Strategies for Diagnosis of Fetal right atrium dilation: Based on fetal cardiac anatomy and hemodynamics

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Abstract

Background

Fetal right atrium (RA) dilation is frequently detected in routine screenings while it remains a challenge to clarify the reasons. This study aimed to analyze the cardiac anatomy and hemodynamics of fetal RA dilation and the changes of hemodynamic indexes.

Methods

420 fetuses with RA dilation were included, which were classified into 4 types: volume overload (Group A, n=117), pressure overload (Group B, n=85), Ebstein's anomaly (Group C, n=16), and physiological enlargement (Group D, n=202). All the types was divided into two control groups according to different gestational weeks (19-31 gestational weeks and 32-36 gestational weeks). The ratio of RA and left atrium (RA/LA) were measured at Four-chamber view (4CV) . Peak velocity of tricuspid regurgitation (V TR) was recorded in each diseases.

Results

RA/LA in 19-31GW were: A: 1.45±0.24, B: 1.28±0.15, C: 1.22±0.10, D: 1.28±0.18. RA/LA in 32-36GW were: A: 1.68±0.25, B: 1.46±0.23, C: 1.64±0.19, D: 1.45±0.27. V TR in Group B (3.29±0.58 m/s) was higher than that in Group A (1.85±0.49 m/s), C (1.86±0.22 m/s), and D (0.88±0.45 m/s), respectively. As for V TR, there was statistical significance among the ductus arteriosus anomalies (3.98±0.41 m/s), the pulmonary artery anomalies (3.03±0.38 m/s) and the restrictive FO (2.23±0.30 m/s) (all $P<0.05$).

Conclusions

We proposed a protocol by which fetal cardiac anatomy and hemodynamics was used to clarify the reasons of fetal RA dilation. We compared the degree of right atrial enlargement in different types of diseases. We also provided a reference value of V TR for each type of reasons of RA dilation.

Background

Congenital heart disease (CHD), accounting for about 0.4–1.3% of all live births [1–4], is the most common congenital malformation leading to perinatal morbidity and mortality and is considered the leading cause of death in newborn with congenital anomalies [5–7]. Undoubtedly, fetal

echocardiography plays an increasingly important role in prenatal diagnosis of fetal cardiac malformations [8]. Right atrium (RA) dilation is frequently detected in routine screenings or fetal echocardiograms while it remains a challenge for sonographers to clarify the reasons of the enlarged chamber, either a normal physiological sign or a secondary event caused by intra-cardiac or extra-cardiac anomalies. In fact, many cardiac abnormalities have an enlarged RA as an associated sign which attracts attention of sonographers rather than the deficiency itself [9]. In the case of fetal pulmonary valve atresia with a well-developed pulmonary artery, the abnormal valve is not evident enough to be observed at first glance while an enlarged RA together with tricuspid regurgitation (TR) could often be identified during routine obstetric examinations. If the fetus is referred to a further examination by an echocardiography specialist, the correct diagnosis may be reached. Unfortunately, many scans just stop here with the cardiac lesions resulting in RA dilation not detected, especially in late pregnancy when enlarged RA is always considered as a normal physiological sign. It is urgent to propose a systematic method valuable for the evaluation of fetal RA dilation. In the current study, we presented data from a 10-year cohort of cases with echocardiographic findings. We summarized the reasons of fetal RA dilation based on the abnormal cardiac hemodynamics and structural anomalies.

1. Materials And Methods

1.1. Study subjects

We retrospectively reviewed the image data obtained during routine obstetric examinations and fetal echocardiogram from the fetal screening center and echocardiography center in our hospital from Jan 2007 to Dec 2016. We searched our database in the diagnosis including RA dilation and found 464 fetuses of the review. Outcome data was obtained from hospital records (postnatal echocardiography, autopsy or operation) and phone-call follow up. In total, 420 fetuses with confirmed diagnosis were included in the current study. All the fetuses were singletons. As gestational age might affect the evaluation of RA dilation, the fetuses were divided into two groups according to gestational age (gestational weeks, GW: 19–31, and 32–36). Fetal biparietal diameter and femur length were used to determine gestational age. RA dilatation between 19 and 31 gestational weeks was defined an estimated RA/LA $>$ 1.1, 32 gestational weeks and above was defined $>$ 1.2, established by Tan J, et al

[10].

