital images were enlarged to ensure accurate and consistent calculation of cardiac axis. The line tool was used to divide the thorax into two equal halves intersecting the fetal spine and sternum, and another line was then placed through the interventricular septum. The axis was then calculated using the angle tool, which automatically calculated the angle between

Correspondence to: Dr S. L. Boulton, 541 Evanswood Place, Cincinnati, OH 45220, USA (e-mail: stacyboulton@yahoo.com)

Accepted: 22 December 2005

Copyright © 2006 ISUOG. Published by John Wiley & Sons, Ltd.
limits of agreement was used to assess the agreement of the calculated. The Bland and Altman method for confidence intervals was used to evaluate the ability of the fetal cardiac axis to predict the presence or absence of CHD, and 95% CI were calculated. Receiver–operating characteristics (ROC) curve analysis was used to determine the ability of the fetal cardiac axis to predict CHD. An alpha of 0.05 was considered significant.

Discrete variables were compared by the Fisher's exact test. An alpha of 0.05 was considered significant.

Continuous variables were expressed as mean ± SD and were tested for equal variances by Levene's test prior to comparison. The Student's t-test was used for the comparison of continuous variables with equal variances, and Welch's ANOVA was used for unequal variances. Discrete variables were compared by the Fisher's exact test. An alpha of 0.05 was considered significant.

Receiver–operating characteristics (ROC) curve analysis was used to evaluate the ability of the fetal cardiac axis to predict the presence or absence of CHD, and 95% CI were calculated. The Bland and Altman method for confidence limits of agreement was used to assess the agreement of the cardiac axis measurements of the two investigators. SPSS 13.0 (SPSS Inc., Chicago, IL, USA) was used for analysis.

RESULTS

There were 85 cases of AWDs identified from April 1991 to March 2004. Three cases of body stalk anomaly were excluded. Twenty-three cases were excluded due to an inability to obtain the necessary landmarks for the four-chamber view, or missing outcome data. The 59 remaining cases were used in the analyses. Forty-two cases had gastroschisis and 17 cases had omphalocele.

The mean gestational age at the time of the cardiac axis measurement was 24.4 ± 5.5 (range, 16.3–35.7) weeks. The two observers’ measurements are plotted along with the best-fit line by the least mean squares method (Figure 2). The absolute difference between each measurement pair ranged from 0–16° (mean, 4.1° ± 3.0°). The mean values of the measurements by the two observers were 54.8° ± 17.5° (range, 22–105°) and 54.6° ± 18.2° (range, 22–104°). The mean difference between the two observers was 0.15° with SD 5.1°, giving 95% limits of agreements −9.9 to +10.2. The standard error of the limits was 1.15. The 95% CI for the limits of agreement is −12.1 to −7.6 for the lower limit, and +7.9 to +12.4 for the upper limit. The mean of the two measurements was used for the subsequent analyses.

The mean cardiac axis measurement was 54.7° ± 17.7° (range, 22–105°). There were 15 fetuses (23.4%) with cardiac axis measurements exceeding 65°, and one that was less than 25°. Ten of 17 fetuses with omphalocele (58.8%) and six of 42 fetuses with gastroschisis (14.3%) had an abnormal cardiac axis. The mean axis was significantly greater in fetuses with omphalocele, 64.0° ± 22.1° (range, 23–105°) compared to those with gastroschisis 50.7° ± 14.0° (range, 25–90°), P = 0.03.

There were seven cases of CHD. Six (86%) of the cases of CHD were diagnosed by antenatal ultrasound, and all had omphalocele and an abnormal cardiac axis (Table 1). Five of the six cases with the antenatal diagnosis of CHD had a cardiac axis that exceeded 65°, and one case had

Figure 1 Ultrasound image showing measurement of the cardiac axis. A fetal four-chamber view of the heart was first obtained and digitized. The line tool was used to divide the thorax into two equal halves intersecting the fetal spine and sternum, and another line was then placed through the interventricular septum. The axis was calculated at 40° using the angle tool, as shown. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

Figure 2 Line graph showing two observers’ cardiac measurements at mean ± SD gestational age of 24.4 ± 5.5 (range, 16.3–35.7) weeks, n = 59. The line is the best fit by the least mean squares method.
an axis measurement of 23°. One fetus with gastroschisis and CHD with a normal cardiac axis (58°) had a small ventricular septal defect (VSD) that was detected after delivery and did not require any intervention.

