Factors controlling fetal echocardiography determine the diagnostic accuracy of isolated ventricular septal defect

Jiao Chen, Liang Xie, Han-Min Liu
Chengdu, China

Background: **Fetal echocardiography (FECG) is a key screening tool for prenatal cardiac abnormalities. Herein, we examined the ultrasonic factors determining prenatal ultrasonic diagnosis of isolated ventricular septal defect (IVSD).**

Methods: **The diagnostic role of ultrasonic factors was investigated in patients in middle or late pregnancy, diagnosed with IVSD by FECG and confirmed using postnatal echocardiography.**

Results: **One hundred and six patients with IVSD were enrolled; the majority had perimembranous VSD. The combined imaging mode of 2 dimentional-echocardiography (2DE) and color doppler flow imaging (CDFI) showed the highest rate (56.6%) of IVSD detection, while CDFI was more efficient than 2DE (32.1% *vs.* 11.3%). The single-view mode was more efficient than multiple-view mode (75.5% *vs.* 24.5%). The highest efficient mode to detect IVSD was achieved using combined imaging mode on the single view of the left ventricular outflow tract view (LVOTV) (28.3%). FECG correctly classified 71.7% of fetal IVSD. There was a significant difference of accuracy rate in classifying IVSD among the three different imaging modes (χ^2=7.141, P<0.05). The single imaging mode of CDFI and the mode of CDFI combined with 2DE correctly classified 75.9% and 75.0% of fetal IVSD, respectively. LVOTV was the most accurate view of fetal IVSD classification (85.2%; χ^2=15.782, P<0.05). There was no difference in accuracies of IVSD classification among multiple-view modes (χ^2=2.343, P>0.05) or between single-view mode and multiple-view mode (χ^2=0.32, P>0.05).**

Conclusion: **Single LVOTV in CDFI or CDFI combined with 2DE of FECG were the most effective diagnostic modes for fetal IVSD diagnosis.**

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Key words: **congenital heart diseases/defects; echocardiography; fetal-ultrasound; isolated ventricular septal defect**

Introduction

Congenital heart disease (CHD) is one of the most common birth defects, of which ventricular septal defects (VSD) account for 20%-32% of CHD cases.[1] VSD is closely associated with chromosomal abnormality, and its prevalence may reach 20%-40% due to accompanying fetal VSD.[2-4] Therefore, prenatal screening of VSD is of increasing importance. Severe cardiac malformation may be easily identified in prenatal diagnosis. However, the detection rate of isolated VSD (IVSD), accounting for about 53.57% of all fetal cardiac malformations,[5] is relatively low.

Currently, fetal echocardiography (FECG) is the most widely used technique for prenatal diagnosis of IVSD.[6] Previous studies have mainly focused on prenatal diagnostic rate, misdiagnosis and missed diagnostic rate, and outcome.[7] However, there are few reports on the value of ultrasonic display mode, and the type and the number of displayed views, for the diagnosis of fetal IVSD. In the present study, to determine the most effective ultrasonic diagnostic mode for prenatal diagnosis of IVSD, we compared two-dimensional echocardiography (2DE) with color doppler flow imaging (CDFI), and correlated the types and the number of views essential for diagnosis.

Methods

Ethics

This study was approved by the Hospital Ethics Committee.

Author Affiliations: Department of Ultrasonography, West China Second University Hospital, Sichuan University, Chengdu, China (Chen J); The Vascular Remodeling and Developmental Defects Research Unit, West China Institute of Women and Children's Health, West China Second University Hospital, Sichuan University, Chengdu, China (Xie L, Liu HM); Department of Pediatric Pneumology, West China Second University Hospital, Sichuan University, Chengdu, China (Liu HM); Key Laboratory of Birth Defects and Related Diseases of Women and Children (Sichuan University), Ministry of Education, West China Second University Hospital, Sichuan University, Chengdu, China (Chen J, Xie L, Liu HM)

Corresponding Author: Han-Min Liu, Department of Pediatric Pneumology, West China Second University Hospital, Sichuan University, Chengdu, Sichuan, China (Tel: +86-28-85503209; Email: hanmin@vip.163.com)

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Informed consent was signed by all participants.

Selection and description of participants

Pregnant women who were registered at our hospital and were resident in Sichuan region were recruited and included in the prospective study cohort. The subjects were observed until delivery or termination of pregnancy. The inclusion criteria of the study were fetuses in middle or late pregnancy diagnosed with IVSD using FECG at the Prenatal Diagnosis Center of our hospital and confirmed by postnatal echocardiography. The exclusion criteria were subjects whose diagnoses were accompanied by other intracardiac/extracardiac malformation or chromosomal abnormality suggested by amniocentesis.