This study was approved by the Ethics Committee of Shengjing Hospital of China Medical University. Written informed consent was obtained from the parents for publication of clinical details, clinical images, and videos.

1.2. Fetal Cardiac Examination

All fetuses with normal or abnormal cardiac structures were examined using ultrasound systems (Voluson 730, E8, and E10, GE Healthcare, Kretztechnik, Zipf, Austria). At first, routine obstetric sonography was performed to detect extra-cardiac malformations. Then detailed cardiac examination was performed by an experienced fetal echocardiographer. The visceral and cardiac position was determined as previously described [11]. Briefly, a long-axis plane of the fetus combined with the transverse planes at both the fetal abdominal level and thoracic level was used to ascertain whether both the stomach and heart were on the left side of the fetus. Four transverse views including the 4CV, the left and right outflow tract view, and the three-vessel-trachea (3VT) view were scanned. In addition, three sagittal views including bi-caval view, aortic arch view, and the ductal arch view were also scanned. Color Doppler, pulsed Doppler, and/or high-definition flow imaging (HDFI) were performed when necessary. All image data was saved as video clips for later analysis. Diameters of RA and LA were measured in systole from the lateral walls of each atrium to the edge of secundum septum at a 4CV, established by Tan J, et al [10]. The ratio of RA/LA in diameter was calculated. Peak velocity of tricuspid regurgitation (V_{TR}) was recorded in each diseases. All dimensions were measured three times, and the average value was used.

1.3. Statistical analysis

Data were expressed as means ± standard. Differences between multiple means were compared by one-way ANOVA, using Tamhane's T2 test or Bonferroni test when the variance was heterogeneous or homogeneous, respectively. All tests were considered significant when $p < 0.05$.

2. Results

2.1 Disease types

In total, 420 fetuses with RA dilation were included in the current study. All the prenatal findings and postnatal outcomes were summarized in Table 1. The reasons of RA dilation were classified into 4

types: RA volume overload (n = 117), RA pressure overload (n = 85), displacement of tricuspid valve (Ebstein's anomaly) (n = 16), and physiological enlargement (n = 202). According to our design, Ebstein's anomaly belongs to a separate category as the lower insertion of tricuspid valve could result in RA dilation morphologically, though tricuspid valve dysplasia and TR always accompany with this malformation. Among the reasons of RA dilation, physiological enlargement was undoubtedly the most common, especially in late pregnancy. For these 202 fetuses, 184 cases showed a normal RA/LA within the first 2 weeks of life by postnatal echocardiogram, 133 of which had an opening FO, 7 had a patent ductus arteriosus. Another 18 neonates showed an enlarged RA with a large-in-sized interatrial left-to-right shunting suspected as atrial septal defect.

For abnormal RA enlargement, the most common reason was pulmonary anomalies (n = 57), including pulmonary valve stenosis and atresia. In a case of pulmonary valve atresia, the 4CV showed an enlarged RA and a hypertrophic right ventricle (RV), together with a severe TR (Video Clip 1). Possibility of RA pressure overload should be considered based on signs above. The reversed blood flow in the ductus and main pulmonary artery, with no blood going through the pulmonary valve during systole (Video Clip 2) could be visualized by scanning 3VT view carefully. In this circumstance, the pulmonary valve was presented as a thick echo dense membrane during systole as shown in the animation (Video Clip 3). The final diagnosis was then reached. In a case of tricuspid valve atresia complicated with hypoplastic RV and a ventricular septal defect, an enlarged RA with a severe deflated RV was showed at 4CV. In addition, a thick echo dense membrane could be visualized at the place of tricuspid valve where no valve movement could be identified (Video Clip 4). Color Doppler flow imaging (CDFI) showed no forward flow crossing the tricuspid valve and a right-to-left shunting through ventricular septum (Video Clip 5).

