The differential diagnosis of double aortic arch and right aortic arch with mirror-image branches in the fetus- A potential novel method

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Abstract

Objective: To explore a new method of differential diagnosis of fetal double aortic aorta (DAA) and right aortic arch with mirror-image branches (RAA-MB). Methods: Clinical data and prenatal echocardiographic features of the DAA (n = 22) and RAA-MB (n = 65) confirmed by postnatal or autopsy findings were analyzed retrospectively. The angles between the two aortic arches in the DAA group and between the right aortic arch and the mirror branch were measured. The differences between both groups and differential diagnosis value of the angles were compared and analyzed based on the ROC curve. Results: Left-sided DAA's proportion (100%) was higher in the double aortic arch group (32.3%) than in the RAA-MB group, (P ¡ 0.05). The proportion of conotruncal anomalies is higher in the RAA-MB group (64.6%) than in the DAA group (18.2%) (P ¡ 0.05). There was a significant difference in the angles between both groups (DAA: 50.3° ± 8.3° vs RAA-MB: 82.9° ± 13.8°) (P < 0.01). When the cut-off value was 62.8°, the sensitivity and specificity of differential diagnosis were 95.5% and 96.9%, respectively. Conclusions: Distinguishing the angle measurement between DAA and RAA-MB is helpful in prenatal prognosis. We recommend a cutoff value of 62.8°.

Introduction

Both the double aortic arch (DAA) and the right aortic arch with the mirror-image branches (RAA-MB) are considered as abnormal development of the aortic arch. However, their prognoses are quite different. Therefore, it is necessary to make a differential diagnosis of the DAA and the RAA-MB in the fetus, which is helpful for the prenatal prognosis consultation. Previous studies suggested that the three-vessel-trachea view and their adjacent view could be used to distinguish them.[1] However, if there is hypoplasia or atresia in the posterior part of the left aortic arch, its manifestations are very similar to those of the RAA-MB, making it very difficult to distinguish both. The 3D STIC technique increased the sensitivity of fetal echocardiography for detecting arch anomalies.[2] The DAA forms an "O" vascular ring, [1, 3] while the RAA-MB itself does not.[4] The main difference between the two is to observe whether the first branch of the ascending aorta is connected with the descending aorta. However, the right aortic arch is usually higher than the left one, which cannot be displayed completely in one view. Moreover, in the same view, the angle between the right aorta and the first vessel branch can be shown. Therefore, we hypothesized that there might be a difference among the angle between the two arches of the DAA and that between RAA and the first branch of the right arch. To our best knowledge, this is the first study to elucidate on that difference. Based on two-dimensional color

echocardiography, the angles between the two aortic arches and the RAA and its first branch were measured to distinguish them in this study.

Methods

Twenty-two fetuses with DAA, 8 cases of which with hypoplastic left arch and 2 cases of which with very hypoplasia of the distal left arch, and 65 fetuses with RAA-MB prenatally diagnosed with post-natal or autopsy findings confirmed from our database of 27652 fetuses were analyzed retrospectively in our center from October 2015 to October 2019. Clinical data and prenatal echocardiographic features of the DAA and RAA-MB were collected. The study design was approved by the ethics review board of our hospital. Fetal autopsy following the termination of the pregnancy was performed with the consent of the parents. Informed consent was unnecessary for the other cases, as this is a retrospective study.

Inclusion criteria: the cases confirmed by postnatal or autopsy findings, clear three-vessel-trachea view, and a visible color in the Doppler image of the first branch of the right aortic arch. Exclusion criteria: the angle of the first branch of the RAA cannot be measured due to the invisible beginning part of the first branch of the RAA.

All the fetal echocardiographic examinations were performed by a physician with over 5 years of experience in our maternal-fetal medicine consultation center, based on the guidelines previously published.[5-7] All fetal echocardiographs were obtained using a Voluson E8/E10 equipped with a 2D/3D probe of 2- to 8-MHz (GE Healthcare, Zipf, Austria).

