

Echocardiographic Characteristics and Prognosis of the Fetuses with Ebstein Anomaly in Pregnancy

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Research

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Abstract

Objective: The aim of this study was to describe the fetal echocardiographic features of Ebstein anomaly (EA) and also to evaluate the prognosis of those fetuses.

Methods: We retrospectively reviewed the clinical records of 53 fetuses with EA who were enrolled from January 2011 to December 2018 in Beijing Anzhen Hospital, and analyzed the ultrasonic features and prognosis of the fetuses.

Results: In this single-institutional study, 53 fetuses were screened after 23~39 weeks of gestation with EA. In these fetuses, patients with complications accounted for a greater percentage (69.81%). Ultrasound imaging showed that the posterior lobe shifted down further than the septal leaflets, and the anterior lobe changed less than 50%. Severe tricuspid valve (TV) regurgitation showed the highest proportion in these fetuses (56.60%). Among the enrolled fetuses, 20 cases were classified into grade \geq II. 40 cases (75.47%) were inducted, and 13 cases (24.5%) were selected for continued pregnancy. However, only one of the fetuses developed till successful delivery.

Conclusion: Echocardiography has become an important diagnostic tool in identifying the fetuses with EA, a rare and heterogeneous congenital heart disorder. The prognosis of the fetuses with EA is relatively poor. Therefore, understanding the echocardiographic characteristics and the prognosis of the fetuses with EA is of great value for pregnancy consultations during the perinatal period.

1 Introduction

Ebstein anomaly (EA) is a congenital defect of the tricuspid valve (TV), characterized by varying degrees of downward displacement of the TV leaflets into the cavity of the right ventricle¹. EA accounts for less than 1% of all cases of congenital heart disease². Current reports predominantly describe postnatal diagnosis of EA in neonates or infants. However, fetal presentation in EA is predicted to have a poor overall prognosis as the age at presentation is dependent on the severity of anatomic and hemodynamic derangements³. In this study, we evaluated the echocardiographic features and the prognosis of the fetuses with EA in pregnancy. Additionally, we analyzed the echocardiographic data that can be used as potential prognostic factors for fetuses with EA and tricuspid valve dysplasia to provide more valuable information on perinatal consultation.

2 Materials And Method

2.1 Study design and patient selection

A total of 34,756 fetuses were examined from January 2011 to December 2018 in Beijing Anzhen Hospital, Capital Medical University, Beijing, China. The cohort of 53 fetuses (all singletons) diagnosed with EA were retrospectively identified in the perinatal databases of the tertiary centers according to the prenatal demographic, clinical, and echocardiographic data. All procedures involving human participants

followed to the ethical standards of the institutional and/or national research committee, and the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

2.2 Echocardiography

All patients underwent ultrasound screening with high resolution ultrasound equipments (Voluson E8; General Electric). Ultrasound settings were standardized. In all cases, patients underwent detailed fetal echocardiographic examinations to evaluate the cardiac structures and function, which included fetal biometric measurements, and visualization of a normal 4-chamber, outflow tract, 3-view, 3-view, 4-view of the heart, and aortic and ductal arches.

Color flow mapping and Pulsed Wave Doppler imaging were also performed. Moreover, extracardiac anomalies of the fetuses were also evaluated. Each study was documented by hardcopy images. The right atria (RA), left atria (LA), atrialized right ventricle (aRV), functional right ventricle (fRV), and left ventricle (LV) were measured separately. In 25 cases, the area ratio of $(RA + aRV)/(LA + LV + fRV)$ was calculated (Fig. 1). According to these data, the tricuspid valve downward shift of the fetuses was grouped into four levels, in which the severity is associated with the prognosis of EA patients. The classification standard was set as follows: Grade I < 0.5 , excellent prognosis; Grade II $0.5-0.99$, good prognosis, survival rate is 92%; Grade III $1-1.49$, poor prognosis, early mortality rate is 10%; Grade IV ≥ 1.5 , extremely poor prognosis, and the mortality rate is 100%.

2.3 Statistical analyses

Statistical analysis was performed using the SPSS software (SPSS version 22.0, SPSS, Inc., Chicago, IL, USA). Data including observational data were expressed as frequency histograms or absolute and percentage frequency values. Continuous data are expressed as mean SD and/or median and range, as appropriate.

3 Results

3.1 Data from prenatal ultrasound

We evaluated the outcomes of 53 pregnant patients with EA. The pregnant women were aged from 17 to 40, with an average of 28. All the women enrolled had a single pregnancy. At the time of initial diagnosis, the gestational age ranged from 23 to 39 weeks, with an average of 28^{+6} weeks. Characteristics of the cases are summarized in Table 1 and Fig. 1.