The most common reason of RA volume overload was restrictive foramen ovale (FO) (n = 51). For fetuses with restrictive FO (R-FO), there are two main forms as the narrow inlet of the FO channel and a stenosis outlet of the FO channel, respectively. In the absence of CHDs, the restrictive FO carries a good prognosis. For the 40 fetuses without CHDs in our study, 32 cases showed a normal RA/LA within the first 2 weeks of life by postnatal echocardiogram. Another 8 neonates with an enlarged RA

showed different degree of TR without other significant cardiac anomalies. Another common reason of RA volume overload was tricuspid valve dysplasia ($n = 43$). In a case of tricuspid valve dysplasia, the 4CV showed an enlarged RA with abnormal thick tricuspid valves (Video Clip 6). CDFI showed a severe TR during systole (Video Clip 7).

2.2 Ratio Of Right Atrium To Left Atrium

The RA/LA for the two groups (19-31GW and 32-36GW) was compared. Right atrium dilation was more obvious in 32-36W (Fig. 2). In 19-31GW, the RA/LA in the volume overload group was significantly higher than other groups (all $P < 0.05$). After 32 weeks of gestation, the RA/LA in the Ebstein's anomaly group was changed obviously. Comparing the ratio in the volume overload group to the Ebstein's anomaly group was not statistically significant in 32-36GW ($P > 0.05$).

2.3 The Velocity Of Tricuspid Regurgitation In Different Diseases

As RA dilation always accompany with TR and the peak velocity of TR (V_{TR}) was easily to be obtained during echocardiographic examinations, we made an analysis in fetuses complicated with TR in our case series. For Ebstein's anomaly group, the fetuses with pulmonary valve stenosis and atresia were not included in this analysis. The mean V_{TR} for volume overload group, pressure overload group, Ebstein's anomaly group, and physiological enlargement group was (1.85 ± 0.49) m/s, (3.29 ± 0.58)m/s, (1.86 ± 0.22)m/s, and (0.88 ± 0.45)m/s, respectively. These records showed that V_{TR} in physiological enlargement group was significantly lower than the other three groups, respectively (all $P < 0.05$). As the V_{TR} is highest in the pressure overload group ($P < 0.05$), we conducted a separate analysis for the pressure overload group. Among all diseases, the V_{TR} in the ductus arteriosus anomalies, the pulmonary artery anomalies and the restrictive FO was most visible (Fig. 3). The ductus arteriosus anomalies included closure of ductus arteriosus and constriction of ductus arteriosus, meanwhile the pulmonary artery anomalies included pulmonary valve atresia and pulmonary valve stenosis. There was statistical significance among the three groups (all $P < 0.05$).

3. Discussion

The CURRENT researches are not rare on the reference values in normal fetal heart. Measurements of normal cardiac anatomical dimensions, including ventricular diameter, aortic diameter, and so like,

have been proposed by many multicenter studies, most of which are positively correlated with gestational age (GA) [12–14]. The normal reference range of fetal heart establishes a quantitative relationship between the cardiac dimensions and the GA, furthermore, it provides an essential reference for clinical evaluation of fetal development. However, compared with the ventricular diameter, the atrial diameter is more susceptible to change in blood volume [15]. Therefore, there are few researches in reference values of RA. The fetal four-chamber heart is symmetrical in normal circumstances, with the ratio of RA/LA close to 1: 1 or slightly larger [12]. Thus, in this study, the ratio of RA/LA was applied to reflect the variation in right atrial diameter.

