Investigating the characteristics of echocardiogram, surgical treatment, chromosome and prognosis for fetal right heart enlargement
A STROBE-compliant article

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Abstract

The prognosis of right heart enlargement varies according to different etiologies. The purpose of this study was to investigate the characteristics of echocardiogram, surgical treatment, chromosome and prognosis for fetal right heart enlargement.

The foetal echocardiogram was performed on 3987 pregnant women, and then 88 fetuses with right heart enlargement were identified. The data about prenatal and postnatal echocardiograms, postnatal cardiac surgical treatment, karyotype analysis and autopsy after induced labor were analyzed in the 88 fetuses.

Except the 1111 cases that had loss of follow-up, 2876 cases had complete data. Among the 2876 cases, right heart enlargement was identified in 88 fetuses. Of the 88 fetuses, 15 had total atrioventricular septal defect (unbalanced type: right ventricular dominance), 15 Ebstein's anomaly, 18 fallot tetrad, 14 double outlet right ventricle, 13 total anomalous pulmonary venous drainage, and 13 premature closure of ductus arteriosus. Chromosomal abnormality was found in 12 cases.

There are many etiological factors causing right heart enlargement. The prognosis is better in the fetuses with single heart malformation than in the fetuses who have extracardiac malformation or/and chromosomal abnormality besides heart malformation. Fetal echocardiography combined with karyotype analysis can provide important bases for evaluating the prognosis of fetuses with right heart enlargement.

Abbreviation: CI = confidence interval.

Keywords: chromosome abnormality, echocardiogram, foetus, prenatal diagnosis, right heart enlargement

1. Introduction

Fetal cardiac malformation with an incidence of 6–8‰ severely affects fetal growth, development and postnatal survival.[1] Fetal cardiac malformation is influenced by both genetic and environmental factors, and is strongly associated with chromosome abnormality.[2] During the fetal period, the 40% of blood from both superior and inferior vena cava enters the left atrium through foramen ovale and the remaining 60% of blood enters the right ventricle through tricuspid valve, so the blood volume is larger in the right heart than in the left heart. The prognosis of right heart enlargement varies according to different etiologies. The purpose of this study was to analyze the etiological factors of fetal right heart enlargement and provide a basis for evaluating the prognosis of the fetuses with right heart enlargement.

2. Materials and methods

All study methods were approved by the Ethics Committee of Henan Provincial Peoples Hospital. All the subjects enrolled in the study gave written informed consent to participate.

2.1. Subjects

A total of 3987 pregnant women with a age of $(29.28 \pm 7.32,$ mean $\pm$ standard deviation) years (range 16–47) and a gestation age of $(26.67 \pm 3.39,$ mean $\pm$ standard deviation) weeks (range 16–40) and from Henan Provincial Peoples Hospital and the Seventh Peoples Hospital of Zhengzhou, underwent fetal echocardiogram. The fetuses with complete data including prenatal and postnatal echocardiograms, postnatal cardiac surgical treatment, karyotype analysis and autopsy after induced labor were enrolled in this study.

2.2. Instrument

The fetal echocardiography was performed using GE Voluson E8 ultrasonic instrument with detecting head of RAB4–8, frequency of 4–8 MHz and the mode of Fetal Cardiac, or using Philips iE33

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ultrasonic instrument with detecting head of C5–1, frequency of 1–5 MHz and the mode of Fetal Echo. Postnatal echocardiography was performed using Philips iE33 ultrasonic instrument with detecting head of X5–1, frequency of 1–5 MHz and the mode of Pediatrics.

2.3. The diagnosis of fetal right heart enlargement

Fetal echocardiography was performed according to the *Standardized Guidelines about Fetal Echocardiography* recommended by American Echocardiogram Association.[3] The standard sections included abdominal transverse section, 4-chamber view, left ventricular outflow view, right ventricular outflow view, 3-vessel view, aortic arch view, ductal arch view, and caval long-axis view. The echocardiographic diagnosis of the right heart enlargement was made based on more than 95% confidence interval of normal transverse diameters of right atrium and right ventricle.[4] In details, the normal high limits of transverse diameter of the right atrium from 14 weeks of gestation to term were 4.87 mm (14 weeks), 5.65 mm (15 weeks), 6.42 mm (16 weeks), 7.17 mm (17 weeks), 7.92 mm (18 weeks), 8.65 mm (19 weeks), 9.37 mm (20 weeks), 10.08 mm (21 weeks), 10.77 mm (22 weeks), 11.46 mm (23 weeks), 12.13 mm (24 weeks), 12.79 mm (25 weeks), 13.44 mm (26 weeks), 14.08 mm (27 weeks), 14.70 mm (28 weeks), 15.32 mm (29 weeks), 15.92 mm (30 weeks), 16.51 mm (31 weeks), 17.09 mm (32 weeks), 17.66 mm (33 weeks), 18.21 mm (34 weeks), 18.76 mm (35 weeks), 19.29 mm (36 weeks), 19.81 mm (37 weeks), 20.32 mm (38 weeks), 20.82 mm (39 weeks) and 21.30 mm (40 weeks); and the normal high limits of transverse diameter of the right ventricle from 14 weeks of gestation to term were 3.72 mm (14 weeks), 4.53 mm (15 weeks), 5.32 mm (16 weeks), 6.10 mm (17 weeks), 6.86 mm (18 weeks), 7.62 mm (19 weeks), 8.35 mm (20 weeks), 9.08 mm (21 weeks), 9.79 mm (22 weeks), 10.49 mm (23 weeks), 11.17 mm (24 weeks), 11.84 mm (25 weeks), 12.50 mm (26 weeks), 13.14 mm (27 weeks), 13.77 mm (28 weeks), 14.38 mm (29 weeks), 14.98 mm (30 weeks), 15.57 mm (31 weeks), 16.14 mm (32 weeks), 16.70 mm (33 weeks), 17.25 mm (34 weeks), 17.78 mm (35 weeks), 18.30 mm (36 weeks), 18.81 mm (37 weeks), 19.30 mm (38 weeks), 19.78 mm (39 weeks) and 20.24 mm (40 weeks).

2.4. Karyotype analysis

Prenatal fetal karyotype analysis: Amniotic fluid (15 ml) was collected from each patient and inoculated into RPMI1640. The chromosomes were prepared by the routine method, and then underwent Giemsa staining followed by analysis of 30 mitotic phases under a microscope.

Postnatal karyotype analysis in newborns: Venous blood (3 ml) was collected from each newborn and inoculated into RPMI1640. The chromosomes were prepared by the routine method, and then underwent Giemsa staining followed by analysis of 30 mitotic phases under a microscope.

Karyotype analysis in aborted fetuses: Cord blood (3 ml) was collected from each aborted fetus and inoculated into RPMI1640. The chromosomes were prepared by the routine method, and then underwent Giemsa staining followed by analysis of 30 mitotic phases under a microscope.

2.5. Follow-up for fetal right heart enlargement

The data including prenatal and postnatal echocardiograms, postnatal cardiac surgical treatment, karyotype analysis of chromosome and autopsy after induced labor were collected. Prenatal karyotype analysis was performed using fetal amniotic fluid. If the prenatal karyotype analysis failed to be carried out, karyotype analysis was performed using cord blood in the fetuses undergoing induced labor or using venous blood in the fetuses undergoing cardiac surgical treatment.

2.6. Repeatability tests between and within observers

For the inside diameters of fetal left atrium, left ventricle, right atrium and right ventricle, Repeatability tests between and within observers were performed using the Bland-Altman method.

3. Results

3.1. Clinical data

In the 3987 pregnant women, their age was (29.28 ± 7.32, mean ± standard deviation) years (range 16–47) and their gestation age was (26.67 ± 3.39, mean ± standard deviation,) weeks (range 16–40). Of the 3987 cases, 2876 cases (72.13%) had complete data and 1111 cases (27.87%) missed follow-up.