Table 1
 Characteristics of pregnant women and echocardiographic characteristics of fetuses with EA

Item	
Pregnant age (years)	17–40
Gestational age at admission (weeks)	23–39
Fetuses with comorbidity n (%)	
Yes	37 (69.81%)
No	16 (30.19%)
The downward displacement of the TV	
Septal leaflets(mm)	6.86 ± 3.40
Posterior leaflets(mm)	9.11 ± 4.76
Changed in anterior leaflets n (%)	19(35.85%)
TV regurgitation	
Mild n (%)	6(11.32%)
Moderate n (%)	15(28.30%)
Severe n (%)	32(56.60%)
Severely n (%)	2(3.77%)
Area ratio class at gestationn (%)	
I	1(4.00%)
II	2(8.00%)
III	20(80.00%)
IV	2(8.00%)
TV = tricuspidvalve; Area ratio=(RA + aRV)/(LA + LV + fRV).	

3.2 Fetal new birthrate and induction rate

In this study, 17 cases (%) of all enrolled fetuses were selected for continued pregnancy. Among the 53 fetuses, 16 cases showed simple EA but 37 cases showed EA-associated malformations (Fig. 2). In the pregnant women who continued with the pregnancy, only one of the fetuses was then delivered successfully. In this study, the birth rate of the fetus was 1.89% (1/53). The prenatal echocardiogram for this fetus is shown in Fig. 3. On the second day after birth, the first postnatal echocardiogram was obtained, in which tricuspid septal displacement deformity, moderate tricuspid regurgitation, and a

slightly dilated left atrium (LA) were presented (Fig. 4). The newborn had no other symptoms of discomfort and regular reexamination was conducted. The distribution histogram was generated according to the number of pregnant women with distinct fetal malformations (Fig. 5). The number of pregnant women who chose to terminate their pregnancy is relatively high, 40 in total (in red) including 10 without complications and 30 with complications, whereas the number of pregnant women who chose to continue their pregnancy is relatively low, 13 in total (in blue) including 6 without complications and 7 with complications .

4 Discussion

Ebstein's anomaly (EA) is a rare congenital heart disorder. Fetal diagnosis and presentations of the disease are typically the most severe and are associated with the highest mortality rates⁴⁻⁵. In the present study, we found that fetal echocardiography is a preferred tool to diagnose the lesion accurately. Two-dimensional echocardiograms were performed in an apical four-chamber view. The images mainly showed that (1) the tricuspid valve septum and posterior lobe can shift down, which may cause severe dysplasia, thus forming membrane-like remnants, and leading to abnormal development of leaflets, chordae, and papillary muscles; (2) although the anterior lobe is attached to the normal level of the annulus, it may be larger, and sail-shaped. The chordae space disappeared or adhered to the right ventricular wall to varying degrees and, in some cases, may be hypoplastic or down; (3) the annulus is enlarged; (4) the arterialized right ventricle and the right atrium is significantly expanded. Nonetheless, each patient has its own characteristics, mainly manifested in the differences among the tricuspid septal lobe, posterior lobe lesions, and occasionally anterior lobular abnormalities that shift down or block the right ventricular outflow tract. Additionally, the right ventricle looks abnormal, the right ventricle cavity below the tricuspid valve is significantly reduced, and the trabecular part also becomes smaller⁶⁻⁷. The funnel part can be narrowed by residual valve tissue or abnormal muscle bundles or fiber bundles⁸. In this study, 53 cases of EA were diagnosed by prenatal echocardiography, all of which had the above typical ultrasonographic manifestations of deformity. EA can be diagnosed prenatally granted the prenatal ultrasound examination reveals the above manifestations of the fetal heart. Since this complex congenital anomaly has a very variable anatomical and clinical spectrum, early diagnosis can provide patients with a timely and effective perinatal treatment plan. This is consistent with previous studies describing⁹⁻¹¹ the high detection rate of other congenital complex diseases with prenatal ultrasound, indicating that echocardiography is worth pursuing in clinical practice.