Right atrium dilation is frequently detected in routine screenings or fetal echocardiograms that can easily draw the examiners' attention. In our center, four transverse planes have been used in routine obstetric sonography since 2005. Theoretically, most cardiac anomalies could be detected if all the planes could be obtained and the image data interpretations could be made correctly, according to the AIUM or ISUOG guidelines [16, 17]. However, the underlying causes behind the enlarged atrium are still not easy to determine for sonographers. Furthermore, when the fetal abnormalities had been diagnosed, the severity could be judged by the extent of RA dilatation.

We have summarized the cases of RA dilation in recent ten years. RA dilation were classified into four types: RA volume overload, RA pressure overload, displacement of tricuspid valve (Ebstein's anomaly), and physiological enlargement. Each of the four types can cause different extent of RA dilation. In addition, RA dilation usually accompanies with various degrees of tricuspid regurgitation [15, 18–20]. Generally, RA pressure overload could always lead to worse tricuspid regurgitation with higher velocity. At the same time, both RA volume overload and physiological dilation usually lead to tricuspid valve dilation and tricuspid regurgitation with lower velocity.

It is meaningful for sonographers to make an accurate diagnosis of some fetal congenital heart disease through finding out the main cause of the RA dilation. First, we need to clarify the reasons of fetal RA dilation based on the abnormal cardiac hemodynamics and structural anomalies. As everyone knows, the foramen ovale (FO) and the ductus arteriosus (DA) are the two peculiar anatomical structures during intrauterine development. Normally, the FO facilitates oxygen-rich IVC blood to

enter the LA, decreasing the volume of blood in the right atrium (right heart) [21]. If its opening were restrictive, the blood volume of the RA would increase, leading to the RA dilation. The DA imports about 90 percent of the blood flow from the pulmonary artery into the descending aorta, reducing both the volume and pressure load of the right heart [22].

When compared with the right atrium, the right ventricle contains much of myocardial tissue, with less effect on the diameter when right heart volume was overload. Due to the lack of muscle fibers in the fetal atrium, the RA would expand when the right blood volume increases, which means the atrium is intolerant of volume overload. Compared with other three types, the RA dilation caused by volume overload is more apparent. Restrictive FO is one of the main causes for the RA volume overload. In our research it has been found that restrictive FO would cause the most obvious expansion of the RA. Certainly, other conditions could also lead to RA volume overload such as tricuspid dysplasia, anomalous pulmonary venous drainage and so on. But the extent of RA dilation may not be as severe as that of restrictive FO since the shunt through FO may increase compensatively in these conditions.

The right heart pressure overload could also lead to RA dilation. In this circumstances, the right atrial blood would be obstructed through the tricuspid valve into the right ventricle which may results in an increase of blood volume and RA dilation. The main causes of right heart pressure overload during intrauterine development are pulmonary stenosis/atresia or premature closure /contraction of DA. Tricuspid regurgitation is a common complication on the right heart pressure overload. When not accompanied with valve diseases, the higher systolic pressure in the right ventricle, the higher V_{TR} would be. When comparing the pulmonary stenosis/atresia with the closure of/constriction of ductus arteriosus, it showed that the V_{TR} in DA disease was higher than that in pulmonary stenosis/atresia. At the same time, the change of right atrial diameter was quite different among the diseases. One of the reasons is the pulmonary disease is chronic while the contractility of the right ventricle may have decreased. Besides, massive shunt through foramen ovale would balance atrial pressure so that the right atrial dilatation would not be obvious. On the contrary, premature closure of DA/ DA contraction

usually occurs late in pregnancy. In this condition, RV systolic pressure would elevate tremendously in a very short term, leading to severe TR with extremely high velocity.

4. Study Limitations

We acknowledge the retrospective nature of our study. The study is also limited that it is a long-period review study, imaging techniques and the examiner's experience improved with time. As the largest fetal echocardiography center and consultation center in northeast China, we were able to obtain relatively large number of fetuses with RA dilation. However, a long-period review could include more cases of various kinds of CHDs, which better fit the study design. In addition, our population had a referral bias, as most of the examinations were done when suspecting of fetal CHDs. However, these limitations, had they been addressed in a multi-center prospective study in a normal screening population, would likely have led to improvements in the completeness of the studies.