3.2. Analysis of etiological factors, chromosome and prognosis for fetal right heart enlargement

Among the 2876 cases, right heart enlargement was identified in 88 fetuses. Of the 88 fetuses, 15 had total atrioventricular septal defect (unbalanced type: right ventricular dominance), 15 Ebstein's anomaly, 18 fallot tetrad, 14 double outlet right ventricle, 13 total anomalous pulmonary venous drainage, and 13 premature closure of ductus arteriosus. Of the 15 fetuses with total atrioventricular septal defect, 10 had no other malformations, 2 aortic coarctation, 1 digestive system abnormalities, and 2 central nervous system malformation; 3 21-trisomy syndrome and 12 normal chromosomes; 6 underwent induced labor and 9 received cardiac surgical correction with good prognosis. Of the 15 fetuses with Ebstein's anomaly, 12 had no other malformations and 3 had pulmonary artery stenosis; one had 13-trisomy syndrome, 1 21-trisomy syndrome and 13 normal chromosomes; 6 underwent induced labor, 2 received cardiac surgical correction with good prognosis and 7 were followed up. Of the 18 fetuses with fallot tetrad, 15 had no other malformations and 3 had absence of pulmonary valve; 4 had 21-trisomy syndrome and 14 had normal chromosomes; 8 underwent induced labor, 7 received radical correction and 3 underwent palliative surgery with good prognosis. Of the 14 fetuses with double outlet right ventricle, 7 had ventricular septal defect, 4 pulmonary artery stenosis, 2 transposition of conducting arteries and 1 intact ventricular septum; 1 had 18-trisomy syndrome, 1 13-trisomy syndrome and 12 normal chromosomes; 4 underwent induced labor, 9 received radical correction and 1 underwent palliative surgery with good prognosis. Of the 13 fetuses with total anomalous pulmonary venous drainage, 9 had no other malformations, 1 had pulmonary vein stenosis and 3 digestive system abnormalities; 1 had cat eye syndrome and 12 had normal chromosomes; 3 underwent induced labor, 9 received cardiac surgical correction with good prognosis and 1 died 5 days after surgical correction (postnatal 28 days). Of the 13 fetuses with premature closure of ductus arteriosus, 13 all had no other malformations but had normal chromosomes and normal postnatal echocardiogram. The etiological factors, chromosome and prognosis for right

Table 1

Etiological factors, chromosome and prognosis of fetal right heart enlargement.

Etiological factors	Cases (n)	Combined with other malformations	Chromosome	Follow-up
Total atrioventricular septal defect (right ventricular dominance)	10	No	Two cases with 21-trisomy syndrome exhibiting unusual facies with wide eye distance, flat nasal root and blepharophimosis	Two cases with 21-trisomy syndrome underwent induced labor, 8 cases received successful surgical correction
	2	Aortic coarctation	Normal	One case underwent induced labor and another received successful surgical correction and plastic operation
	1	Digestive system abnormalities	Normal	Induced labor
	2	Central nervous system malformations	One case with 21-trisomy syndrome exhibiting unusual facies with wide eye distance, flat nasal root and blepharophimosis	Two cases underwent induced labor
Ebstein's anomaly	12	No	Normal	Three cases underwent induced labor, 2 cases received surgical correction and 7 cases did not receive surgery
	3	Pulmonary artery stenosis	One case with 13-trisomy syndrome exhibiting microcephaly, narrow eye distance and ear deformity, and one case with 21-trisomy syndrome exhibiting unusual facies with wide eye distance, flat nasal root and blepharophimosis	All the 3 cases underwent induced labor
Fallot tetrad	15	No	Four cases with 21-trisomy syndrome exhibiting unusual facies with wide eye distance, flat nasal root and blepharophimosis	Six cases underwent induced labor, 6 cases received radical operation and 3 cases received palliative operation
	3	Absence of pulmonary valve	Normal	Two cases underwent induced labor and one case received surgical correction
Double outlet right ventricle	7	Ventricular septal defect	One case with 18-trisomy syndrome exhibiting occipital posterior process, narrow forehead, microcephaly, wide anterior fontanelle, low ear with malformation, short rima oculi, small submaxilla and clenched fist	Two cases underwent induced labor and 5 cases received corrective provedure
	4	Pulmonary artery stenosis	Normal	Three cases received radical operation and one case received bilateral Glenn operation
	2	Great artery transposition	One case with 13-trisomy syndrome exhibiting microcephaly, narrow eye distance and ear deformity	One case underwent induced labor and one case received surgical correction
	1	Intact ventricular septum	Normal	Induced labor
Total anomalous pulmonary venous drainage	2	No	Normal	All the 9 cases received successful procedure
	1	Pulmonary vein stenosis	Cat eye syndrome (chromosome 22-long arm-trisomy syndrome) exhibiting unusual facies with large nostril, microcrania, wide eye distance and fistula before ears	The case received surgical correction and 5 days later died
	3	Digestive system abnormalities	Normal	All the 3 cases underwent induced labor
Premature closure of ductus arteriosus	13	No	Normal	Postnatal ultrasonic cardiogram was normal in the 13 cases

heart enlargement are shown in Table 1 and Figures 1–6. The diameter of each heart chamber in the 88 fetuses is shown in Table 2.

3.3. Analysis of consistency

Bland-Altman indicated good repeatability in the measurement of inside diameters of left atrium, left ventricle, right atrium and right ventricle within and between observers. For the left atrium, the 95% confidence interval (CI) was [−2.383, 2.233] within observers, and the 95% CI was [−2.985, 2.275] between observers. For the right atrium, the 95% CI was [−1.837, 1.569] within observers, and the 95% CI was [−2.475, 2.025] between observers. For the left ventricle, the 95% CI was [−2.089, 1.870] within observers, and the 95% CI was [−2.263, 2.423] between observers. For the right ventricle, the 95% CI was [−2.633, 2.282] within observers, and the 95% CI was [−2.594, 2.004] between observers (Figs. 7–14).

Table 2

The diameter of each heart chamber in the 88 fetuses with right heart enlargement ($\bar{x} \pm s$) (n = 88, mm).

Gestation weeks	Case (n)	Left atrium	Right atrium	Left ventricle	Right ventricle
16	2	4.53 ± 0.14	6.62 ± 0.20	3.80 ± 0.21	5.97 ± 0.08
17	2	5.08 ± 0.08	7.35 ± 0.19	4.56 ± 0.28	6.80 ± 0.19
18	3	6.59 ± 0.21	8.23 ± 0.20	5.23 ± 0.25	6.98 ± 0.23
19	2	6.42 ± 0.17	8.95 ± 0.22	5.69 ± 0.15	7.89 ± 0.12
20	2	7.99 ± 0.17	9.88 ± 0.19	6.56 ± 0.27	8.98 ± 0.14
21	3	8.65 ± 0.21	10.24 ± 1.98	7.98 ± 0.20	9.67 ± 0.18
22	4	8.79 ± 0.19	10.97 ± 0.26	8.45 ± 0.30	10.03 ± 0.12
23	6	9.48 ± 0.15	11.69 ± 0.22	8.88 ± 0.25	10.78 ± 0.17
24	9	9.97 ± 0.28	12.43 ± 0.24	9.43 ± 0.26	11.81 ± 0.22
25	8	10.49 ± 0.29	12.99 ± 0.22	9.78 ± 0.17	11.98 ± 0.25
26	8	10.97 ± 0.17	13.69 ± 0.29	10.43 ± 0.19	12.76 ± 0.27
27	6	11.59 ± 0.27	14.34 ± 0.24	11.17 ± 0.19	13.45 ± 0.27
28	5	11.95 ± 0.21	14.97 ± 0.11	11.23 ± 0.15	13.89 ± 0.09
29	3	12.39 ± 0.13	15.65 ± 0.32	11.45 ± 0.17	14.65 ± 0.16
30	2	12.79 ± 0.23	16.37 ± 0.11	12.69 ± 0.23	15.45 ± 0.16
31	2	13.17 ± 0.15	16.78 ± 0.17	12.98 ± 0.17	15.78 ± 0.09
32	3	14.64 ± 0.16	18.32 ± 0.23	13.43 ± 0.23	16.67 ± 0.25
33	2	14.98 ± 0.23	18.54 ± 0.19	13.65 ± 0.16	16.93 ± 0.25
34	3	15.37 ± 0.18	18.65 ± 0.23	14.87 ± 0.17	17.56 ± 0.17
35	2	16.72 ± 0.22	18.87 ± 0.21	14.98 ± 0.22	17.97 ± 0.26
36	2	17.12 ± 0.16	19.54 ± 0.16	15.45 ± 0.08	18.68 ± 0.22
37	3	17.38 ± 0.26	19.95 ± 0.19	15.65 ± 0.08	19.04 ± 0.22
38	2	18.67 ± 0.24	20.65 ± 0.21	12.76 ± 0.18	19.67 ± 0.07
39	2	18.95 ± 0.19	20.91 ± 0.14	12.87 ± 0.22	20.21 ± 0.91
40	2	19.29 ± 0.17	22.32 ± 0.16	12.98 ± 0.14	21.43 ± 0.21
Total	88	12.16 ± 0.16	14.76 ± 0.17	10.68 ± 0.18	13.08 ± 0.17