Fetuses diagnosed with EA have a poor prognosis, and the total mortality rate is as high as 80% or more¹². Mild EA had better prognosis compared to severe EA. However, worse prognosis is observed when EA is combined with other diseases, consistent with the conclusions in our study. Other studies also reported that factors, including fetal edema, cardiac hypertrophy, outflow obstruction, and cardiothoracic ratio > 0.55 , are suggestive of poor prognosis for the fetuses¹³. Upon longer duration of TV malformation, the disease will be getting severe gradually; the right heart will be overloaded, thus inducing right heart failure, and increasing the burden of the right heart. In severe cases, the right heart can be twice size as

the left heart, indicating that the prognosis of the fetus is extremely poor and requires timely treatment to ensure the safety of the child. Issues regarding the importance of the atrialized chamber have also been raised¹⁴⁻¹⁵. In this study, only one fetus was regularly followed up and examined by our center with an induction rate of 98.11% (1/53), which is much higher than the mortality rate of EA patients in previous studies. The main reason is that fetuses with severe or severely late tricuspid regurgitation as well as those with combined malformations account for a large proportion of cases. Our center is a cardiovascular hospital, and most of the patients are mothers with critically ill fetuses. Although the diagnosis can be made in time, the efforts seeking for treatment during the perinatal period cannot be exerted, which may contribute to a low birth rate of patients. The high proportion of grade Ⅲ and grade Ⅳ in the grading area associated with prognosis can also be explained by such a high rate of induction. On the other hand, it also shows that with the development of examination assistive technology, more congenital heart diseases can be identified in the fetal period. It is noteworthy that the high detection rate is also a factor contributing to the increase of the death rate, although this needs further verification.

Although this is one of the largest cohorts of fetuses with EA, the sample size is still relatively small, which is therefore limited to provide a strong conclusion. Additionally this is a single-institutional retrospective study. Many patients were referred to us from other centers. As a result, there is potential patient selection bias which may have led to the data, and results presented here may not be directly applicable to other centers and populations.

5 Conclusions

Echocardiography has become an important tool in identifying the fetuses with EA, a rare and heterogeneous congenital heart disorder. The prognosis of EA patients during the fetal period is relatively poor. Therefore, understanding the echocardiographic characteristics and the prognosis of fetal EA is of great value for pregnancy consultations during the perinatal period.

Abbreviations

EA

Ebstein anomaly; TV:Tricuspid valve; RA:Right atria; LA:Left atria; aRV:Atrialized right ventricle; fRV:functional right ventricle; LV:Left ventricle.

Declarations

Acknowledgements

Not applicable.

Authors' contributions

Yuduo Wu was responsible for data collection, data analysis, and manuscript preparation; Xiaoyan Gu was responsible for data interpretation; Yihua He was responsible for manuscript revision and finalization. Funding was secured by Hongjia Zhang.

Founding

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Availability of data and materials

The datasets analyzed for the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The human study were approved by the ethics committee of Beijing Anzhen Hospital. Written informed consent was obtained from all subjects.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

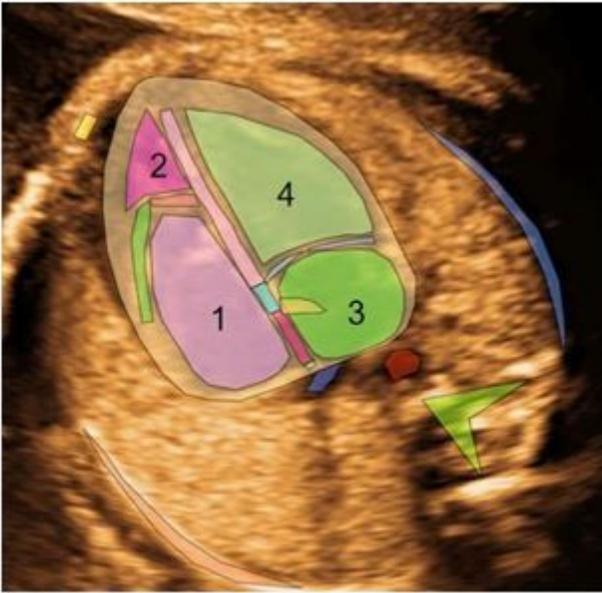


Figure 1

Measurements were done in a four-chamber section of the heart at the end of diastole. Area ratio = $(RA + aRV) / (fRV + LA + LV)$. 1=RA+ aRV, 2=fRV, 3=LA, 4=LV. Among the enrolled fetuses, twenty-five cases were graded according to the EA severity. One case in grade I, twenty cases in grade II, two cases in grade III, and two cases in grade IV. RA: right atria; LA: left atria; aRV: atrialized right ventricle; fRV: functional right ventricle; LV: left ventricle.

