Measurement of the Great Vessels in the Mediastinum Could Help Distinguish True From False-Positive Coarctation of the Aorta in the Third Trimester

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Objective. We investigated the utility of analyzing prenatal mediastinal measures of the great arteries in distinguishing true coarctation of the aorta (CoA) from false-positive CoA. ***Methods.*** All fetuses in this study had suspicion of CoA based on the presence of right-left heart disproportion. We defined 3 study groups: group 1, true fetal CoA; group 2, false-positive fetal CoA with a narrow aortic arch; and group 3, false-positive fetal CoA without a narrow aortic arch. ***Results.*** In group 1, the mean mediastinal pulmonary artery (PA) to ascending aorta (Ao) diameter ratio ± SD was 2.03 ± 0.48, and in group 2, the ratio was 1.60 ± 0.23. The difference was statistically significant (P = .0018, t test). In group 3, the mean PA:Ao ratio was 1.35 ± 0.14. The difference between groups 1 and 3 was statistically significant (P = .0002, t test). In our study group, for a PA:Ao ratio of 1.60, sensitivity was 83.0%; specificity, 85.0%; positive predictive value, 62.5%; and negative predictive value, 94.0%. ***Conclusions.*** In the third trimester, the main PA:Ao ratio as measured in the fetal mediastinum can be a helpful tool in distinguishing true CoA requiring neonatal cardiac surgery from false-positive CoA and simple disproportion requiring medical attention but no surgery in the first month of postnatal life. ***Key words:*** coarctation of the aorta; great vessels; mediastinum; third trimester.

Abbreviations
Ao, ascending aorta; CoA, coarctation of the aorta; PA, pulmonary artery

Antenatal diagnosis of coarctation of the aorta (CoA) is a challenge, although it is critically important for early treatment of the neonate.[1–3] Echocardiography allows for identification of groups at high risk but does not predict with certainty the presence of a CoA after birth. Echocardiographic markers suggestive of CoA in the fetus are many and include a visual disproportion in size between the ventricles, with the right heart larger than the left, visualization of a narrow aortic isthmus or aortic shelf, the presence of a left superior vena cava, and a bicuspid aortic valve.[4–11] However, these prenatal findings are nonspecific for predicting a postnatal diagnosis of CoA (Figures 1 and 2).

In the third trimester of pregnancy in an otherwise structurally normal heart, substantial right-left heart size disproportion raises the possibility of the diagnosis of CoA with the need for delivery at an appropriately equipped center for performance of a cardiovascular evaluation and postnatal echocardiography. However,
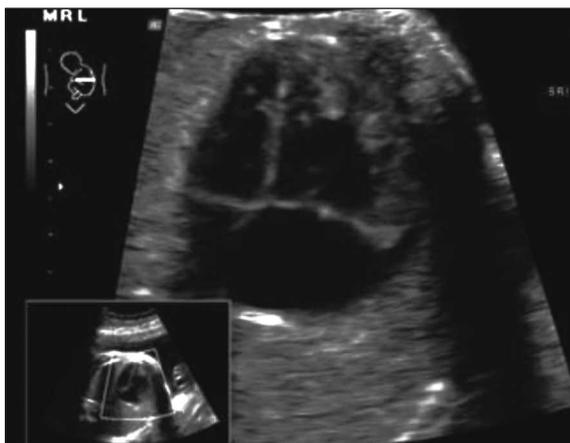
Figure 1. False-positive diagnosis of fetal CoA at 34 weeks: disproportion in the 4-chamber view.

oftentimes in such cases, prenatal evaluation reveals a false-positive finding in which the postnatal echocardiogram may be normal, and parents are unnecessarily stressed. To better predict the presence of CoA, we investigated the utility of analyzing prenatal mediastinal measurement of the great arteries in distinguishing true from false-positive CoA.

Material and Methods

We performed a retrospective analysis of fetuses suspected of having CoA. All fetuses had suspicion of CoA based on the presence of right-left

Figure 2. False-positive diagnosis of fetal CoA at 34 weeks (another fetus): long-axis view of the fetal aortic arch showing a narrow transverse aortic arch (3.90 mm), narrow aortic isthmus (arrow), elongated fetal aortic shelf (ductal aneurysm in the differential diagnosis), and descending aorta of 5.70 mm. Neonatal echocardiographic findings were normal.