4. Discussion

The development of fetal heart structure has been completed in the eighth gestational weeks.[5] Heart malformations are mainly caused by the abnormalities occurring during embryo development. With the improvement of ultrasonic equipment, fetal echocardiography can evaluate cardiac structure, function and hemodynamics. Prenatal diagnosis can provide counseling for pregnant women and their family.

In this study, the 88 fetuses with right heart enlargement included 15 with total atrioventricular septal defect (unbalanced type: right ventricular dominance), 15 with Ebstein's anomaly, 18 with fallot tetrad, 14 with double outlet right ventricle, 13 with total anomalous pulmonary venous drainage, and 13 premature closure of ductus arteriosus. Based on cardiac abnormalities and whether combined with extracardiac abnormalities or/and chromosome abnormality, stratified analysis indicated that in the 88 fetuses with right heart enlargement, single heart malformation occurred in 62 fetuses including 58 who were followed up or received surgical correction with good prognosis and 4 who underwent induced labor, multiple heart malformations occurred in 9 fetuses including 4 who received surgical correction with good prognosis and 5 who underwent induced labor, heart malformation combined with extracardiac malformation occurred in 5 fetuses all receiving induced labor, heart malformation combined with chromosomal abnormality occurred in 9 fetuses including 8 who underwent induced labor and 1 died 5 days after surgical correction (postnatal 28 days), and heart malformation combined with both extracardiac malformation and chromosomal abnormality occurred in 3 fetuses all receiving induced labor. Pont SJ et al[6] studied birth defects associated with trisomy 18 and trisomy 13 among US liveborn infants using the Healthcare Cost and Utilization Project's Kids' Inpatient Database and Nationwide Inpatient Sample, 2 large, current and nationally representative databases. The occurrence of 39 commonly reported comorbid birth defects among infants with trisomies 18 and 13 was compared to the occurrence of malformations among newborns without trisomies. The prevalences of trisomy 18 and 13 were 1.29/10,000 and 0.85/10,000 live births, respectively. Among infants with trisomy 18, 61% were female and 45.4% with heart defects. Among those with trisomy 13, 53% were female, 38.4% had heart defects, 24.5% had orofacial anomalies, and 11.2% had central nervous system abnormalities. More than half of the newborns with both conditions died prior to discharge. This updated information can be conducive to clinical decision-making. ICD-9-CM diagnosis codes for data from the Healthcare Cost and Utilization Project were used to identify infants with and without Down syndrome (DS), and to classify birth defects.[7] The study population consisted of liveborn infants discharged from the hospital from 1993 through 2002. Odds ratio (OR) for the association between the occurrence of congenital malformations and the presence of DS were computed using logistic regression models for survey data. Discharge data included 11,372 DS and 7,884,209 non-DS births, representing national estimates of 43,463 DS and 39,716,469 non-DS births respectively. In addition to congenital heart defects that co-occurred most often in DS infants compared to infants without DS, the risks for gastrointestinal malformations (OR 67.07), genitourinary malformations (OR 3.62), orofacial malformations (OR 5.63), and abdominal wall malformations (OR 3.25) were also elevated in infants with DS. There was no difference in the risk of spina bifida between infants with and without DS. Our results were consistent with the results above, namely that the
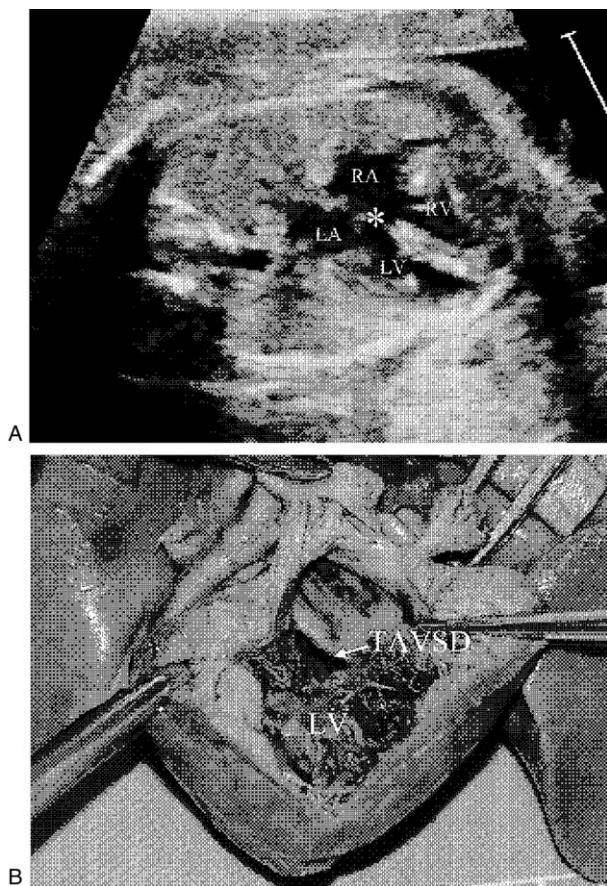
Figure 1. Complete atrioventricular septal defect. (a) The 4-chamber view of fetal echocardiography shows right heart enlargement combined with TAVSD in 23 gestational weeks. (b) Fetal cardiac autopsy displays TAVSD. * indicates complete atrioventricular septal defect. LA = left atrium, LV = left ventricle, RA = right atrium, RV = right ventricle and TAVSD = total atrioventricular septal defect.
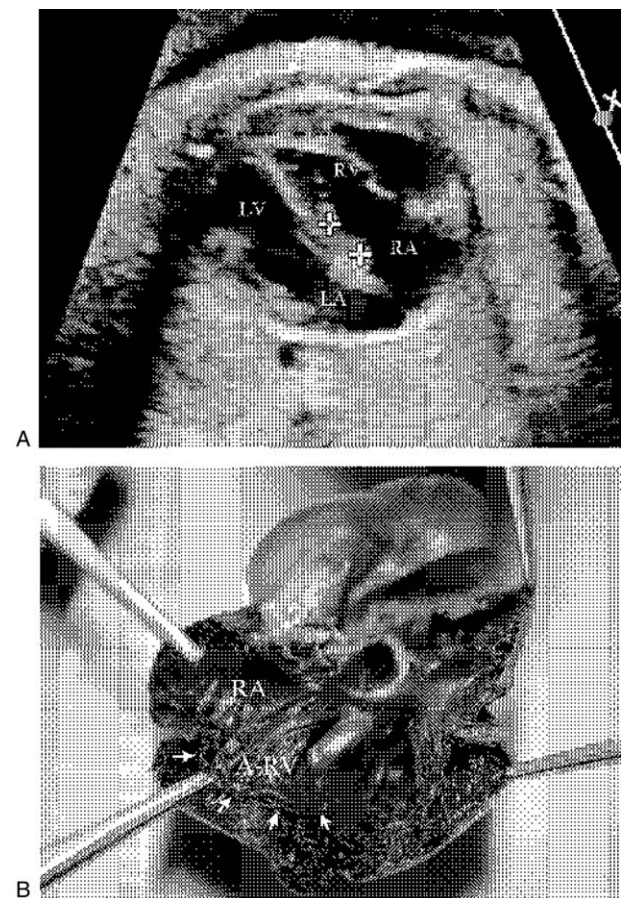

Figure 2. Ebstein's anomaly. (a) The four-chamber view of fetal echocardiography shows right heart enlargement combined with Ebstein's anomaly in 22 gestational weeks. (b) Fetal cardiac autopsy displays Ebstein's anomaly. ** and ↑ indicate Ebstein's anomaly. A-RV = atrialized right ventricle, LA = left atrium, LV = left ventricle, RA = right atrium and RV = right ventricle.

prognosis is poor in the fetuses that have heart malformation combined with chromosome abnormality.