5. Conclusion

We proposed a protocol by which fetal cardiac anatomy and hemodynamics was used to clarify the reasons of fetal RA dilation. We compared the degree of right atrial enlargement in different types of diseases. We also provided a reference range of V_{TR} for each type of reasons of RA dilation.

Abbreviations

RA: right atrium; RA/LA: the ratio of right atrium to left atrium; 4CV: Four-chamber view; TR: tricuspid regurgitation; VTR: velocity of tricuspid regurgitation; CHD: congenital heart disease; 3VT: three-vessel-trachea; RV: right ventricle; CDFI: color Doppler flow imaging; FO: foramen ovale; R-FO: restrictive foramen ovale; GA: gestational age; GW: gestational week

Declarations

Our study has been approved by the ethics committee of Shengjing Hospital of China Medical University. All women who participated in this study gave written consents.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

LSZ, YZ designed the study. LSZ, YZ, YW collected the data. LSZ, YZ, YW performed the data analyses. LSZ, YZ, YW revised the article critically. All authors read and approved the final manuscript.

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Table

Table 1.

The prenatal findings and postnatal outcomes of fetuses with right atrium dilation in our case series.

Diagnosis	GW		Indication reasons					Associated cardiac anomaly	Outcome		
	19-32	33-36	CHD?	A-4CV	TR	Routine	Arrhythmia		TOP	IFUD	NNA
Volume overload											
TV-D	28	15	0	4	32	7	0	VSD(3); PE(14); TR(43)	2	0	41
TAPVC	16	3	9	6	0	4	0	VSD(5); PLSVC(3)	2	1	16
Galen aneurysm	2	2	4	0	0	0	0	Ascites(4); SUA(2)	0	0	4
R-FO	3	48	6	25	18	0	2	HLHS(9); PV-S(5)*; TR(21)	9	0	42
Pressure overload											
TV-A	9	0	6	3	0	0	0	VSD(5); PV-S(5)*; HRHS(7); PE(3)	6	0	3
PV-S	32	12	5	19	8	10	2	VSD(8); PE(6); PLSVC(2); TR(35)	2	0	42
PV-A	13	0	2	6	5	0	0	VSD(5); DORV(2); HRHS(4); PE(2); TR(8)	4	0	9
P-DA	2	7	2	0	7	0	0	VSD(3); RAA(2); PE(3); TR(9)	2	0	7
C-DA	3	7	2	0	7	1	0	TR(10)	0	0	10
Displacement of TV											
Ebstein's anomaly	13	3	4	0	10	2	0	PV-A(3)**;PV-S(4)*;VSD(4); TCA(2);PE(2);TR(16)	5	0	11
Physiologica	52	150	4	26	29	163	0	TR(101)	0	0	202

*Cases not repeatedly recorded in the pulmonary valve stenosis group

** Cases not repeatedly recorded in the pulmonary valve atresia group

GW: gestational weeks, CHD: congenital heart disease, A-4CV: asymmetrical four-chamber view, TR: tricuspid valve regurgitation, TOP: termination of pregnancy, IFUD: intrauterine fetal death, NNA: neonatal alive, TV-D: tricuspid valve dysplasia, VSD: ventricular septal defect, PE: pericardial effusion, TAPVC: total anomalous pulmonary venous connection, PLSVC: persistent left superior vena cava, SUA: single umbilical artery, R-FO: restrictive foramen ovale, HLHS: hypoplastic left heart syndrome, HRHS: hypoplastic right heart syndrome, C-DA: constriction of ductus arteriosus, P-DA: premature closure of ductus arteriosus, PV-S: pulmonary valve stenosis, PV-A: pulmonary valve atresia, TV-A: tricuspid valve atresia, DORV: double outlet right ventricle, RAA: right aortic arch, TCA: truncus arteriosus, TV: tricuspid valve.