Excluding cases with CHD, the mean cardiac axis was 52.9° ± 16.0° (range, 23°–93°). The fetuses with omphalocele and without CHD (n = 11) still had a significantly greater cardiac axis than those with gastroschisis and without CHD (n = 41), 61.2° ± 20.0° vs. 50.6° ± 14.2°, respectively (P = 0.04). There were 10 cases (four with omphalocele and six with gastroschisis) with an abnormal cardiac axis and no CHD.

A ROC curve was used to evaluate the cardiac axis for the diagnosis of CHD in fetuses with AWDs. Utilizing a cut-off of > 65° or < 25°, the area under the curve was 0.89 (CI 0.78–0.99), P = 0.001, the sensitivity was 86%, specificity 81%, positive predictive value (PPV) 38% and negative predictive value (NPV) 97.7%.

**DISCUSSION**

Fetuses with AWDs in our study sample had a high frequency of abnormal cardiac axes (58.8% omphalocele, 14.3% gastroschisis), even in the absence of CHD. There were sixteen (27.1%) cases in the study population with an abnormal cardiac axis, and 10 cases did not have CHD. Fetuses with omphalocele are more likely to have abnormal axes and have significantly greater cardiac levorotation than fetuses with gastroschisis. Despite our study’s finding of an increased percentage of fetuses with AWDs and abnormal cardiac axes, a normal cardiac axis in this population still had a high NPV (97.7%) to exclude CHD. The PPV however was quite low at 38%. We speculated that the PPV was low because the axis in these fetuses may be related to the fact that they had an AWD.

This study was limited by the retrospective collection of data and the reliance on fetal echocardiography and newborn examinations to determine if CHD was present. In our experience, the antenatal diagnoses of omphalocele and gastroschisis by ultrasound are highly accurate. In contrast, the antenatal diagnosis of specific heart defects is often more challenging. We assumed a normal fetal echocardiogram and normal newborn cardiac examination excluded CHD; however, it is possible some defects may be missed. In fact, a small VSD in one fetus with gastroschisis was not detected antenatally. There may have been other fetuses with a normal fetal echocardiogram with undetected CHD.

An explanation for our findings may be found in the embryologic development of the fetus. At approximately 8 weeks’ gestational age, the fetal heart undergoes vertical and horizontal rotation, and at the same time the midgut enters the umbilical cord, rotates and subsequently returns to the abdomen. A common anatomic disruption at this point in embryogenesis may result in an omphalocele and an abnormal cardiac axis in the absence of CHD.

Gastroschisis occurs when there is a defect in or near the median plane of the ventral abdominal wall from incomplete fusion of the lateral folds, and there are several proposed etiologies including abdominal wall ischemia due to involution of the vitelline artery or right umbilical vein, and interruption of the mesenchymal somatic migration. These proposed etiologies of gastroschisis would not appear to have an effect on embryo cardiac development and fail to explain our findings of increased levorotation or abnormal axes in 14% of our patients.

AWDs are common birth defects and neonatal prognosis is dependent on the presence of associated anomalies, as well as the development of other neonatal complications (necrotizing enterocolitis, bowel obstruction, bowel necrosis, biliary obstruction etc.). When an AWD is detected antenatally, serial targeted ultrasound examinations are often done to search for other anomalies. Fetal omphalocele is associated with additional anomalies in 60–70% of cases, while gastroschisis is almost always an isolated finding. The finding of CHD with either AWD will affect the subsequent prognosis. Fetuses with AWDs and normal cardiac axes are less likely to have structural heart problems when compared to similarly affected fetuses with an abnormal axis. An abnormal cardiac axis warrants a more detailed scan of the fetus.

**REFERENCES**