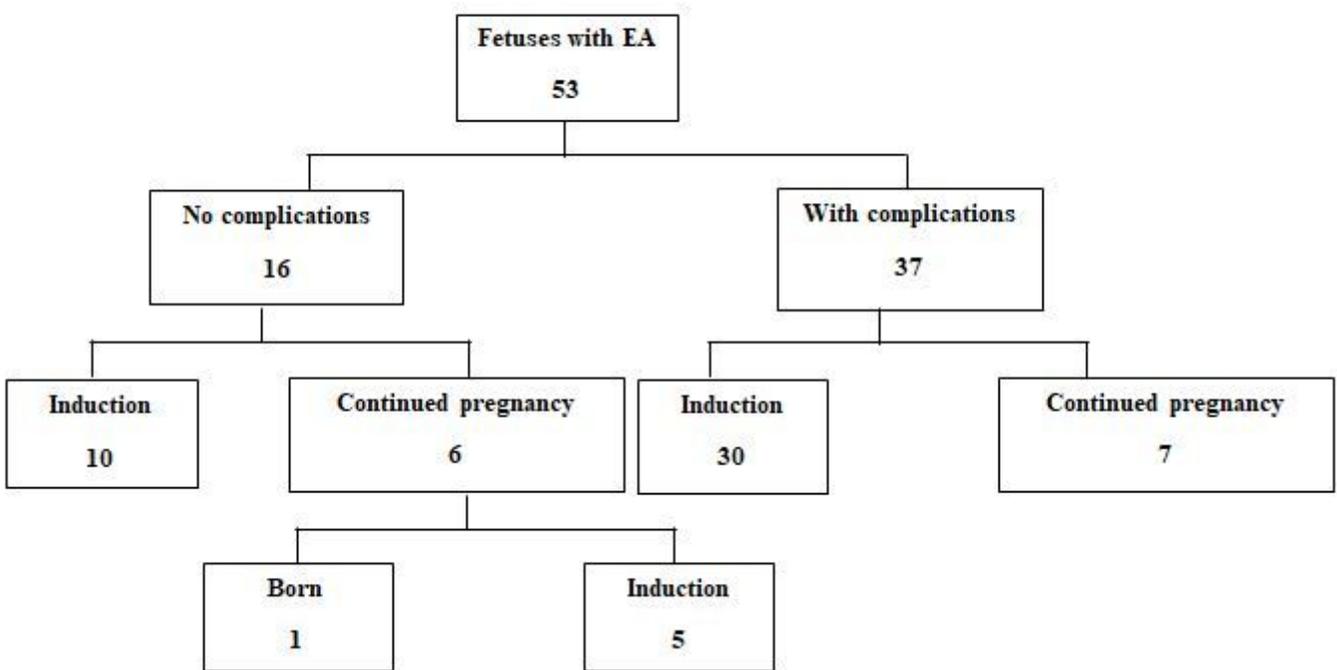


Figure 2

A schema of echocardiographic analysis for the enrolled fetuses with EA.

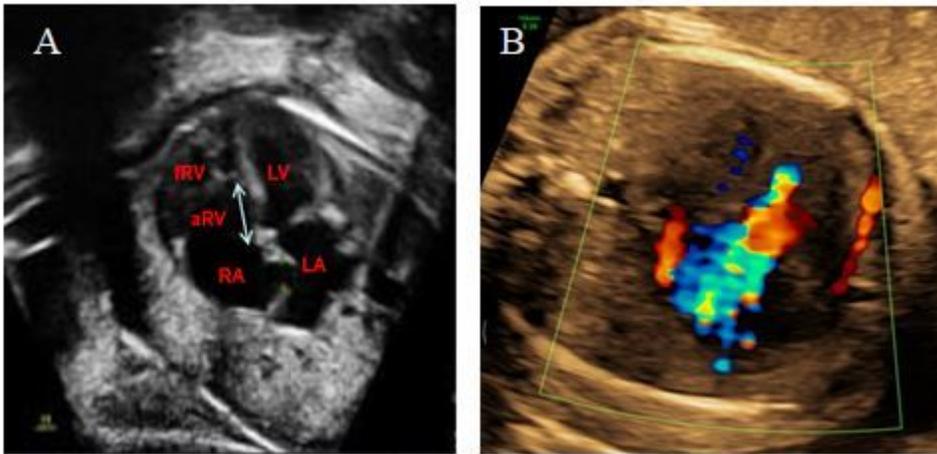


Figure 3

Prenatal ultrasound examinations for the developing fetus in a four-chamber view. (A) Two-dimensional ultrasound. Two-way arrows indicate the downward shift of septum tricuspid at 28 wks of gestation. (B) Color flow mapping. Color Doppler flow imaging indicates a moderate tricuspid regurgitation before birth (the arrow mark). tRA: right atrium, aRV: Atrialized right ventricle, fRV: Functional right ventricle, LA: left atrium; LV: left ventricle.