Supplemental Videos

Video clip 1. Simultaneous imaging of two-dimensional (2D) and color Doppler flow showing the four-

chamber view (4CV) of a fetus with pulmonary valve atresia at 24 weeks’ gestation.

A severe tricuspid regurgitation (TR) and dilated RA could be visualized. LV-left ventricle, RV-right ventricle, RA-right atrium, LA-left atrium

Video clip 2. Color Doppler flow imaging (CDFI) showing the three-vessel-trachea (3VT) view of the same fetus with Movie clip 1.

A reversed flow (arrow) in the ductus and pulmonary artery could be visualized. RV-right ventricle, DAO-descending aorta, AO-aorta, PA- pulmonary artery

Video clip 3. 2D imaging showing the right ventricle outflow tract of the same fetus with Movie clip 1&2.

The pulmonary valve was presented as a thick echo dense membrane (indicated by icon) during systole. RV-right ventricle, AO-aorta, PA- pulmonary artery

Video clip 4. 2D imaging showing the 4CV of a fetus with tricuspid valve atresia at 24 weeks’ gestation.

An enlarged RA with a deflated RV and a thick echo dense membrane (indicated by icon) at the place of tricuspid valve could be visualized. LV- left ventricle, RA-right atrium, LA-left atrium

Video clip 5. CDFI showing the 4CV of the same fetus with Movie clip 4.

CDFI showed no forward flow crossing tricuspid valve (indicated by icon) during diastole and a right-to-left shunt flow signal through ventricular septal (arrow). LV-left ventricle, RA-right atrium, LA-left atrium

Video clip 6. 2D imaging showing the 4CV of a fetus with tricuspid valve dysplasia at 25 weeks’ gestation.An enlarged RA and thick tricuspid valves (indicated by icon) could be visualized. LV-left ventricle, RV-right ventricle, RA-right atrium, LA-left atrium

Video clip 7. CDFI showing the 4CV of the same fetus with Movie clip 6.

CDFI showed a severe TR during systole. LV-left ventricle, RV-right ventricle, RA-right atrium, LA-left atrium