The angle between the right aortic arch and its first branch was measured by color Doppler imaging (Figure. 1) on the 3VT view. In the DAA, the angle between the proximal parts of the two arches was measured, while in the RAA-MB, the angle between the RAA and the left brachiocephalic artery was measured.

Two observers completed the measurements of angles of the DAA and RAA with mirror branches. They were blinded to the final results. Twenty cases were randomly selected to measure the angle to determine the internal and interval variability of the observers by using the same view. The interval between the two measurements for the same observer was two weeks.

Statistical analysis

All echocardiographic measurement data are expressed as mean ± SD. Professional statistical software (SPSS 20.0) was used for all analyses. Student's t-test was used to compare the differences in measurement data between both groups. $P < 0.05$ was considered statistically significant. The ROC curve was used to analyze the sensitivity and specificity of the angle in the diagnosis of DAA or RAA with MB.

Results

In DAA group, the average age of pregnant women was 28.1 ± 4.6 years old (ranged from 20 to 38 y), and the average gestational age was 27.2 ± 4.1 weeks (22-36 weeks). In RAA-MB group, the average age of pregnant women was 29.1 ± 4.4 years old (ranged from 21 to 36 y), and the average gestational age was 26.6 ± 3.6 weeks (ranged from 21 to 36 weeks).

The proportion of the left-sided DA (100%) was higher in the double aortic arch group (32.3%) than in the RAA-MB group, ($P < 0.05$). The proportion of conotruncal anomalies in the RAA-MB group (64.6%) was higher than that in the double aortic arch group (18.2%) ($P < 0.05$). Other data are shown in Table 1.

There was a significant difference in the angles between the DAA group (ranged from 33.6° to 71.7°, 50.3° ± 8.3°) and the RAA-MB group (ranged from 57.7° to 111.8°, 50.3° ± 8.3°) ($P < 0.01$) (Figure 2). Based on the ROC curve analysis, when the cut-off value was 62.8°, the sensitivity and specificity of differential diagnosis were 95.5% (95% CI: 77.2% - 99.9%) and 96.9% (95% CI: 89.3% - 99.6%), respectively (Figure. 3).

The Bland-Altman plots showed that the intra- and inter-observer agreements of LD and DA measurements were almost within 95% limits of agreement (Figure. 4).

Discussion

Based on the position and branching pattern, aortic arch anomalies include a variety of congenital abnormalities. According to the theory of double aortic arch by Edwards JE,[8] in a double aortic arch, both the embryonic right and left arches persist, arising from the ascending aorta, passing on both sides of the trachea and esophagus, and joining posteriorly to form the descending aorta. If the posterior segment of the left arch is hypopastic or even atretic, the aortic arch branching pattern may mimic the right aortic arch with mirror-image branches. However, the right aortic arch with mirror-image branches is the mirror image of the normal left aortic arch and branches. This condition results from regression of a segment of left aorta arch between the left subclavian artery and descending aorta and the right aortic arch persist. The left subclavian artery fused with the left common carotid artery to form the left brachiocephalic artery, which is the first branch of the right aortic arch. The ductus arteriosus usually is left-sided, arising anteriorly from the base of the innominate artery or the left subclavian artery rather than posteriorly from the descending aorta.[1]

A double aortic arch completely encircles the trachea and esophagus, also called complete vascular ring. Under this condition, the ductus arteriosus is most often left-sided. The DAA can be isolated, or it may be associated with other cardiac anomalies. The right aortic arch may be associated with other cardiac anomalies or may be isolated. Right aortic arch with mirror-image branches often associate with intracardiac anomalies, particularly the conotruncal anomaly, which is consistent with the previous literature.[9, 10,11] When the right aorta arch is diagnosed prenatally, it is necessary to confirm whether there is chromosome abnormality, especially trisomy 21 and microdeletion of 22q11.[1, 9, 12, 13]