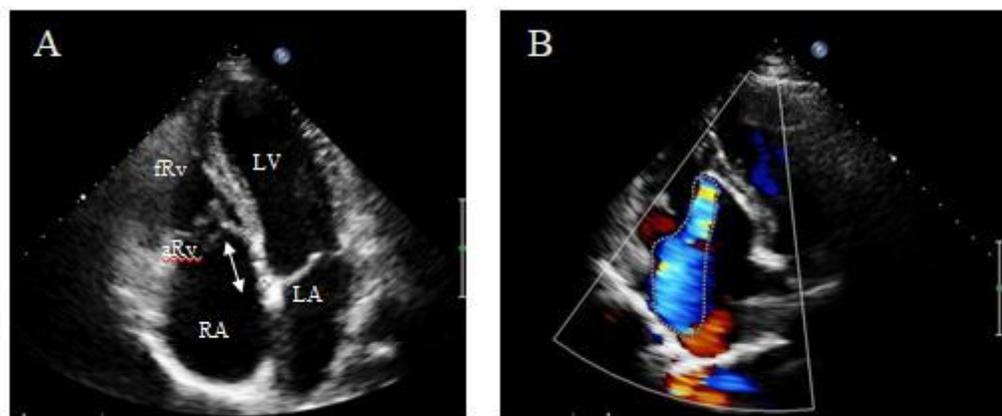


Figure 4

The postnatal ultrasound examination from the developing fetus in the four-chamber view. (A) Two-dimensional ultrasound. Two-way arrows indicate the TV septal descending. (B) Color flow mapping. Color Doppler indicates the tricuspid regurgitation. TV=tricuspid valve.

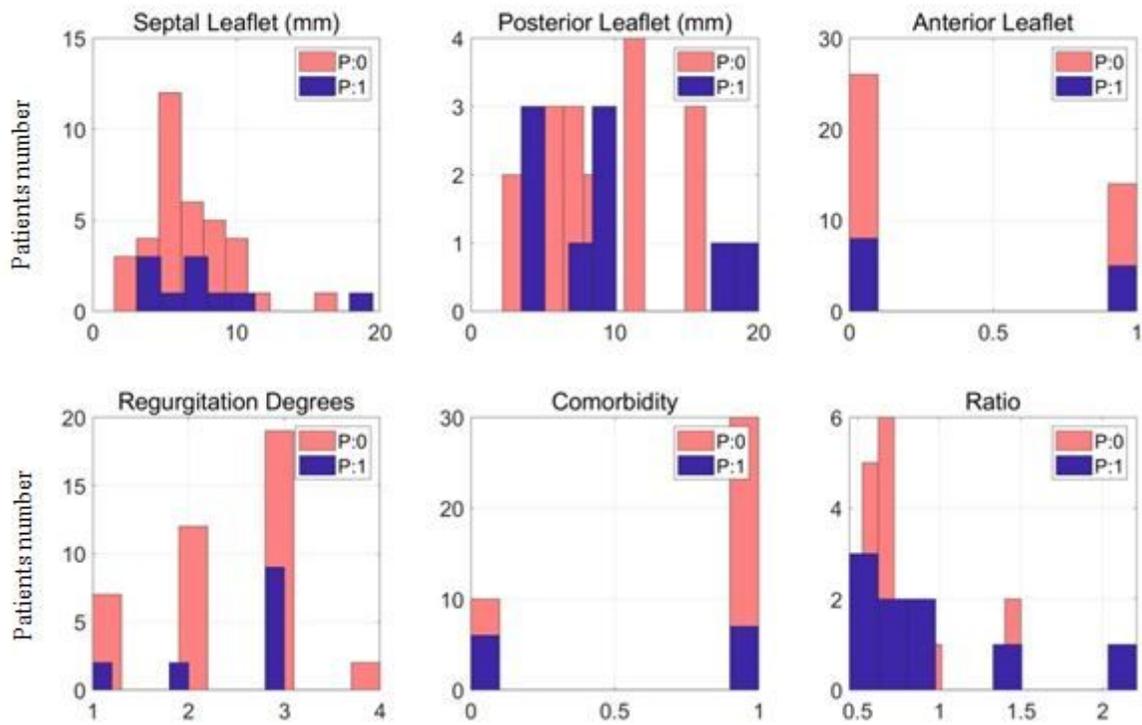


Figure 5

The distribution of patients was presented under each relevant indicator. P=0 termination of pregnancy (red), P=1 continuation of pregnancy (blue).