Figures

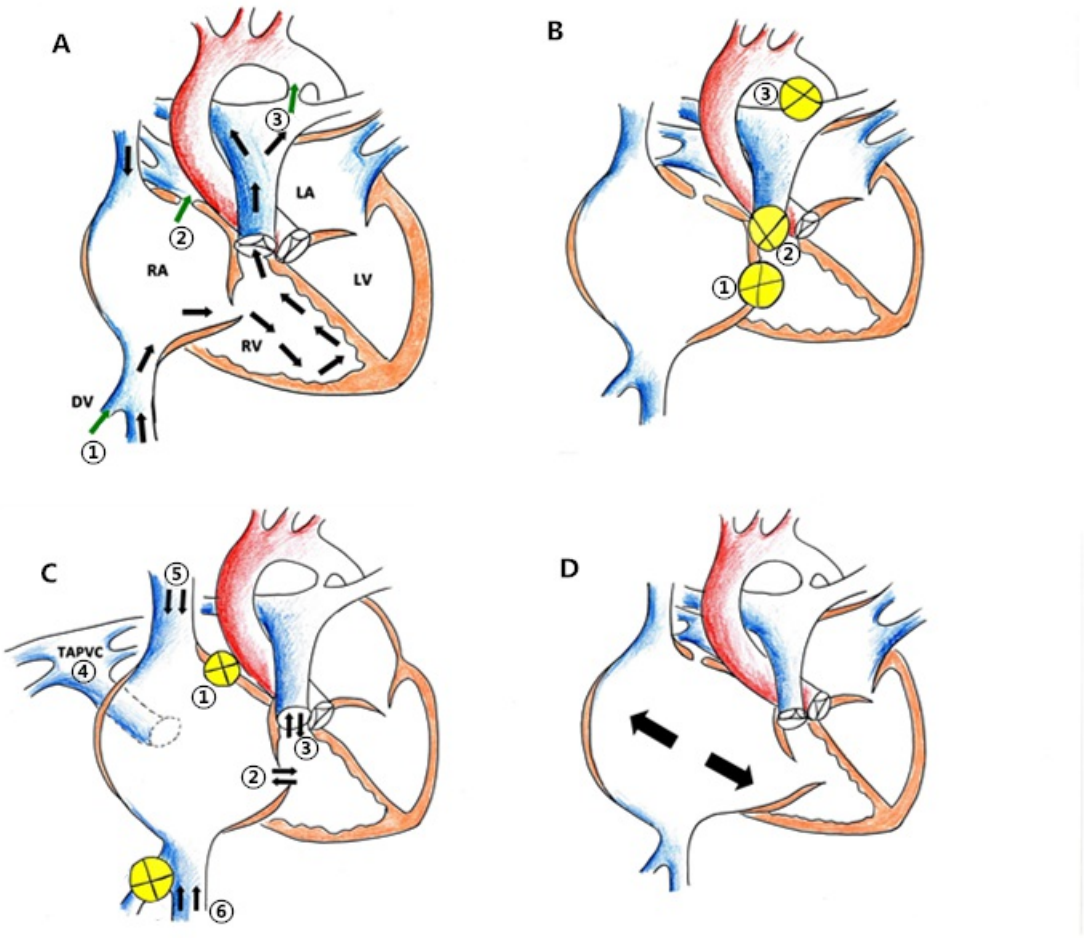

Figure 1

(A) Fetal hemodynamics and characteristic anatomic structures such as ductus venosus (green arrow①), FO (green arrow②) and ductus arteriosus (green arrow③). Black arrows indicate the path of RA stream in and out. (B) Reasons of RA pressure overload such as tricuspid valve atresia (①), pulmonary valve stenosis or atresia (②) and premature closure or constriction of ductus arteriosus (③). (C) Reasons of RA volume overload such as restrictive FO (①), tricuspid dysplasia (②) associated with tricuspid regurgitation (arrows), absent pulmonary valve (③) associated with pulmonary regurgitation (arrows), TAPVC (④) and abnormal enlarged superior vena cava (⑤) or inferior vena cava (⑥).Yellow circle indicates the absence of ductus venosus. (D) Abnormal displacement of tricuspid valve downwardly from the atrioventricular junction (indicated by arrows) causes a morphologic dilatation of RA. LV-left ventricle, RV-right ventricle, RA-right atrium, LA-left atrium, DV-

ductus venosus, TAPVC-total anomalous pulmonary vein connection, FO-foramen ovale