heart disproportion, defined as right atrium larger than left atrium, right ventricle larger than left ventricle, and tricuspid valve larger than mitral valve (minimum ratio, 1.6) on the 4-chamber view. Additional inclusion criteria were as follows: (1) a foramen ovale larger than 4 mm, to rule out premature closure or restriction of the foramen ovale; (2) good-quality imaging of the fetal upper mediastinum with visualization of the 3-vessel view, allowing measurements in a single tomographic plane of the main pulmonary artery (PA) before bifurcation and the ascending aorta (Ao)[12–14]; (3) fetuses with disproportion in the mediastinum between the right and left sides with the PA at least 2 mm larger than the Ao (Figures 3 and 4); (4) a ductus arteriosus pulsatility index of greater than 2.0, to exclude premature ductal constriction as a cause of right-left disproportion; and (5) neonatal echocardiography performed in our center. The exclusion criteria were as follows: (1) extracardiac malformations; (2) twin gestation; and (3) other complex cardiac anatomy such as an interrupted aortic arch, Shone syndrome, and hypoplastic left heart syndrome. No pregnant woman was taking medication. All neonates were delivered in our institution. Postnatal CoA if present was diagnosed by neonatal echocardiography and confirmed after birth.

Patients were divided into 3 study groups: group 1, true fetal CoA by the presence of fetal right-left disproportion and a narrow aortic arch with confirmed CoA after birth (n = 12); group 2, false-positive fetal CoA by virtue of the presence of fetal

Figure 3. Fetus from Figure 1 with a mediastinal PA:Ao ratio of 1.42. The neonate had pneumonia, anemia, and normal echocardiographic findings.

right-left disproportion and suspicion of a narrow aortic arch but a normal aortic arch at neonatal evaluation (n = 20); and group 3, false-positive fetal CoA by virtue of the presence of fetal disproportion without a narrow aortic arch and normal neonatal echocardiographic findings (n = 20). We measured the aortic arch in the long-axis view of the aorta (Figure 2) and defined a narrow aortic arch in the third trimester of pregnancy as less than 4 mm.[7] Detailed retrospective analysis of fetal echocardiograms with a focus on measurement of the mediastinal great vessels was performed. A *t* test was used to distinguish differences between the groups, with *P* < .05 indicating significance.

Results

Data for the 3 study groups, including the number of fetuses in each group, mean maternal age, gestational age, mean fetal weight, heart area to chest area ratio, isthmus size, PA diameter, and Ao diameter (as measured in the 3-vessel mediastinum view) are provided in Table 1.

In group 1, the mean mediastinal PA:Ao ratio ± SD was 2.03 ± 0.48, and in group 2, the ratio was 1.60 ± 0.23. The difference was statistically significant (*P* = .0018, *t* test; Figure 5). In group 3, the mean PA:Ao ratio was 1.35 ± 0.14. The difference between groups 1 and 3 was statistically significant (*P* = .0002, *t* test; Figure 5).

In our study group, for a PA:Ao ratio of 1.60, sensitivity was 83.0%; specificity, 85.0%; positive predictive value, 62.5%; and negative predictive value, 94.0%.

Figure 4. Mediastinum in true fetal CoA with a PA:Ao ratio of 2.20. The neonate underwent cardiac surgery.
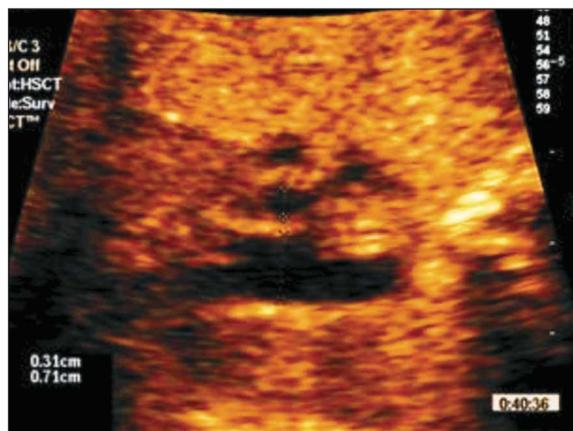
Discussion

Prenatal diagnosis of CoA, although possible, is still a very difficult diagnosis to make accurately.[4,15] It is important because prenatal diagnosis of CoA improves survival and reduces neonatal morbidity.[1] In addition, a false-positive diagnosis of CoA creates unnecessary parental stress and anguish for a neonate that will end up with a normal heart.

Severe CoA has been reported as early as 14 to 16 weeks' gestation.[6] However, there might also be a normal-appearing heart in the first and second trimesters, and CoA may present later on in the third trimester. The possibility of progression from a normal aortic arch to a hypoplastic aortic arch and CoA during fetal life has been recognized previously.[5] In addition, it is also possible to have a normal aortic arch during fetal life and then have CoA later on during postnatal or adult life.[16]

One might think that the easiest way to diagnose CoA in the fetus is through visualization of the aortic arch on a longitudinal view, 2-dimensional sonogram, or 3-dimensional reconstruction.[9] Unfortunately, this is not possible in every case because of the fetal position or technical problems. Second, the size of the aortic isthmus after 30 weeks' gestation becomes relatively smaller compared to the descending aorta and may be a source of false-positive diagnoses (Figure 2).