Imaging techniques

For ultrasonic examination, FECG was used to examine the pregnant women in supine position using GE VIVID7 (General Electric Medical Systems, Milwaukee, WI, USA), GE E9 (General Electric Medical Systems), and Philips IE33 (Philips Medical Systems Nederland B.V., Veenpluis, The Netherlands) ultrasound diagnostic devices. The probe frequency was set at 1-5 MHz and the pulse transmitting frequency was less than 100 Mw/cm^2. The scale of color doppler was set at 50 cm/s.

Neonatal echocardiography proceeded with a probe frequency set at 3-8 MHz and pulse transmitting frequency <100 Mw/cm^2. The IVSD types were classified as perimembranous, muscular, subarterial, or mixed types based on the location of the defects.[8] The imaging modes included 2DE and CDFI, and the view modes including the left ventricular outflow tract view (LVOTV), large-vessel short-axis view (LVSAV), and four-chamber view (FCV), were recorded in the scan. The type and the size of VSD were recorded.

Statistical analysis

Statistical software SPSS 18.0 was used for all statistical analyses. Measurement data are expressed as mean±SD, and the count data as percentage (%). The mean comparison between the two groups of data was performed using *t* test. The component ratios were compared using Chi-square test. The variables were correlated using linear correlation analysis and the dependency relation between the variables was determined using linear regression analysis. Differences were considered statistically significant at $P<0.05$.

Results

General information

A total of 106 postnatal cases of fetal IVSD were confirmed, including 56 males (56/106, 52.8%) and 50 females (50/106, 47.2%), aged 1-9 days (1.96±1.75 days). The initial diagnosis of fetal IVSD was made at 22-32 weeks of gestation (26.33±2.85 weeks). Fetal heart rate was 125-173 bpm (147.25±7.29 bpm). Of the 106 cases of IVSD, 58 (58/106, 54.7%) cases were perimembranous type, 22 (22/106, 20.8%) cases were muscular type, 16 (16/106, 15.1%) cases were subarterial type, and 10 (10/106, 9.4%) cases were mixed type.

Ultrasonic imaging modes for detection of fetal IVSD

The combined imaging mode of 2DE and CDFI was the most effective mode for detection of fetal IVSD (56.6%; Table). The single 2DE and single CDFI imaging modes exhibited lower rates of detection (43.4%), while CDFI was more efficient than 2DE (32.1% *vs*. 11.3%, respectively).

Ultrasonic view modes for detection of fetal IVSD

The single-view mode was more efficient than the multiple-view mode in detecting fetal IVSD (75.5% *vs*. 24.5%, respectively). In the single-view mode, the most efficient mode was LVOTV, which detected 50.9% of fetal IVSD. In the multiple-view mode, LVOTV was also the most effective mode of detection, followed by the basic view combined with LVSAV or/and FCV. In a comprehensive analysis of ultrasonic factors, the most efficient mode for detection of IVSD was the combined imaging mode on the single view of LVOTV (28.3%). The most efficient mode to show the shunt was the single CDFI mode on the single view of LVOTV (17.0%).

Accuracy of IVSD classification

FECG correctly classified 71.7% fetal IVSD, with a high accuracy for both perimembranous VSD (81%) and muscular VSD (81.8%), but a poor accuracy for subarterial VSD (37.5%).

Comparison of imaging modes for classification of fetal IVSD

The single imaging mode of CDFI (75.9%) had a similar accuracy to the combined imaging mode of

Table. Number of cases diagnosed with different imaging modes and view modes

View modes/imaging modes	2D	CDFI	2D+CDFI	Total
Single-view mode LVOTV	6	7	19	54
LVSAV	1	1	2	9
FCV	2	3	8	17
Multiple-view mode LVOTV+LVSAV	1	4	8	13
LVOTV+FCV	1	2	5	8
LVOTV+LVSAV+FCV	1	1	3	5
Total	12	34	60	106

LVOTV: left ventricular outflow tract view; LVSAV: large-vessel short-axis view; FCV: four-chamber view; 2D: two-dimensional; CDFI: color doppler flow imaging.

2DE and CDFI (75.0%) for IVSD classification; both displayed high classification accuracy. The single imaging mode of 2DE (33.3%) showed the lowest classification accuracy. The relationship between the different imaging modes and IVSD classification was statistically significant (χ^2=7.141, P<0.05).

Comparison of view modes

In the three views of the single-view modes, LVOTV was the most accurate view for fetal IVSD classification (85.2%), while LVSAV and FCV (44.4% and 41.2%, respectively) showed significantly lower accuracy than LVOTV (χ^2=15.782, P<0.05). The accuracy of classification was 76.9% using LVOTV combined with LVSAV, 50.0% using LVOTV combined with FCV, and 83.3% using all three modes. The difference in accuracies of IVSD classification among the three multiple-view modes were not different (χ^2=2.343, P>0.05).

There was no significant difference between the single-view mode and the multiple-view mode in accurate classification rate (χ^2=0.32, P>0.05). While there was a significant difference in the classification accuracy between the six types of view modes, single LVOTV and LVOTV combined with LVSAV and/or FCV displayed a very high classification accuracy (χ^2=18.092, P<0.05).