In the 15 fetuses with total atrioventricular septal defect (unbalanced type: right ventricular dominance), except the 3 with 21-trisomy syndrome including 1 with digestive system abnormalities and 2 with central nervous system malformations, other fetuses received surgical correction and obtained better therapeutic effects. In total atrioventricular septal defect (unbalanced type: right ventricular dominance), the common atrioventricular valve is located at the right of the interventricular septum, so the blood from heart atrium directly flows into the right ventricle with right heart enlargement. In anatomical structure, the common atrioventricular valve does not match cardiac muscle mass. In total atrioventricular septal defect (unbalanced type: right ventricular dominance), right ventricle pressure and pulmonary pressure are equal to left ventricular pressure due to left-to-right shunt, and fetuses will have progressive pulmonary hypertension after birth.[8] Fetal pulmonary arterial pressure may markedly increase within a few months after birth, especially in the fetuses with 21-trisomy syndrome.[9,10] Common atrioventricular valve regurgitation increases ventricular volume load, aggravating pulmonary hypertension and congestive heart failure. In this study, there were 15 cases with Ebstein's anomaly. In the 15 cases with Ebstein's anomaly, 2 had chromosome

abnormalities including 1 with 13- trisomy syndrome and 1 with 21- trisomy syndrome. Of the 15 cases with Ebstein's anomaly, 6 underwent induced labor, 7 did not receive surgery due to no complications such as heart failure, cardiac dilatation and severe arrhythmia, and 2 received surgical correction due to heart failure, progressive cyanosis and severe arrhythmia 6 to 12 months after birth. In Ebstein's anomaly, the anterior leaflet of tricuspid valve enlarges, the parietal leaflet and posterior leaflet move down, and the tricuspid valve is attached to the right ventricular wall, leading to right atrial enlargement.[11,12] During fetal period, increased right atrial pressure caused by acleistocardia and severe tricuspid valve regurgitation leads to right-to-left shunt. In early stage after birth, the infants have cyanosis due to right-to-left shunt. When heart function falls to grade III or IV, the infants will have more severe cyanosis and cardiac enlargement (the ratio of heart to chest >0.65). Prognosis is poor in the infants with Ebstein's anomaly because severe arrhythmia can be life-threatening.[13,14] Therefore, in this study, of the 15 cases with Ebstein's anomaly, 3 with single severe downward displacement of tricuspid valve, 1 with intracardiac abnormalities and 2 with both intracardiac abnormalities and chromosome abnormality all underwent induced labor. In the 18 cases with fallot tetrad, there were 4 cases with 21-trisomy syndrome. Of the 18 cases with fallot tetrad, 8 underwent
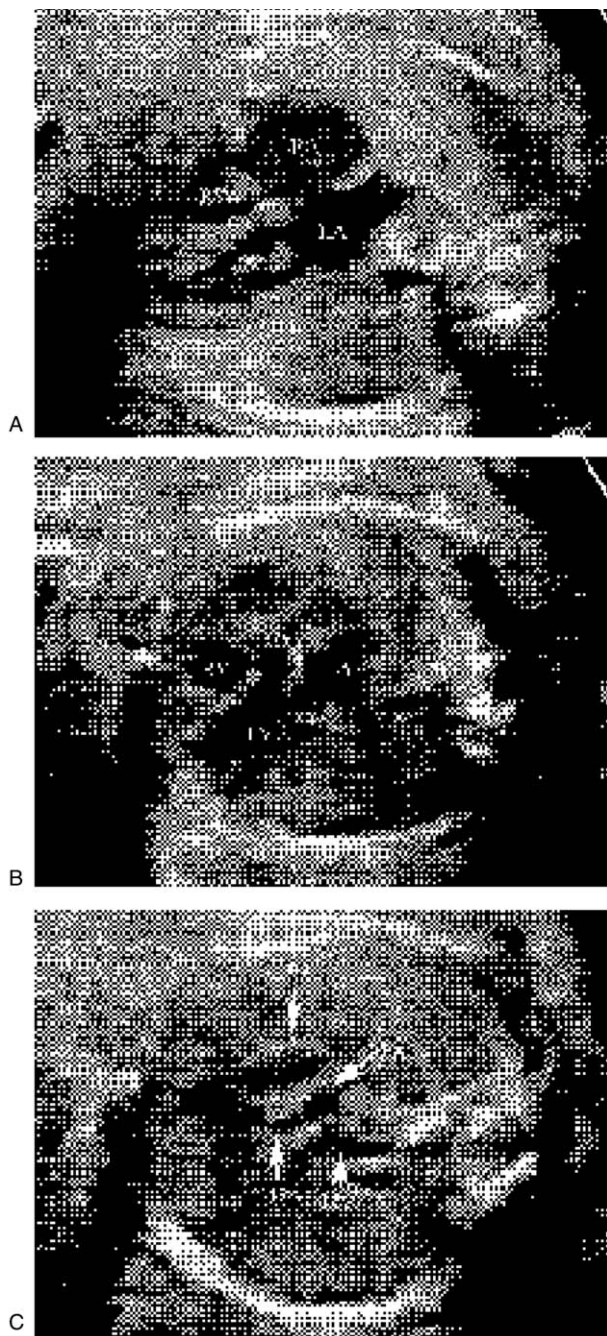
Figure 3. Fallot tetrad in 21 gestational weeks. (a) The 4-chamber view of fetal echocardiography shows fetal right heart enlargement. (b) Ventricular septal defect combined with aortic overriding interventricular septum. (c) 3-vessel view of fetal echocardiography shows stenoses of MPA, LPA and RPA. * indicates ventricular septal defect. AO = aorta, LA = left atrium, LV: left ventricle, LPA = left pulmonary artery, MPA = main pulmonary artery, RA = right atrium, RPA = right pulmonary artery and RV = right ventricle.
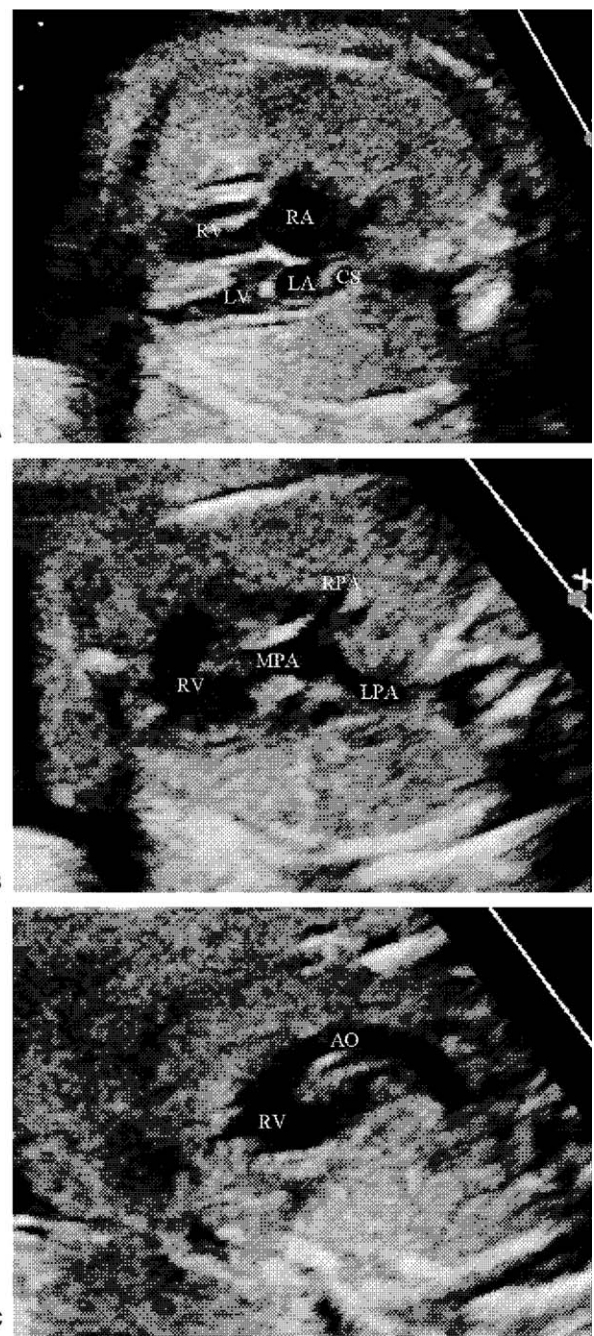
Figure 4. Double outlet right ventricle in 23 gestational weeks. (a) The 4-chamber view of fetal echocardiography shows right heart enlargement. (b) The pulmonary artery originates from the right ventricle. (c) The AO originates from the right ventricle. AO = aorta, CS = coronary sinus, LA = left atrium, LPA = left pulmonary artery, LV = left ventricle, MPA = main pulmonary artery, RA = right atrium, RPA = right pulmonary artery and RV = right ventricle.