In our study, we were interested in focusing on borderline CoA in late gestation, in which evidence of a discrete CoA narrowing or shelf was absent. All fetal echocardiograms were obtained after 26 weeks' gestation and were based on the 3-vessel view. The value of analyzing 3-vessel and trachea views was initially proposed by Yoo et al[12] and Yagel et al,[14] and the notion of analyzing the fetal mediastinum and 3-vessel view for possible detection of CoA was introduced by Viñals et al.[17] They suggested that mediastinal disproportion between the PA and Ao may be a marker but did not provide specific measurements.

Our goal was to calculate the main PA:Ao diameter ratio in the mediastium (as shown in an example, measurements were taken in a single line going across the 3 vessels). We consider this an easy approach to perform, which can be used by less experienced sonographers (Figures 3 and 4).

Table 1. Comparison of Data From the 3 Study Groups

Parameter	Group 1, True CoA	Group 2, False + CoA	Group 3, False + CoA
Characteristics	Disproportion and narrow aortic arch isthmus, CoA confirmed after birth	Disproportion and narrow aortic arch isthmus, no CoA after birth	Disproportion without narrow aortic arch, no CoA after birth, normal neonatal echocardiographic findings
Fetuses, n	12	20	20
Maternal age, y	28.20 ± 4.80	28.40 ± 4.40	27.20 ± 5.40
Gestational age, wk	31.50 ± 4.30	34.00 ± 2.48	33.60 ± 4.60
Fetal weight, g	1939 ± 962	2517 ± 695	3393 ± 488
HA:CA ratio	0.36 ± 0.05	0.38 ± 0.06	0.35 ± 0.03
Ao isthmus, mm	2.5–4.0	3.0–4.0	4.1–6.0
PA diameter, mm	8.47 ± 2.05	9.90 ± 1.25	8.50 ± 1.76
Ao diameter, mm	4.21 ± 1.83	5.50 ± 0.80	6.60 ± 1.44
PA:Ao ratio	2.03 ± 0.48	1.60 ± 0.23	1.35 ± 0.14
Birth weight, g	2920 ± 570	2986 ± 559	3393 ± 488
Survivors, %	50	100	100

Values are mean ± SD unless otherwise indicated. CA indicates chest area; and HA, heart area. Statistics for PA:Ao ratio in groups 1 and 2: $P = .0018$, t test. Statistics for PA:Ao ratio in groups 1 and 3: $P = .0002$, t test.

Our data show that this ratio may distinguish between a fetus with CoA requiring neonatal intervention and a fetus with simple disproportion in great arterial size but a heart not requiring neonatal intervention for CoA.

The disproportion in the great arteries is probably related to blood flow redistribution in cases of a narrow transverse arch or aortic isthmus or CoA. In these circumstances of increased resistance at the any point of the left ventricular outflow tract, the blood flow would mainly be redistributed via the tricuspid valve and right ventricular outflow tract. It can be only a temporary redistribution that normalizes after birth or a permanent redistribution seen in cases requiring cardiac surgery after delivery.

Further questions can be asked with the use of this index of disproportion between the main PA and Ao in the mediastinum. Is it possible to distinguish CoA from an interrupted aortic arch? Will the degree of disproportion potentially predict for the development of late postnatal CoA? Application of this index in the fetus with follow-up in future studies may address these questions.

Our study had the following limitations. Our approach was dedicated only to a selected group of fetuses and neonates with suspected or proved CoA, which required cardiac surgery in the first month of life. We recommend a neonatal echocardiogram for any fetus with substantial right-left disproportion. It would be interesting to follow patients with false-positive CoA during the first year of life to see whether CoA develops later on. We did not focus on false-negative cases in this study group or on additional measurements done by other groups because our intent was to add one new piece of valuable information to the spectrum of fetal cardiovascular sonography. We did not make a differential diagnosis for false-positive cases, but we excluded a restricted foramen ovale and other structural cardiac and extracardiac anomalies.