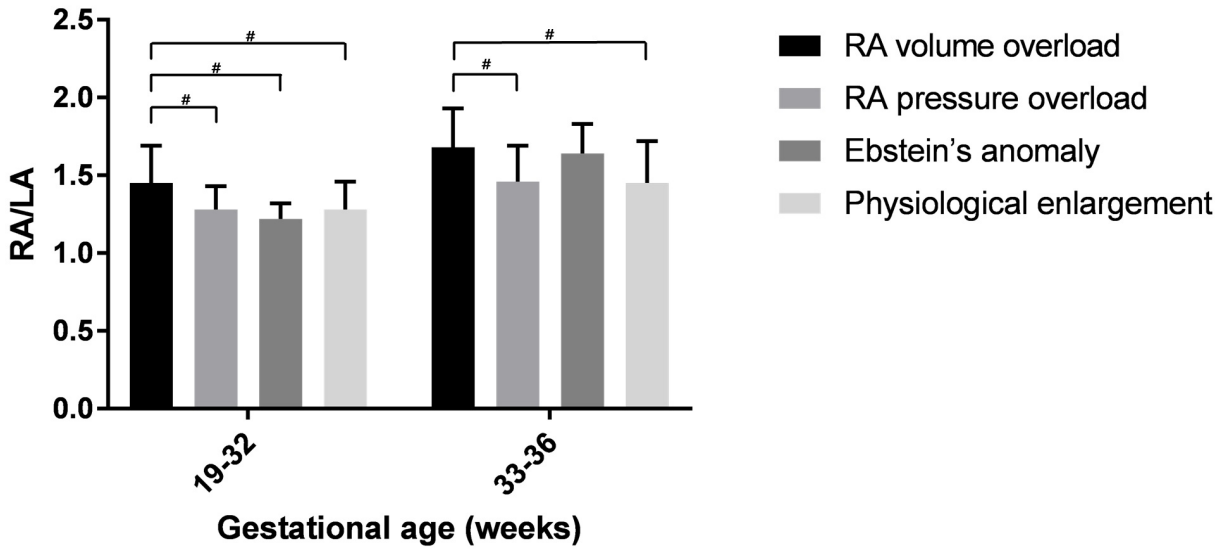

Figure 2

The ratio of RA and left atrium (RA/LA) in four types at vary gestation weeks (19-32GW and 33-36GW) . RA/LA: right atrium/left atrium, # indicating P < 0.05.

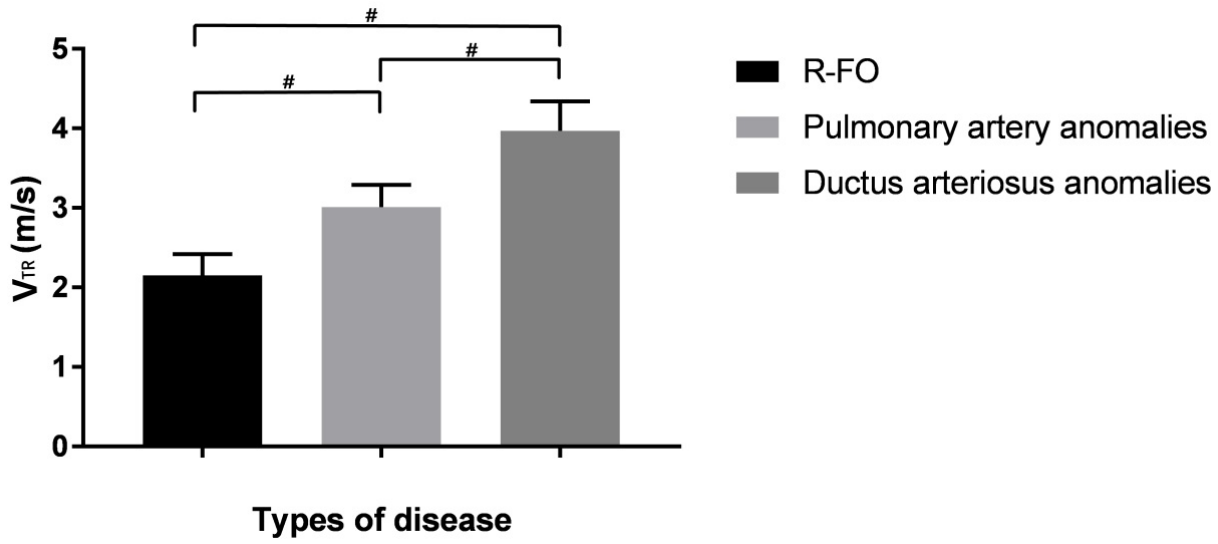

Figure 3

Peak velocity of tricuspid regurgitation in three types of disease. VTR: velocity of tricuspid regurgitation, R-FO: restrictive foramen ovale , # indicating P < 0.05.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

Video clip6.avi
Video clip4.avi
Video clip7.avi
Video clip5.avi
Video clip2.avi
Video clip3.avi
Video clip1.avi