induced labor, 6 received radical operation due to progressive cyanosis 6 to 12 months after birth, 3 received B-T palliative operation due to severe delayed growth 5 to 9 months after birth and 1 received surgical correction 8 months after birth. Fallot tetrad shows right heart enlargement, thick right ventricular anterior wall, ventricular septal defect, aortic overriding, right ventricular outflow tract obstruction and/or pulmonary artery stenosis. Most infants with fallot tetrad only have mild cyanosis

after birth; with the extension of time, cyanosis is progressive 6 to 12 months after birth but the development of pulmonary valve annulus is good. A few infants with fallot tetrad have severe cyanosis soon after birth due to outflow obstruction caused by dysplasias of pulmonary valve annulus and/or pulmonary artery.[15,16] The presence of thick body-pulmonary arterial collateral branch can lead to congestive failure.[17] The absence of pulmonary valve can result in respiratory insufficiency.[18,19]
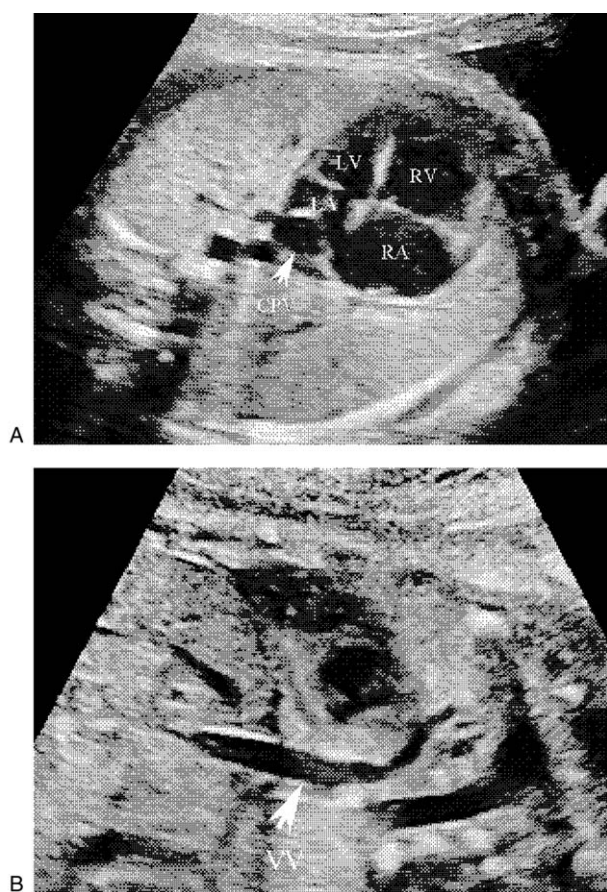
Figure 5. Total anomalous pulmonary venous drainage (infracardiac type) in 24 gestational weeks. (a) The 4-chamber view of fetal echocardiography shows right heart enlargement combined with CPV. (b) The CPV descends to liver through VV. CPV = common pulmonary vein, LA = left atrium, LV = left ventricle, RA = right atrium, RV = right ventricle, VV = vertical vein.

In this study, there were 14 cases with double outlet right ventricle. In the 14 cases with double outlet right ventricle, there were 2 had chromosome abnormalities including one with 18-trisomy syndrome and another with 13-trisomy syndrome. Of the 14 cases with double outlet right ventricle, 2 had ventricular septal defect with long distance between 2 large arteries and underwent induced labor; 5 has subaortic ventricular septal defect, received surgical correction 8 to 12 months after birth and obtained better therapeutic effects; 4 had pulmonary artery stenosis (3 received surgical correction 6 to 12 months after birth and 1 received bilateral Glenn operation 3 months after birth with better therapeutic effects); 2 had great artery transposition (1 underwent induced labor and 1 received surgical correction 6 months after birth with better therapeutic effects); and 1 had intact ventricular septum and underwent induced labor. In the prenatal diagnosis of double outlet right ventricle, we mainly evaluate ventricular septal defect size, position relation between heart ventricle and large artery and development of pulmonary artery, because they are strongly associated with postnatal clinical symptoms. Non-restrictive ventricular septal defect exhibits congestive heart failure in the absence of pulmonary artery stenosis, severe cyanosis in the presence of pulmonary artery stenosis, and early cyanosis and congestive heart failure in the presence of great artery transposition.[20,21] The aim of surgical intervention for double outlet right ventricle is to achieve
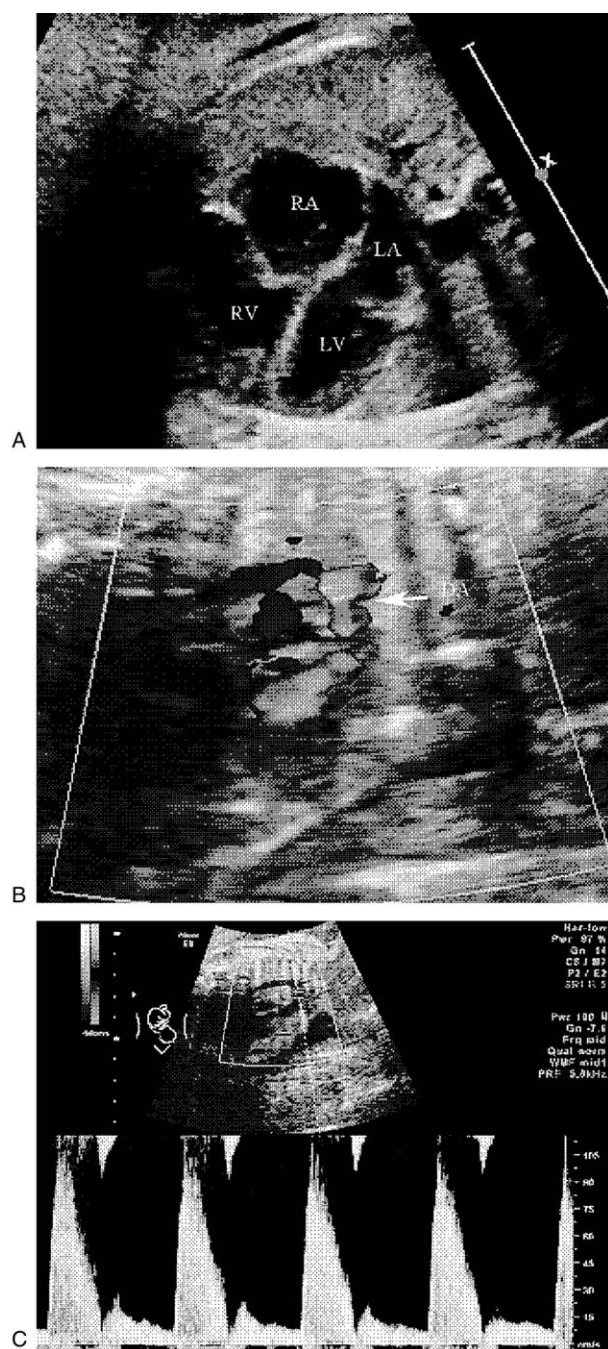