The identification of isolated RAA-MB is crucial for distinguishing it from the DAA.[4,14] In the DAA, especially the hypoplasia of the posterior part of the left arch, which is easily confused with the RAA-MB. The left arch of DAA runs backward at the left side of the trachea and is connected with the descending aorta. The left and right arches are generally not in the same plane. Generally, the wider arch is higher than the thinner one. The continuity between the left arch and the descending aorta should be carefully observed by adjusting the probe in the multiple views. The left brachiocephalic artery of the RAA-MB runs from right to left in front of the trachea to the left shoulder, and has no connection with the descending aorta. However, it may be misdiagnosed as a double aortic arch when the blood flow of left DA overlaps with the left brachiocephalic artery; thus, the interference of DA should be avoided. The technology of the 3D spatiotemporal image correlation of the fetal echocardiography is an accurate diagnostic tool for arch anomalies. [2]

The three-vessel view and three-vessel-trachea view are used to screen the fetal aortic arch for abnormalities.[15, 16] Whether it is DAA or RAA-MB, the first proximal branch of RAA is normally clearly demonstrated. Therefore, when the first branch of the RAA is observed in the three-vessel view, the angle between the first branch and the RAA can be sufficiently measured. Our results show that the duplicability of the measurement of the angle is also satisfactory. Regardless of incidence of hypoplasia of the left arch, the angle between the beginning of the two aortic arches is not changed by the hypoplasia of the posterior part of the left arch. Therefore, the measurement of this angle has good specificity. The right aortic arch is associated with the mirror branches, which do not form a vascular ring. Meanwhile, the DAA form an "O" shape ring. Therefore, there is a significant difference between the two angles as our results convey. We found that the angle in the DAA group was significantly higher than that in the RAA-MB group. According to the ROC curve analysis, when the cut-off value was 62.8°, the sensitivity and specificity for the differential diagnosis were 95.5% and 96.9%, respectively.

The DAA can compress the trachea, which can result in the stridor in newborns, of whom some need surgical treatment.[10] In contrast, there was no vascular ring in the RAA-MB itself, and no clinical symptoms because of no compression of the trachea.[3, 9, 17] However, a U-shaped vascular ring is formed when the right aortic arch is associated with the left-sided DA. RAA-MB is often associated with intracardiac malformation, especially the conotruncal anomalies. Further, the RAA-MB is often associated with chromosomal abnormalities, which need further genetic examination.

This study has limitations. First, it is a retrospective study, and there may be selective bias. Further, the number of the cases is limited,particularly limited number of the DAA with very hypoplasia or atresia of the distal left arch. Thus, large prospective samples are needed for further study.

Therefore, measuring the angle of the first branch of the RAA can distinguish the fetal DAA and the RAA-MB, which is easy and reproducible. We recommend a cutoff value of 62.8deg.

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Table 1. General data and ultrasound features in the fetuses with DAA and RAA with MB

		DAA (22)	RAA with MB (65)
Age (y)		28.1±4.6	29.1±4.4
GA (w)		27.2±4.1	26.6±3.6
Ductus arteriosus*	Left-sided	22(100%)	21(32.3%)
	Right-sided	0	12 (18.5%)
	Double	0	3 (4.6%)
	Anterior	0	13 (20%)
	Absence	0	16 (24.6%)
Conotruncal defects*		4(18.2%)	42(64.6%)
	TOF	3	24
	DORV	0	6
	TA	1	3
	TGA	0	3
	PA/VSD	0	6
Angles*		50.3 ± 8.3 °	82.9 ± 13.8 °

* P <0.05.

Figures and legends

Figure 1. Echocardiographic and schematic images of the angle (*) measurement in the double aortic arch with 51.35°(A) and right aortic arch with mirror-image branches with 85.76°(B). LAA: left aortic arch; RAA: right aortic arch; DA: ductus arteriosus; MB: mirror-image branches; Sp.: spine.

Figure 2. Scatter plot of the angles in the double aortic arch and right aortic arch with mirror-image branches

Figure 3. ROC curve: The area under ROC was 0.9853 (95% CI was 0.9609 to 1.010). When the cut-off value was greater than 62.8deg, the sensitivity was 95.5%, 95% CI: 77.2% - 99.9; the specificity was 96.9%, 95% CI: 89.3% - 99.6%.

Figure. 4 Bland-Altman plots showing the intra- (a) and inter- (b) observer variability for the angle measurements.