Discussion

Not all IVSDs can be diagnosed correctly in the prenatal period, with echocardiography having a diagnostic sensitivity for detection of fetal IVSD of approximately 73.4% (missed diagnostic rate of 26.6%).[9,10] In the present study, the combined imaging mode of 2DE and CDFI showed a prenatal IVSD diagnosis rate of 56.6%, suggesting that combined 2DE and CDFI can improve the diagnosis rate of IVSD before birth, even when the defect shown in 2DE and the shunt detected in CDFI occur at the interventricular septum (IVS).

CDFI is generally thought to be a more sensitive imaging mode than 2DE for detection of IVSD. Due to the thin membranous tissue of the interventricular septum, a pseudo echo drop-out tends to occur in 2DE scanning. In addition, the size of the perimembranous VSD is typically less than 3 mm, which is difficult to detect with 2DE.[11] By contrast, in the present study, the sensitivity of CDFI was higher than that of 2DE, and the color signal was more attractive compared with the background of the 2DE black-and-white image. Therefore, we suggest that that the optimized operating mode of detecting IVSD before birth involves using CDFI to find the shunt in IVS, followed by standard view 2DE to determine the echo continuity of IVS.

In the present study, the single-view mode was far more efficient than the multiple-view mode for detection of IVSD. The sensitivity of 50.9% for diagnosis of fetal IVSD with the single LVOTV was similar to that previously reported.[9,12] We found that LVOTV provided the most effective diagnostic view of fetal IVSD, as there was a wider observation range of IVS and as the view enables control of the angle between the acoustic beam and IVS. Although FCV was reported to be the most effective technique for prenatal screening of abnormalities in the fetal heart,[11-14] LVOTV was superior in diagnosis of fetal IVSD. Perimembranous VSD, the primary fetal IVSD in the present study, was predominantly diagnosed using LVOTV and LVSAV. However, in FECG it is easier to obtain LVOTV than LVSAV. Thus, LVOTV is the most effective view for IVSD prenatal diagnosis. Therefore, an increased emphasis on LVOTV may prevent missed diagnosis of IVSD if no abnormality is observed in the FCV.

We found that perimembranous VSD accounted for 69.8% of fetal IVSD cases, similar to that previously reported.[9] Wang et al[15] reported that the prenatal diagnostic accordance rate of IVSD classification with 2DE was 72.7%, which increased to 90.9% when used with spatio-temporal image correlation technology. We found a similar high accuracy rate of classification for both perimembranous VSD and muscular VSD, although the classification of subarterial VSD in the prenatal period was low, with a tendency of misdiagnosis as perimembranous VSD. The defective regions of perimembranous VSD and subarterial VSD lying adjacent to each other may lead to misdiagnosis and increase the difficulty of identifying the position of fetal pulmonary valve annulus in FECG.[16] For accurate prenatal classification of subarterial VSD, LVSAV may be used to distinguish between perimembranous VSD and subarterial VSD, as LVSAV is the most effective view for identification of pulmonary valve annulus and to view the anatomical relationship between the defect and the valve annulus.[17]

We found that the accurate classification of fetal IVSD mainly relied on the imaging mode of CFDI, independent of use of single mode or combined mode. Thus, use of CDFI or combined CDFI and 2DE is recommended for classification of IVSD before birth. We also found that the multiple-view mode was not superior to the single-view mode for accurate IVSD classification, while the single-view mode of LVOTV showed the highest efficiency and accuracy among all modes. Further, use of LVOTV in combination with CDFI and 2DE was preferable for the diagnosis of fetal IVSD because of its higher sensitivity in detecting and identifying the shunt beam, as well as higher accuracy in defining the site and type, in the prenatal diagnosis of IVSD.[18,19]

There were some limitations in this study. The sample size was small, especially in subarterial VSD and mixed VSD. Further studies on these types of VSD are required.

In conclusion, the use of various imaging and view modes, and acquisition of a number of views, are important factors underlying the accuracy of prenatal diagnosis of IVSD.[20] When single LVOTV is employed, the imaging mode of CDFI or CDFI combined with 2DE may provide a higher diagnostic accuracy in fetal IVSD. Fetal echocardiography may be used for the correct positioning, classification, and prenatal diagnosis of IVSD. The standard view and identification of anatomy represent the key elements for accurate classification of fetal IVSD. Therefore, improved scanning and investigational skills are critical to determine the IVSD diagnostic points in clinical practice.

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Competing interest: The authors have declared that no competing interests exist.

Contributors: Chen J and Liu HM conceived and designed the researches. Chen J performed the researches. Chen J and Xie L analyzed the data. Chen J, Xie L and Liu HM wrote the first draft of the paper. All authors approved the final version of the paper.

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