Figure 6. Premature closure of ductus arteriosus in 34 gestational weeks. (a) The 4-chamber view of fetal echocardiography shows right heart enlargement. (b) The aortic arch view of fetal echocardiography shows that the signal of blood flow becomes thin in the DA. (c) The blood flow accelerates in the DA. DA = ductus arteriosus, LA = left atrium, LV = left ventricle, RA = right atrium, RV = right ventricle.

double ventricular correction, namely the left ventricle is connected to the aorta, the right ventricle is connected to the pulmonary artery and the ventricular septal defected is repaired. The surgical schema for double outlet right ventricle is dependent on anatomic structure. The type of double outlet right ventricle is very important for evaluating prognosis. Of the 13 cases with total anomalous pulmonary venous drainage, 1 case had cat eye syndrome and received surgical correction 28 days after birth
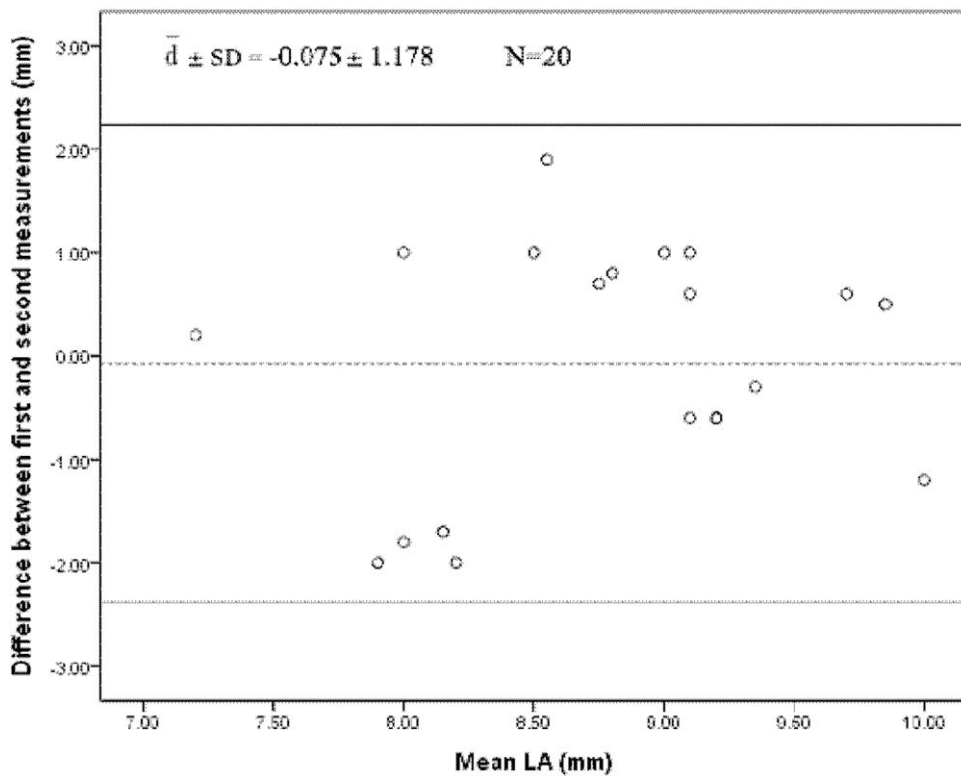
Figure 7. Repeatability in the measurement of the left atrium within observers.
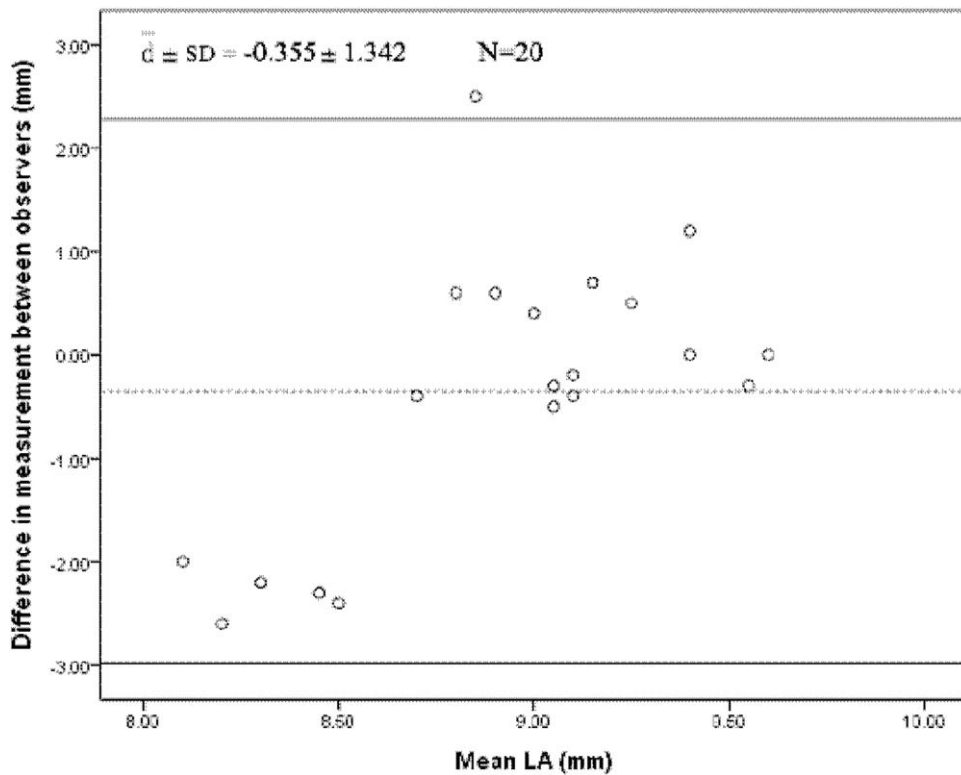