Before the PA:Ao ratio of 1.60 becomes more clinically applicable, we need to evaluate a larger population. Despite an overlap between normal cases and true CoA (Figure 5), our numbers are helpful for identifying cases needed further evaluation and special attention. Our method is simple to use in daily life, as opposed to sophisticated methods of analysis presented before.[18]

Figure 5. Statistical analysis.
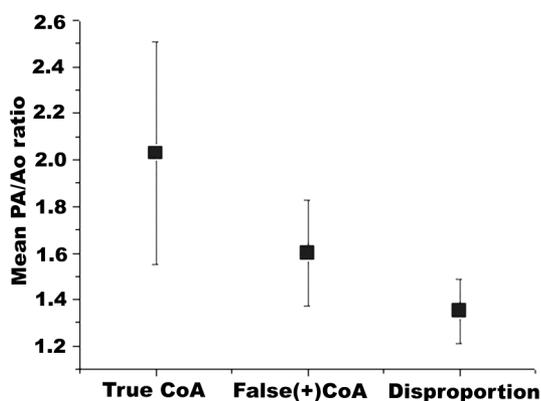
In conclusion, in the third trimester, the main PA:Ao diameter ratio as measured in the fetal mediastinum can be a helpful tool for distinguishing true CoA requiring neonatal cardiac surgery from false-positive CoA and simple disproportion requiring medical attention but no surgery in the first month of postnatal life. Taking into consideration that fetal CoA continues to be very difficult to diagnose despite advances in technology,[19] we think that our data can contribute to improved counseling for parents.

References

1. Franklin O, Burch M, Manning N, Sleeman K, Gould S, Archer N. Prenatal diagnosis of coarctation of the aorta improves survival and reduces morbidity. Heart 2002; 87:67–69.

2. Head CE, Jowett VC, Sharland GK, Simpson JM. Timing of presentation and postnatal outcome of infants suspected of having coarctation of the aorta during fetal life. Heart 2005; 91:1070–1074.

3. Paladini D, Volpe P, Russo MG, Vassallo M, Sclavo G, Gentile M. Aortic coarctation: prognostic indicators of survival in the fetus. Heart 2004; 90:1348–1349.

4. Allan LD, Crawford DC, Anderson RH, Tynan M. Spectrum of congenital heart disease detected echocardiographically in prenatal life. Br Heart J 1985; 54:523–526.

5. Allan LD, Crawford DC, Tynan M. Evolution of coarctation of the aorta in intrauterine life. Br Heart J 1984; 52: 471–473.

6. Bronshtein M, Zimmer EZ. Sonographic diagnosis of fetal coarctation of the aorta at 14–16 weeks' gestation. Ultrasound Obstet Gynecol 1998; 11:254–257.

7. Hornberger LK, Weintraub RG, Pesonen E, et al. Echocardiographic study of the morphology and growth of the aortic arch in the human fetus: observations related to the prenatal diagnosis of coarctation. Circulation 1992; 86:741–747.

8. Hornberger LK, Sahn DJ, Kleinman CS, Copel J, Silverman NH. Antenatal diagnosis of coarctation of the aorta: a multicenter experience. J Am Coll Cardiol 1994; 23:417–423.

9. Molina FS, Nicolaides KH, Carvalho JS. Two- and three-dimensional imaging of coarctation shelf in the human fetus. Heart 2008; 94:584.

10. Nomiyama M, Ueda Y, Toyota Y, Kawano H. Fetal aortic isthmus growth and morphology in late gestation. Ultrasound Obstet Gynecol 2002; 19:153–157.

11. Pasquini L, Fichera A, Tan T, Ho SY, Gardiner H. Left superior caval vein: a powerful indicator of fetal coarctation. Heart 2005; 91:539–540.

12. Yoo, SJ, Lee YH, Kim ES, et al. Three-vessel view of the fetal upper mediastinum: an easy means of detecting abnormalities of the ventricular outflow tracts and great arteries during obstetric screening. Ultrasound Obstet Gynecol 1997; 9:173–183.

13. Yoo SJ, Lee YH, Cho KS, Kim DY. Sequential segmental approach to fetal congenital heart disease. Cardiol Young 1999; 9:430–444.

14. Yagel S, Arbel R, Anteby EY, Raveh D, Achiron R. The three vessels and trachea view (3VT) in fetal cardiac scanning. Ultrasound Obstet Gynecol 2002; 20:340–345.

15. Sharland GK, Chan KY, Allan LD. Coarctation of the aorta: difficulties in prenatal diagnosis. Br Heart J 1994; 71:70–75.

16. Rosenthal E. Coarctation of the aorta from fetus to adult: curable condition or life long disease process? Heart 2005; 91:1495–1502.

17. Viñals F, Heredia F, Giuliano A. The role of the three vessels and trachea view (3VT) in the diagnosis of congenital heart defects. Ultrasound Obstet Gynecol 2003; 22:358–367.

18. Pasquini L, Mellander M, Seale A, et al. Z-scores of the fetal aortic isthmus and duct: an aid to assessing arch hypoplasia. Ultrasound Obstet Gynecol 2007; 29:628–633.

19. Stos B, Le Bidois J, Fermont L, Bonnet D. Is antenatal diagnosis of coarctation of the aorta possible? Arch Mal Coeur Vaiss 2007; 100:428–432.