Figure 8. Repeatability in the measurement of the left atrium between observers.
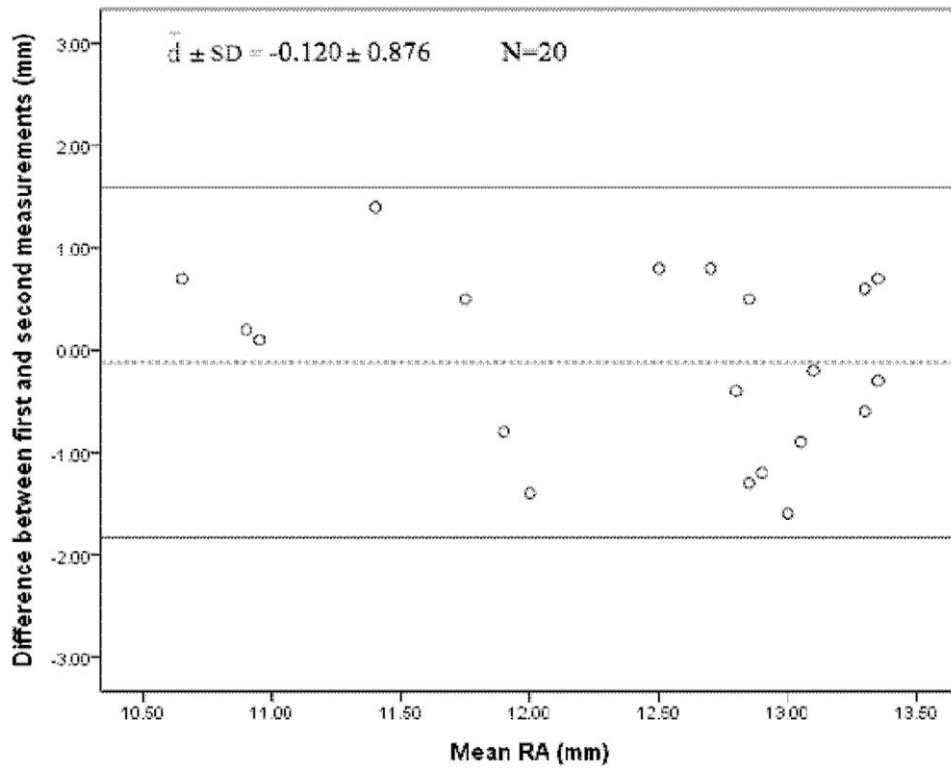
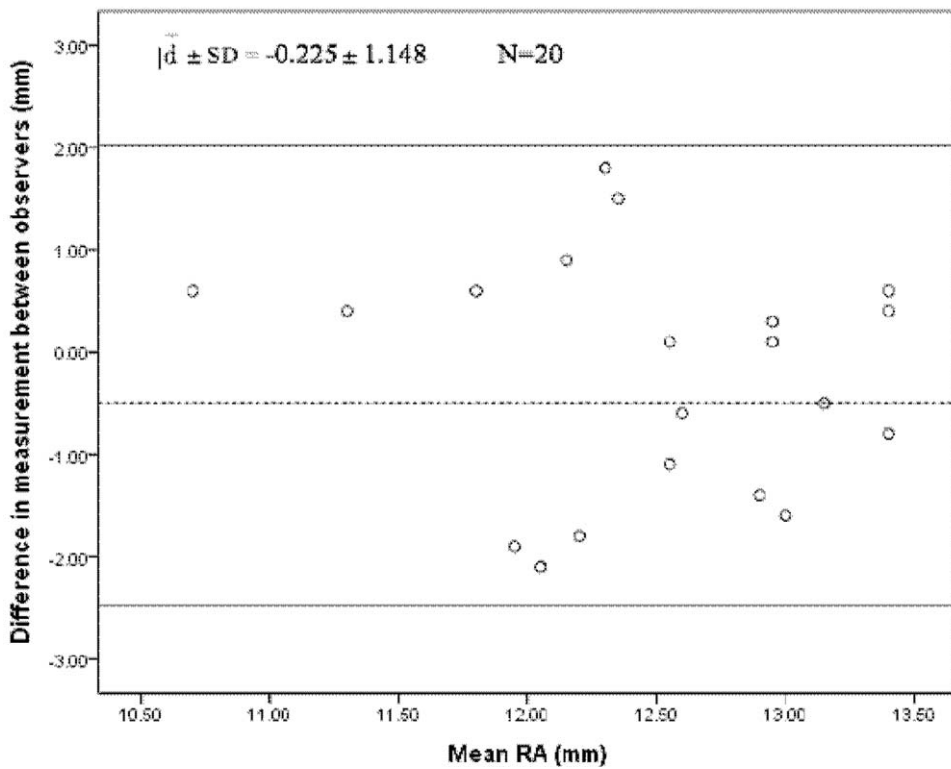**Figure 9.** Repeatability in the measurement of the right atrium within observers.

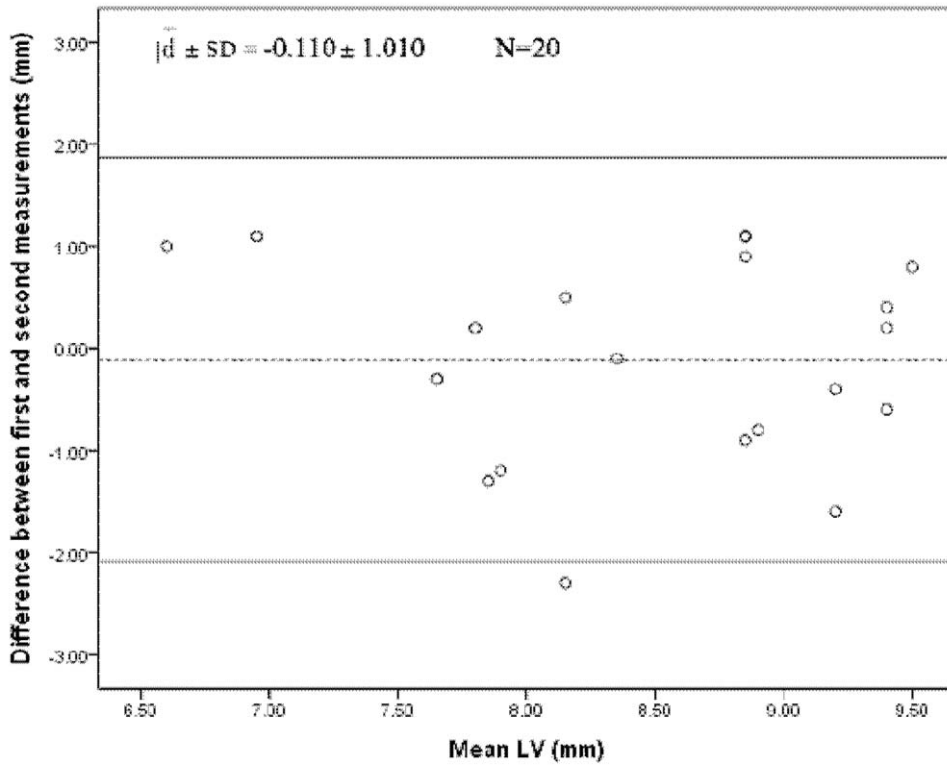**Figure 10.** Repeatability in the measurement of the right atrium between observers.

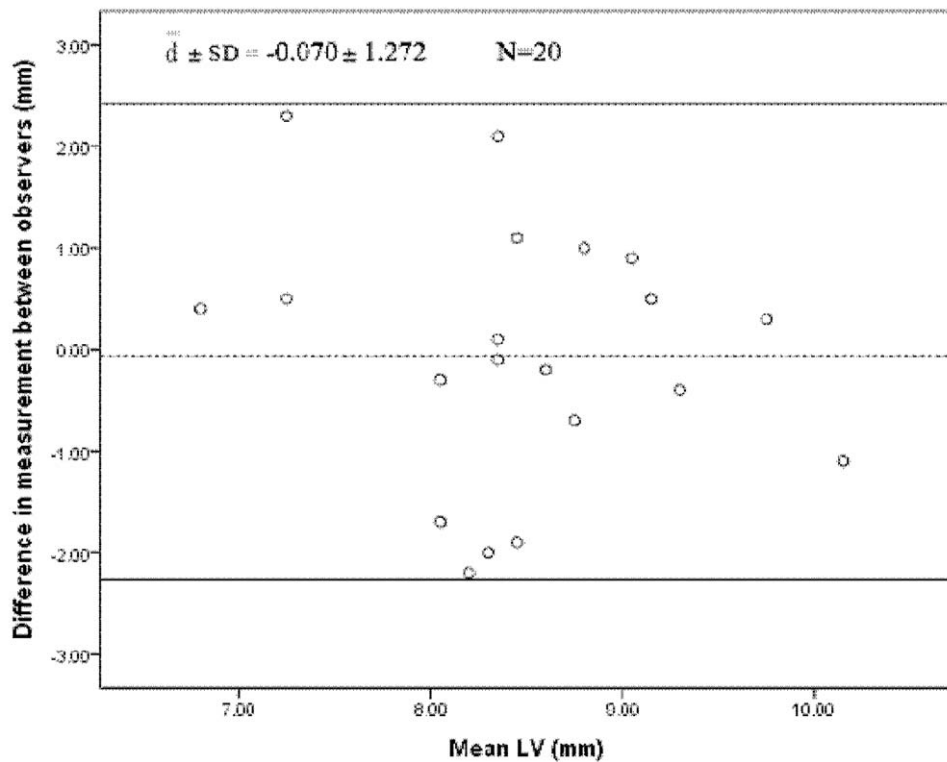**Figure 11.** Repeatability in the measurement of the left ventricle within observers.

Figure 12. Repeatability in the measurement of the left ventricle between observers.
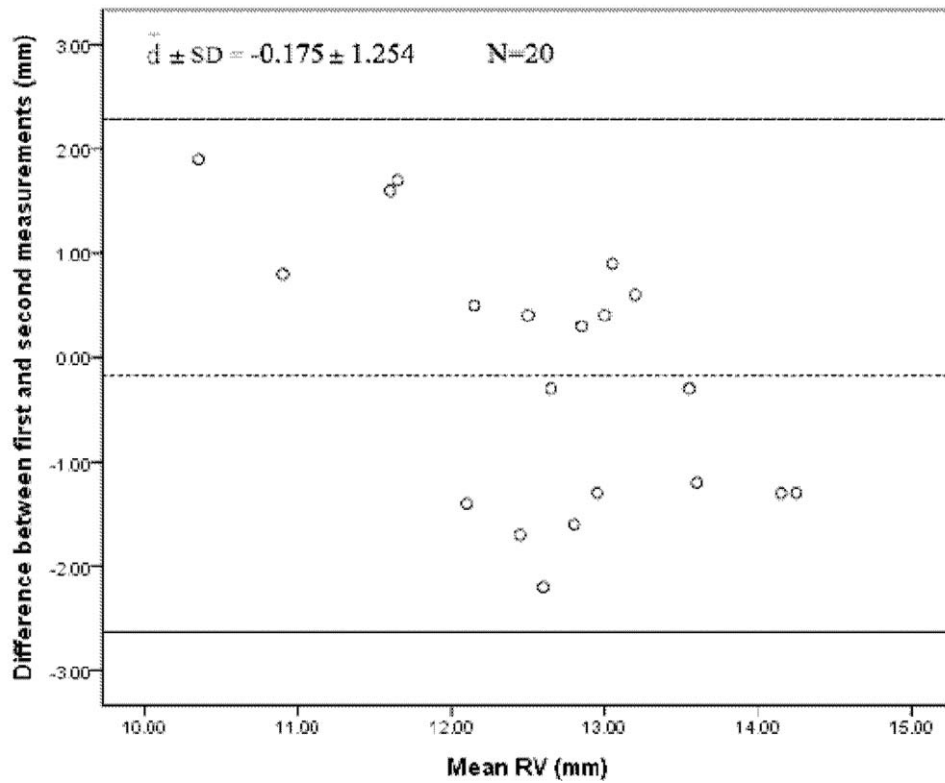
Figure 13. Repeatability in the measurement of the right ventricle within observers.
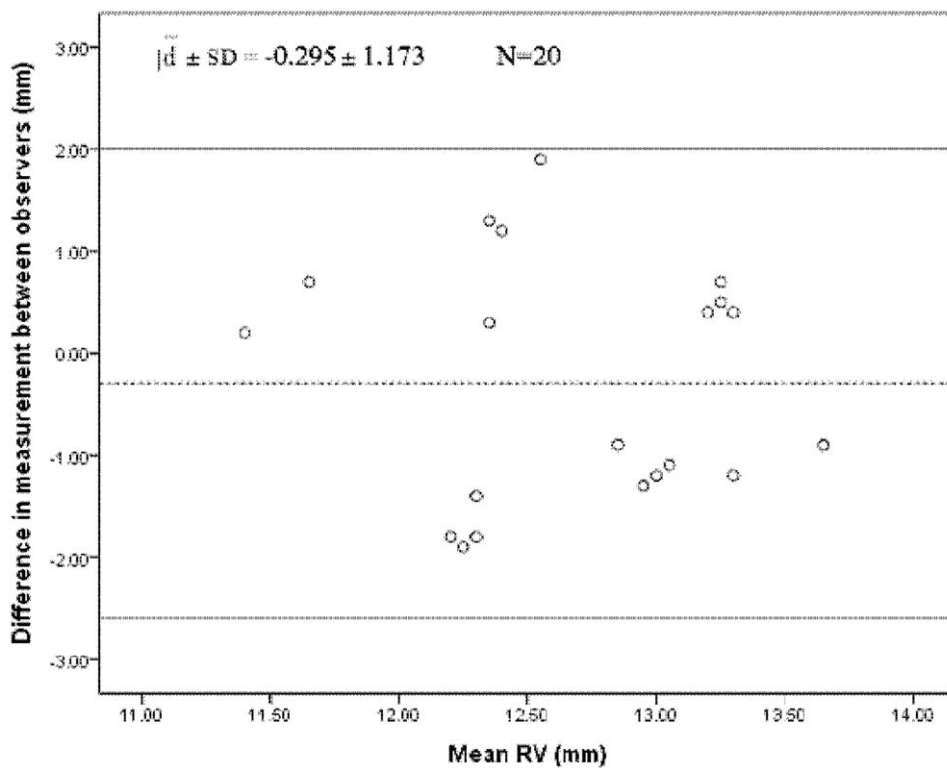

Figure 14. Repeatability in the measurement of the right ventricle between observers.

followed by death 5 days later; 9 cases without other malformations received successful surgical correction within 3 months after birth; and 3 cases with digestive system abnormalities underwent induced labor. In total anomalous pulmonary venous drainage, pulmonary venous blood flows into the right heart system, and then enters the left heart through foramen ovale, leading to right heart enlargement. The fetuses with total anomalous pulmonary venous drainage will have cyanosis after birth, and their prognoses are related to the presence of other malformations, and the obstructed degrees of pulmonary venous return and atrial shunt.[22,23] Although total anomalous pulmonary venous drainage can cause hemodynamic instability and physiological disorder; if pulmonary hypertension is actively treated and surgical correction is performed based on accurate diagnoses for anatomic features and other malformations, fetal prognosis will be good. Premature closure of ductus arteriosus can lead to right heart enlargement, compensatory thickening of the right ventricular wall, tricuspid valve regurgitation and pulmonary valve regurgitation. The ductus arteriosus exhibits a funnel-like change, and Doppler shows systolic (200–300 cm/s) and diastolic turbulence (over 35 cm/s).[24,25] In this study, there were 13 cases with premature closure of ductus arteriosus who all had no other malformations. They were carefully observed and were smoothly born. Postnatal echocardiography indicated that tricuspid valve regurgitation disappeared, the right heart returned to normal limits and heart function was normal. It should be diagnosed as premature closure of ductus arteriosus that fetal echocardiography shows tricuspid valve regurgitation and funnel-like ductus arteriosus with high flow rate at the absence of other malformations. Early diagnosis and close follow-up are conducive to evaluating fetal prognosis.

There are some limitations in this study. In this study, the sample size is relatively small. The duration of postoperative follow-up is short. Chromosomal microarray was not performed when karyotype was normal. These should be improved in future studies.

5. Conclusion

In summary, there are many etiological factors causing right heart enlargement. Based on cardiac abnormalities and whether combined with extracardiac abnormalities or/and chromosome abnormality, stratified analysis suggests that the prognosis of single heart malformation is good, but the prognosis of combined extracardiac malformation or/and chromosome abnormality besides heart malformation is poor. Fetal echocardiography combined with karyotype analysis can provide important bases for evaluating the prognosis of fetuses with right heart enlargement.

Author contributions

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